Systematic review of venous thromboembolism risk categories derived from Caprini score

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ABSTRACT

Objective: Hospital-acquired venous thromboembolism (VTE, including pulmonary embolism [PE] and deep vein thrombosis [DVT]) is a preventable cause of hospital death. The Caprini risk assessment model (RAM) is one of the most commonly used tools to assess VTE risk. The RAM is operationalized in clinical practice by grouping several risk scores into VTE risk categories that drive decisions on prophylaxis. A correlation between increasing Caprini scores and rising VTE risk is well-established. We assessed whether the increasing VTE risk categories assigned on the basis of recommended score ranges also correlate with increasing VTE risk.

Methods: We conducted a systematic review of articles that used the Caprini RAM to assign VTE risk categories and that reported corresponding VTE rates. A Medline and EMBASE search retrieved 895 articles, of which 57 fulfilled inclusion criteria.

Results: Forty-eight (84%) of the articles were cohort studies, 7 (12%) were case-control studies, and 2 (4%) were cross-sectional studies. The populations varied from postsurgical to medical patients. There was variability in the number of VTE risk categories assigned by individual studies (6 used 5 risk categories, 37 used 4, 11 used 3, and 3 used 2), and in the cutoff scores defining the risk categories (scores from 0 alone to 0-10 for the low-risk category; from ≥5 to ≥10 for high risk). The VTE rates reported for similar risk categories also varied across studies (0%-12.3% in the low-risk category; 0%-40% for high risk). The Caprini RAM is designed to assess composite VTE risk; however, two studies reported PE or DVT rates alone, and many of the other studies did not specify the types of DVTs analyzed. The Caprini RAM predicts VTE at 30 days after assessment; however, only 17 studies measured outcomes at 30 days; the remaining studies had either shorter or longer follow-ups (0-180 days).

Conclusions: The usefulness of the Caprini RAM is limited by heterogeneity in its implementation across centers. The score-derived VTE risk categorization has significant variability in the number of risk categories being used, the cutpoints used to define the risk categories, the outcome being measured, and the follow-up duration. This factor leads to similar risk categories being associated with different VTE rates, which impacts the clinical and research implications of the results. To enhance generalizability, there is a need for studies that validate the RAM in a broad population of medical and surgical patients, identify standardized risk categories, define risk of DVT and PE as distinct end points, and measure outcomes at standardized follow-up time points. (J Vasc Surg Venous Lymphat Disord 2022;10:1401-9.)

Keywords: Venous thromboembolism; Deep vein thrombosis; Pulmonary embolism; Risk assessment model; Caprini score

Venous thromboembolism (VTE), encompassing pulmonary embolism (PE) and deep vein thrombosis (DVT), is a major health problem with more than 900,000 cases leading to 100,000 deaths per year in the United States.[1] VTE associated with hospitalization is largely preventable. PE, the most serious presentation of VTE, is one of the most preventable causes of in-hospital death.[2] In 2008, the US Surgeon General called on the country to decrease the incidence of VTE through improved screening, prevention, and treatment.[3] In response, the National Quality Forum, the Joint Commission, and the Centers for Medicare and Medicaid Services established standards of care that required hospitals in the United States to track in-hospital VTE events and determine if appropriate prophylaxis had been instituted.[2]

Several risk assessment models (RAMs) have been developed to predict the risk for VTE. The most

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commonly used one was developed by Caprini in 1991 using data from 538 patients.[4] A Caprini score is calculated as the sum of several risk factors, some with a score multiplier (Supplementary Table I, online only). The total score corresponds with an estimated risk of a VTE event, but it does not distinguish between PE risk and DVT risk. The Caprini RAM has been evaluated in more than 200 studies that have confirmed that a higher score represents a higher risk for VTE.[5-7] The RAM has been updated several times since its inception. An update in 2005 expanded the list of risk factors (eg, serious lung infection and family history of venous thrombosis) and changed the scoring multiplier for several factors considered to be high risk.[8] A 2010 update made minor adjustments to the list of risk factors (eg, history of cancer and current cancer were separated and assigned different score multipliers).[9] Most recently, a 2013 update (Table I) included additional risk factors (eg, smoking, blood transfusion, and a body mass index of >40).[5,10]

Caprini scores were originally grouped into three risk categories, low risk (0-1 points), moderate risk (2-4 points), and high risk (>4 points).[4] The 2005 revision (and the 2010 and 2013 revisions) defined four groups: low risk (0-1), moderate risk (2), high risk (3-4), and highest risk (≥5) (Table I).[5,8,9] Despite these validated risk categories, authors have developed and used many different categorizations, both in terms of the number of risk categories and the cutpoints defining the risk categories. The grouping has varied from two (eg, low and high risk) to as many as five categories. Even when the same number of categories are used, there are variations in the cutpoints defining a similarly named category. The variation and lack of agreement on risk categorization can lead to suboptimal patient care because it forms the basis for decisions regarding VTE prophylaxis and for communication between physicians. The lack of agreement has also led to confusion in the medical literature.

To determine the degree of variation in the interpretation and categorization of Caprini scores in the literature, we conducted a systematic review of articles that report VTE risk categories. We examined the variation in (1) the number of risk categories assigned to Caprini scores and the cutpoints used to define similar risk categories, (2) the outcome measures reported and the duration of follow-up after which they were measured, and (3) the risk of VTE for similarly defined risk categories.

Table I. Caprini Risk Assessment Model (*RAM*) 2013 (with risk categories and score ranges)

1 point each	
Age 41-60 years	
Planned minor surgery (<45 minutes)	
Major surgery in past 1 month (>45 minutes)	
Visible varicose veins	
History of inflammatory bowel disease	
Swollen legs (current)	
BMI ≥25	
Myocardial infarction	
Congestive heart failure	
Serious infection	
Existing lung disease	
On bed rest or restricted mobility for <72 hours	
1 point each (females only)	
Current birth control or HRT use	
Pregnancy (current or in past month)	
History of unexplained stillborn infant, recurrent spontaneous abortion, premature birth with toxemia or growth-restricted infant	
2 points each	
Age 60-74 years	
Current or past malignancy (excluding nonmelanoma skin cancers)	
Planned major surgery (>45 minutes)	
Immobilizing plaster cast in past 1 month	
Central venous access	
On bed rest for >72 hours	
3 points each	
Age ≥75 years	
History of DVT and/or PE	
Family history of DVT and/or PE	
Personal or family history of increased risk of blood clotting	
5 points each	
Elective hip or knee arthroplasty	
Hip, pelvis, or leg fracture	
Serious trauma	
Spinal cord injury resulting in paralysis	
Stroke	
Risk category	**Score range**
Low	0-1
Moderate	2
High	3-4
Highest	≥5

BMI, Body mass index; *DVT*, deep vein thrombosis; *HRT*, hormone replacement therapy; *PE*, pulmonary embolism.

METHODS

Data sources and search strategy. We conducted a systematic review of published literature reporting the interpretation of Caprini risk assessment scores that followed the PRISMA guidelines[11] and that was registered with PROSPERO (Prospective Register of Systematic Reviews, registration number: CRD42021278151). We searched MEDLINE and EMBASE for articles published from January 1, 1991 (the date of the first description of the Caprini RAM),[4] to November 1, 2021. In addition to reviewing each article retrieved, we reviewed the references listed in the articles to determine if any should be included in our review.

Table II. Highest and lowest risk categories of venous thromboembolism (*VTE*) used across studies with their corresponding Caprini score cutpoints and reported VTE rate

Lowest risk category		Highest risk category	
Caprini score range	Reported VTE rate, %	Caprini score range	Reported VTE rate, %
0	0	≥5	0.6
0-1	0	≥5	0.8
0-1	0.2	≥5	1.5
0-2	3.5	≥5	1.8
0-2	0.67	≥5	1.94
0-2	0	≥5	2.0
0-2	0.8	≥5	2.2
0-2	0	≥5	2.7
0-4	0	≥5	3.6
0-4	1.1	≥5	4.2
0-4	1.6	≥5	14.5
0-4	12.3	≥5	17.3
0-6	0.4	≥8	0
0-7	0.5	≥8	11.5
0-10	0.1	≥9	1.6
–	–	≥9	2.2
–	–	≥9	5.8
–	–	≥9	10.3
–	–	≥9	17.4
–	–	≥9	18.3
–	–	≥9	22.5
–	–	≥9	28.5
–	–	≥9	37.5
–	–	≥9	40
–	–	≥10	1.8

Our search strategy (Supplementary Table II, online only) identified studies in humans in which Caprini scores were used to define discrete risk categories. We included all patient populations (eg medical, surgical, critical care). Studies in nonmedical journals, that were not in the English language, that did not use the Caprini scoring system, that did not group the Caprini scores into categories of risk, that did not report the number of patients and number of VTE events in the risk categories, or that included duplicated cohorts were excluded. We also excluded systematic reviews, meta-analyses, commentaries, editorials, statements, or opinion pieces.

Data extraction. One investigator (H.H.) screened the titles and abstracts of the articles and selected those that merited further review. Two investigators (H.H., R.C.) read and summarized the selected articles and reviewed their references. Disagreements were resolved by a third investigator (B.K.L.). Data extracted from each article included year of publication, description of the population, study design, number of patients and of VTE events within each risk category, and, if reported, the frequency of PE and DVT events. The number of risk categories used to quantify risk was recorded, as were the cutpoints and ranges defining the risk categories. Categories, Caprini scores, and corresponding VTE rates were summarized using a series of scatter plots. We also plotted the mean Caprini score of each category against the reported VTE rate for the respective risk category to compute the correlation between risk category and VTE rate.

RESULTS

General characteristics of articles

We identified 892 articles (Supplementary Fig 2, online only), of which 313 were duplicates and were removed. One-hundred ninety-eight articles were excluded for the following reasons: (1) non-English language (n = 37), (2) systematic review, meta-analysis, commentary, editorial, statement, or opinion pieces (n = 146), and (3) nonmedical (n = 15). An additional 80 articles were excluded because they did not report Caprini scores and 206 articles for which categories and/or cutpoints were not fully reported. Thirty-eight were excluded for not reporting number of VTE events. All articles found through a review of references of the selected articles were either duplicates or met exclusion criteria. Fifty-seven articles were included in our analysis, 48 (84%) were cohort studies, 7 (12%) were case control studies, and 2 (4%) were cross-sectional studies. Populations studied included surgical (eg, postoperative thymectomy, lung resection, orthopedic surgery, and otolaryngology surgery) and medical (eg, patients in the intensive care unit, medical inpatients, and patients with a stroke). Although several studies also calculated VTE risk using other RAMs, we recorded only those data obtained using the Caprini RAM. Key details of the selected studies are summarized in Supplementary Table III (online only).

Categories of risk

Number of risk categories and cutpoints. All studies included in this review described their patient population and used Caprini scores to assign them to a VTE risk category. There was heterogeneity in the number of categories used. Only part of this heterogeneity was from the change in categories introduced between the original Caprini RAM (1991; 3 risk categories; low risk, 0-1 points; moderate risk, 2-4 points; and high risk, ≥5 points) and the revised Caprini RAMs (2005, 2010, and 2013; 4 risk categories; low risk, 0-1 points; moderate risk, 2 points; high risk, 3-4 points; highest risk, ≥5 points).[4,5,8,9] Eleven of 57 studies (19%) used the revised Caprini RAMs to compute their patient's scores, but incorrectly grouped patients into three risk categories. All 11 studies used

Table III. Variations in time to outcome measurement across the 57 studies included in this review[a]

Duration of follow-up	Study count (%)
Preoperatively	1 (1.8)
7 days postoperatively	1 (1.8)
21 days postoperatively	2 (3.5)
28 days postoperatively	1 (1.8)
30 days postoperatively	14 (24.6)
30 days after intensive care unit admission	1 (1.8)
30 days or during admission (whichever shorter)	1 (1.8)
30 days post-Caprini score calculated	1 (1.8)
60 days postoperatively	5 (8.8)
60 days after admission	1 (1.8)
60 days after discharge	1 (1.8)
90 days postoperatively	6 (10.5)
90 days after admission	1 (1.8)
120 days postoperatively	1 (1.8)
180 days postoperatively	1 (1.8)
Postoperatively (not otherwise specified)	2 (3.5)
During admission	11 (19.3)
Not reported	6 (10.5)

[a]The Caprini Risk Assessment Model (RAM) is designed to predict risk for a thromboembolic event 30 days after the time of risk assessment.

nonstandard score cutpoints (ie, cutpoints that did not correspond to those established in the 1991 Caprini RAM) to define their three risk categories. Thirty-seven of 57 studies (65%) grouped their patients into four risk categories as recommended by the revised Caprini RAMs (2005, 2010, and 2013). Of these studies, 14 (25%) used the validated categories and cutpoints, and 26 (46%) did not. They either assigned different category names or used different score cutpoints for their four categories. Several studies defined risk categories that were different from any version of the Caprini categories. Three of 57 studies (5%)[10,12,13] grouped patients into two risk categories (low and high). An additional 6 of 57 studies (10%)[14-19] grouped them into five risk categories (eg, very low, low, moderate, high, and highest). The names of the risk categories varied across these studies. No rationale was provided for the development of these new risk categories or for the new score cutpoints.

Low-risk VTE grouping. The Caprini RAM-recommended scores indicating the lowest risk for VTE are 0 to 1. In the studies reviewed, there was heterogeneity in the Caprini score cutpoints used to define the lowest risk category for a VTE event. The range of scores varied from 0 alone,[16-18,20-29] to 0 to 10.[10] The range 0 to 10 defined as low risk by Krauss et al[10] completely encompasses the entire scale of categories (lowest risk through highest risk) for the majority of studies included in our systematic review. The Caprini RAM-recommended risk categories (and respective score cutpoints) are based on VTE risks, with the lowest score being associated with near zero rate for VTE (Fig 1). In the studies reviewed, the VTE rate associated with the lowest risk category varied from 0%[12,16,17,24-26,30-39] to 12.3%.[40] A full list of lowest risk VTE group score cutpoints and VTE rates is presented in Table II.

High-risk VTE grouping. We next analyzed the highest risk categories designated in the selected studies. There was heterogeneity in the Caprini scores used to define the category of patients with the highest risk for a VTE event. The scores assigned to the highest risk ranged from 5 or more to 10 or more.[10] Some studies reported the rate of VTE events associated with their highest risk grouping. That rate of VTE events varied from 0%[40,41] to 40%.[36] A full list of the highest risk VTE group score cutpoints and VTE rates is presented in Table II.

Outcome measures reported and duration of follow-up

All versions of the Caprini RAM are designed to predict the risk of a composite of VTE events (PE and DVT) 30 days from the time of score computation. Although each article in this review described the number of outcome events of interest that occurred during follow-up, the outcome measures reported and the duration of follow-up varied widely across studies.

Outcome measures. The Caprini RAM predicts the risk of VTE events and does not distinguish between risk for PE and risk for DVT. Two of 57 studies (3.5%) reported only one of the two thrombotic events[12,42]; Shen et al[12] reported PE alone as the outcome measure, whereas Chen et al[42] reported on patients with confirmed DVT alone. The remaining 55 of the 57 studies (96%) reported a composite of VTE events (PE and DVT). Many of the studies did not specify the types of DVTs included in their outcome measure (upper extremity, lower extremity, intra-abdominal, or intrathoracic DVT). We found only 2 of 57 studies (3.5%) that listed the types of DVT (upper and lower extremity) in their composite outcome measure.[14,18]

Duration of follow-up. The Caprini score is designed to predict risk of VTE within 30 days after hospitalization or after surgery. We found that follow-up in the reviewed studies varied from a fixed number of days or until the occurrence of a sentinel event resulting in significant heterogeneity in the time point at which VTE was measured (Table III). A total of 17 studies (30%) measured VTE events at 30 days, 7 studies (12%) at 60 days, and 7 studies (12%) at 90 days after the procedure or after admission. A total of 6 studies (11%) used time periods ranging from 7 to 180 days after surgery. Other studies measured VTE at variable time points in the preoperative period (n = 1 [1.8%]), postoperative period (n = 2 [3.5%]), or during the entire duration of the admission (n = 11 [19%]). For those that reported a range of duration of admission, the follow-up ranged from 0 to 131 days.[19,33,43]

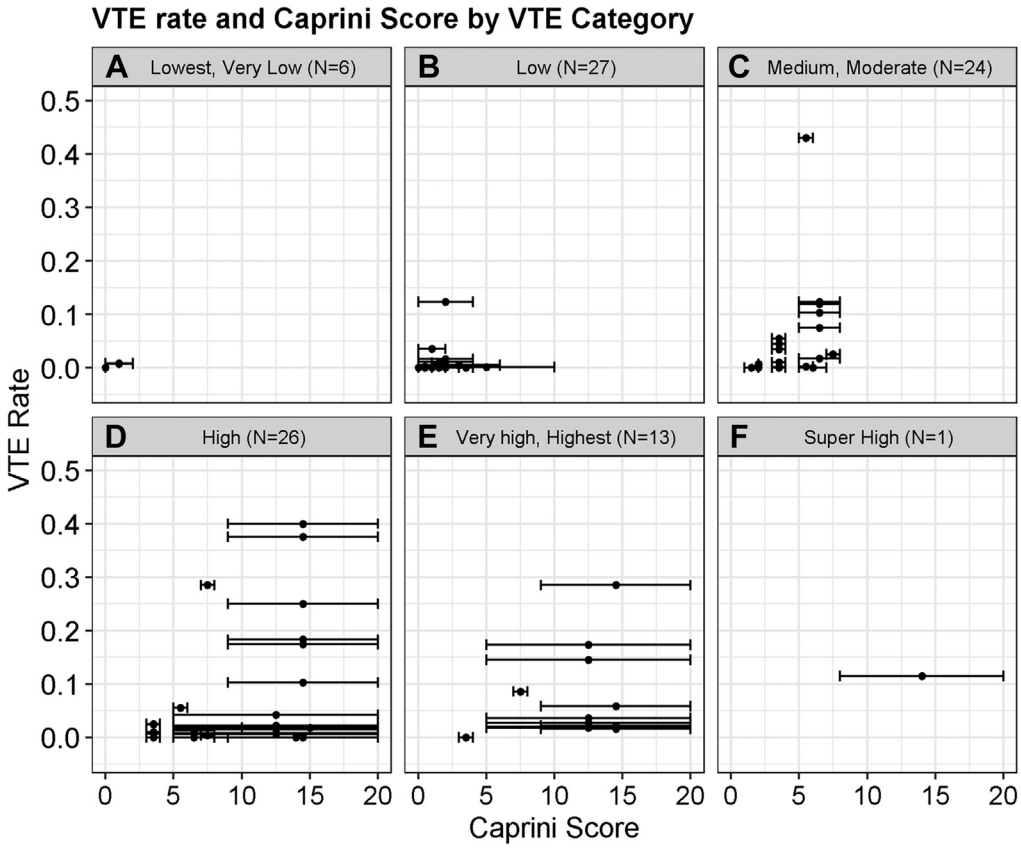

Fig 1. Reported rates of venous thromboembolic (*VTE*) events corresponding to risk categories derived from the Caprini scores across studies. **(A-F)** The reported VTE event rates for progressively increasing risk categories. Some of the categories (eg, **[A]** lowest, very low) are incorporated in a single graph owing to a paucity of available data. The number of studies using the specific risk category depicted in each graph are listed in parentheses.

VTE incidence for the risk categories

We only included studies that reported the number of VTE events for the respective risk categories defined in the study during follow-up. The majority (72%) of studies reviewed had fewer than 50 VTE events. The nine studies (16%)[14,21,24,25,44-48] that did have larger numbers of events ($n > 200$) were limited in their external validity and generalizability, given their focus on a specific subpopulation of patients. The range of the number of events reported varied from 1[28,38,41,49,50] to 3068[44] (median, 27; interquartile range, 8-62). Excluding case control studies, the overall VTE incidence for the entire cohort in each study ranged from 0.10%[38] to 27.9%.[43] The studies also reported the rates of VTE associated with their respective risk categories. We plotted the VTE rates reported for the low risk, medium or moderate, high, very high, and superhigh categories of risk defined in these studies and observed significant overlap in VTE rates across the categories (Fig 1). In a plot of the various risk categories against their reported VTE rates (Fig 2), the correlation between the two was low ($R^2 = 0.23$).

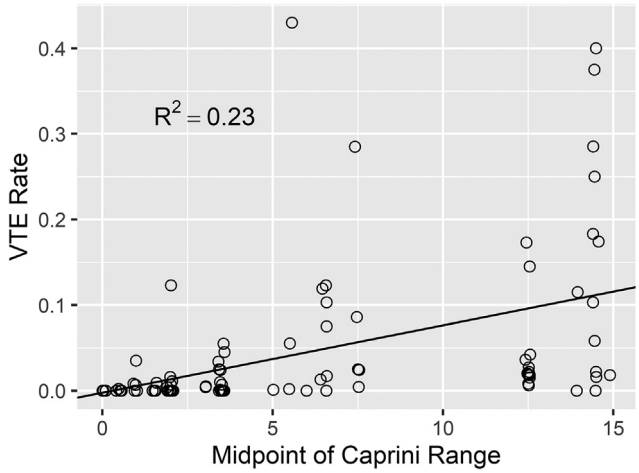

Fig 2. Plot of the midpoint of Caprini category ranges reported in studies against the reported rate of venous thromboembolism (*VTE*, %) in the respective categories.

DISCUSSION

After generating a score, the Caprini RAM (2013) recommends grouping patients into four VTE risk categories (low, moderate, high, and highest) defined by specific score ranges, to facilitate decisions on the choice of VTE prophylaxis. We found significant heterogeneity in

the VTE risk categories being used in the studies reviewed and in the corresponding rate of VTE in each risk category. Studies grouped patients into as few as two risk categories (low and high) to as many as five. The Caprini score ranges used to assign patients to similarly named risk categories varied across the studies. Several reports used a previous version of the Caprini RAM to generate risk scores, but grouped patients according to a subsequently revised version of the RAM. As a result, the scores that constituted a low or a high risk for VTE varied across studies. Therefore, although previous studies have consistently shown a strong correlation between increasing Caprini scores and increasing rates of VTE,[51,52] we were not able to define a similarly strong relationship between rising risk categories and increasing rates of VTE. Within a given study, the risk of VTE increased with progressively more severe risk categories. However, across the spectrum of articles, the variation in number of risk categories, and cutpoints defining the categories, resulted in an association between risk category and risk for VTE as less than ideal, explaining only 23% of the variance in the mean Caprini score within each range of values. Further, the Caprini RAM was designed to predict 30-day risk. Follow-up for determination of outcome among the identified studies varied from 0 to 180 days. As a result of the differences in the implementation and interpretation of the Caprini RAM, a given VTE risk category did not correspond with the same numeric risk of VTE across the studies.

The association between an increasing Caprini score and increasing risk of VTE has been well-established and is not the focus of this review. Caprini risk categories were created by grouping scores based on the risk for a subsequent VTE (Supplementary Fig 1, online only). The categories were designed to help physicians to make decisions on VTE prophylaxis. It is, therefore, vital that not only should the Caprini risk categories show a strong correlation to VTE rates in a given study, but also that the Carpini risk categories should correspond with the same VTE rate across different studies. We aimed to assess the implementation of the Caprini RAM by determining whether the VTE risk categories used by different clinical centers was associated with increasing risk of VTE. We found that the power of most studies to make this determination was low. Using data from the studies that reported VTE rates, we were only able to demonstrate a weak association between categories and VTE rates owing to the variation in the definition of the categories between studies ($R^2 = 23\%$) (Fig 2). There was significant heterogeneity in how the risk categories were assigned across studies. The differences included the names, total number, cutoff scores, and score ranges assigned to the risk categories. There were inconsistencies between the version of RAM used to generate the score and the version of RAM used to assign the category.

As a result of the extensive variation in the definition of Caprini risk categories, a given patient could be defined as low risk for VTE in one study and high risk in another. For example, using the criteria of the revised Caprini RAM, a 56-year-old (1 point) man, undergoing abdominal wall reconstruction (major surgery with duration >45 minutes, 2 points), with a history of ulcerative colitis (1 point) would score 4 points. Applying the risk categorization from Seruya et al[53] for patients undergoing plastic and reconstructive surgery, this individual would be deemed at high risk for VTE. Applying the risk categorization from Yago et al[35] for patients undergoing plastic and reconstructive surgery, this individual would be deemed low risk. The difference in risk categorization could lead to confusing recommendations for prophylaxis ranging from sequential compression devices to prophylactic enoxaparin. The lack of consistency in risk categorization could lead to misunderstandings within physician specialties or across specialties when discussing the care of this patient. It could also complicate the evaluation of the effectiveness of prophylaxis. These factors decrease the clinical usefulness of the Caprini RAM and leave the clinician with no clear guidance on risk-appropriate prophylaxis. There is a need to establish Caprini risk categories that define identical risks for VTE across and within patient subpopulations, and across and within specialties. Previous systematic reviews or meta-analyses have addressed prognostic factors for VTE including the Caprini RAM, but have not addressed clinical translation of the Caprini RAM through risk categories. They were also not able to come up with an analysis that adequately accommodated the wide inconsistencies of cohorts, end points, risk categories and follow-up time points of available studies on the Caprini RAM. One report concluded that their results were limited by "inconsistency in methods of measurement used across studies."[54] The other report assessed a previous version of the Caprini score and concluded that "follow-up time for postoperative VTE was variable among included studies. Some studies reported on inpatient VTE, while others reported to 90 days."[52] To establish reliable categorization, thousands of VTE events would have to be studied in several million hospitalized patients (because overall VTE event rates are low), and the population would need to include the full range of medical and surgical patients.

The clinical implications of PE and DVT, and of subtypes of DVT (ie, lower extremity, upper extremity, intra-abdominal, or intrathoracic), are different. Acute PE is associated with a higher mortality than DVT. Both conditions are associated with clinically important, although distinct long-term complications, namely, post-thrombotic syndrome after DVT[55] and chronic thrombotic pulmonary hypertension after PE.[56] Upper extremity DVTs are less prevalent than lower extremity DVTs, and the rate of PE and chronic post-thrombotic

disability after upper extremity DVT are not well-established.[57] However, they do contribute to morbidity, particularly when post-thrombotic syndrome affects the dominant arm.[55,58-60] Although most of the studies included in our review (96%) reported composite DVT and PE events, they inconsistently stated the types of DVTs that were included in their assessment. Two studies (3.5%) indicated that upper extremity DVT was included as an outcome measure.[14,18] The uncertainty in how VTE was defined complicates the interpretation of the reported Caprini scores, particularly with respect to variability in the clinical implications of the reported VTE risk. As an example, a 2% risk of VTE based on a Caprini score of 2 would be categorized as low risk, but if the 2% risk is for PE, it would be associated with a higher risk of mortality compared with a 2% risk of DVT. Conversely, a 14% risk of VTE based on a Caprini score of 12 seems to be high, but if the risk is primarily that of an upper extremity DVT, it would be associated with different morbidity compared with a 14% risk of PE. A consistent and explicit definition of the individual components of VTE being evaluated in the cohort is essential to an accurate interpretation of results. Ideally, a generalizable VTE RAM would quantify the risk for two distinct outcome measures, PE and DVT. A revision of the Caprini RAM to achieve such a formulation would, require a much larger cohort with a much larger number of event rates than those reported in the studies reviewed.

Limitations. The heterogeneity in study design, assignation of risk categories, and computation of outcome measures across the studies precluded an accurate validation of Caprini RAM-derived risk categories. Detected VTE rates vary depending on the intensity with which VTE is sought for. Because all studies did not describe a systematic search for VTE in their patients, we suspect that their reported VTE rates are based on testing performed after clinical suspicion. The VTE rates also vary depending on the type, if any, of VTE prophylaxis being implemented. None of the studies accounted for the effect of prophylaxis taken to mitigate VTE risk. Finally, VTE rates vary with the duration for which patients are followed. Although the Caprini RAM was developed to predict VTE risk at 30 days, published articles have reported their VTE rates ranging from 1 day to as long as 180 days, rendering validation across studies unreliable.

CONCLUSIONS

The usefulness of Caprini score-derived VTE risk categorization is limited by variability in the number of risk categories being used, the cutpoints used to define the risk categories, and the follow-up durations at which VTE is being measured. There are differences in the outcomes being measured (VTE vs PE vs DVT). The inconsistency of categorization has resulted in similar risk categories being associated with varied VTE rates, which impact the clinical and research implication of the results. Additionally, studies do not consistently employ the most recent Caprini RAM version (2013), which should be the version used to enhance generalizability and serve as a starting point for any future modifications or improvements. To enhance the clinical applicability of the Caprini RAM, there is a need to arrive at a uniform and generalizable tool with validated standard categories of VTE risk. To achieve that goal, we need studies that test a single version of the Caprini RAM in a broad population of medical and surgical patients, to identify standardized risk categories, that define specific risk of DVT and PE as distinct end points, measured at standardized follow-up time points.

AUTHOR CONTRIBUTIONS

Conception and design: BL
Analysis and interpretation: HH, RC, BE, PN, SS, MM, TS, DT, YY, JS, BL
Data collection: HH, RC
Writing the article: HH, JS, BL
Critical revision of the article: HH, RC, BE, PN, SS, MM, TS, DT, YY, JS, BL
Final approval of the article: HH, RC, BE, PN, SS, MM, TS, DT, YY, JS, BL
Statistical analysis: HH, BE, JS
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Overall responsibility: BL

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Supplementary Table I (online only). Caprini risk assessment model (*RAM*) 1991 (with risk categories and score ranges)

1 point each	
Age 41-60 years	
Planned operation >2 hours	
Leg edema, ulcers, stasis	
Sepsis	
Varicose veins	
Malignancy	
Past immobilization (>72 hours)	
Cardiovascular disease	
Trauma	
History of fracture	
Obesity (>20% ideal body weight)	
Stroke	
Previous major surgery	
Protein C, S, or antithrombin III deficiency	
Plasminogen disorders	
Nephrotic syndrome	
Paroxysmal nocturnal hemoglobinuria	
Lupus anticoagulant	
Polycythemia vera	
Inflammatory bowel disease	
1 point each (females only)	
Estrogen or other hormone	
Pregnancy	
2 points each	
Age 61-70 years	
3 points each	
Age 70 years	
History of DVT or PE	
Risk Category	**Score Range**
Low	0-1
Moderate	2-4
High	≥5

DVT, Deep vein thrombosis; *PE*, pulmonary embolism.

Supplementary Table II (online only). Search strategy[a]

#	Search Terms
1	Caprini
2	Category
3	Categories
4	Validation
5	Venous thromboembolism
6	Deep venous thrombosis
7	Pulmonary Embolism
8	1 AND (2 OR 3 OR 4 OR 5 OR 6 OR 7)

[a]The search was performed within MEDLINE and EMBASE. No restrictions were imposed regarding or the publication type.

Supplementary Table III (online only). Articles included in the analysis

Article	Population	Category of Risk (VTE rate if reported)	Study design	No. of patients	No. of events	VTE rate	Follow-up duration
Shuman et al (2012)[61]	Otolaryngology	Low 0-6 (0.4%) Medium 7-8 (2.5%) High ≥9 (22.5%)	Retrospective cohort	2016	27	1.3%	30 days postoperatively
Stroud et al (2014)[30]	Gynecologic oncology	Low 0-1 (0%) Moderate 2 (0%) High 3-4 (0%) Highest ≥5 (3.6%)	Retrospective cohort	1123	37	3.3%	90 days postoperatively
Bahl et al (2010)[31]	General, urologic, and vascular surgery	Low 0-1 (0%) Moderate 2 (0.7%) High 3-4 (1.0%) Highest ≥5 (1.94%)	Retrospective cohort	8216	118	1.4%	30 days postoperatively
Seruya et al (2008)[53]	Plastics and reconstructive surgery	Low ≤1 Moderate 2 High 3-4 Highest ≥5	Retrospective cohort	120	9	7.5%	Postoperatively (not otherwise specified)
Obi et al (2015)[14]	Surgical intensive care unit patients	Low 0-2 (3.5%) Moderate 3-4 (5.5%) High 5-6 (5.5%) Highest 7-8 (8.6%) Superhigh ≥8 (11.5%)	Retrospective cohort	4844	364	7.5%	During admission
Krauss et al (2019)[10]	Joint arthroplasty	Low <10 (0.1%) High ≥10 (1.8%)	Retrospective cohort	1078	8	0.74%	60 days postoperatively
Zhou et al (2014)[45]	Inpatients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Case control	998	347	Not applicable	During admission
Yarlagadda et al (2014)[62]	Otolaryngology	Low 0-1 Moderate 2 Higher 3-4 Highest ≥5	Retrospective cohort	704	15	2.1%	During admission
Hachey et al (2016)[32]	Lung cancer surgery	Low 0-4 (0%) Moderate 5-8 (1.7%) High ≥9 (10.3%)	Retrospective cohort	232	12	5.2%	60 days postoperatively
Sterbling et al (2018)[63]	Lung and esophageal cancer surgery	Low 0-4 Moderate 5-8 High ≥9	Prospective interventional cohort	366	24	6.6%	60 days postoperatively
Tadesse et al (2020)[33]	Surgical inpatients	Low 0-1 (0%) Moderate 2 (0%) High 3-4 (2.4%) Highest ≥5 (2.7%)	Retrospective cross-sectional	155	3	1.9%	During admission
Zhu et al (2020)[15]	Stroke	Very low 0-2 (0.67%) Low 3-4 (0%) Moderate 5-6 (0.18%) High 7-8 (0.41%) Very high ≥9 (2.2%)	Retrospective cohort	3824	21	0.55%	Not reported
Yang et al (2020)[34]	Thymectomy	Low 0-4 (0%) Moderate 5-8 (10.3%) High ≥9 (37.5%)	Prospective cohort	192	17	8.9%	30 days or during admission (whichever shorter)
Cui et al (2020)[40]	Lung resection surgery	Low 0-4 (12.3%) Moderate 5-8 (7.5%) High ≥9 (0%)	Retrospective cohort	437	47	10.8%	During admission

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Supplementary Table III (online only). Continued.

Article	Population	Category of Risk (VTE rate if reported)	Study design	No. of patients	No. of events	VTE rate	Follow-up duration
Kim et al (2020)[16]	Breast surgery	Lowest 0 (0%) Low 1-2 (0%) Moderate 3-4 (0%) High 5-8 (1.3%) Highest ≥9 (1.6%)	Retrospective cohort	881	6	0.68%	30 days postoperatively
Yago et al (2020)[35]	Plastics and reconstructive surgery	Low 0-4 (0%) Moderate 5-6 (43%) High 7-8 (28.5%) Highest ≥9 (28.5%)	Prospective cohort	89	7	7.9%	7 days postoperatively
Wu et al (2020)[64(p202)]	Nononcologic urologic inpatients	Low 1-2 Moderate 3-4 High ≥5	Retrospective cohort	1453	34	2.3%	During admission
Bahl et al (2014)[65]	Otolaryngology	Low ≤6 (0.5%) Medium 7-8 (2.4%) High ≥9 (18.3%)	Retrospective cohort	3498	45	1.3%	30 days postoperatively
Liu et al (2016)[46]	Medical inpatients	Low 0-1 Middle 2 High 3-4 Superhigh ≥5	Case control	640	320	Not applicable	Not reported
Grant et al (2016)[47]	Medical inpatients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Retrospective cohort	63,548	670	1.1%	90 days after admission
Heft et al (2020)[20]	Urogynecologic	Very low 0 Low 1-2 Moderate 3-4 High ≥5	Retrospective cohort	783	2	0.26%	30 days postoperatively
Hanh et al (2019)[44]	Surgical patients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Prospective observational cohort	2,790,027	3068	0.11%	90 days postoperatively
Lobastov et al (2016)[43]	Abdominal surgery and neurosurgery patients	Low 0-1 Medium 2 High 3-4 Very high ≥5	Prospective observational cohort	140	39	27.9%	During admission
Shi et al (2019)[17]	Gynecologic oncology surgery patients	Low 0-1 Moderate 2 High 3-4 Higher 5-7 Super high ≥8	Retrospective cohort	974	17	1.8%	28 days postoperatively
Nemoto et al (2019)[21]	Endovenous thermal ablation patients	Lowest 0 Low 1-2 Moderate 3-4 High ≥5	Retrospective cohort	43,203	402	0.93%	90 days postoperatively
Shen et al (2020)[12]	Lung surgery	Low 0-4 (0%) High ≥5 (0.6%)	Prospective observational cohort	581	3	0.52%	60 days postoperatively
Fu et al (2018)[66]	Intensive care unit patients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Case control	141	47	Not applicable	Not reported
Yang et al (2019)[67]	Gynecologic	Low 0-1 Medium 2 High 3-4 Extremely high ≥5	Case control	159	53	Not applicable	Not reported

Supplementary Table III (online only). Continued.

Article	Population	Category of Risk (VTE rate if reported)	Study design	No. of patients	No. of events	VTE rate	Follow-up duration
Tham et al (2019)[68]	Head and Neck Cancer	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Retrospective cohort	306	7	2.3%	30 days postoperatively
Xu et al (2018)[22]	Intensive care unit after cancer surgery	Very low 0 Low 1-2 Moderate 3-4 High ≥5	Retrospective cohort	2,127	66	3.1%	30 days post ICU admission
Chamoun et al (2019)[50]	Medical floor patients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Prospective observational cohort	297	1	0.34%	30 days post VTE risk assessment
Chen et al (2018)[42]	Inpatients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Case control	390	189	Not applicable	Not reported
Jeong et al (2014)[13]	Complex reconstructive and abdominal contouring surgery	Low 0-4 (1.1%) High ≥5 (1.8%)	Retrospective cohort	1,598	24	1.5%	30 days postoperatively
Wang et al (2021)[69]	Thoracolumbar fractures caused by high-energy injuries	Low 0-1 (n/a) Moderate 2 (n/a) High 3-4 (n/a) Highest ≥5 (14.5%)	Retrospective cross-sectional	429	62	14.5%	Preoperatively
Shi et al (2018)[17]	Urologic tumor surgery	Very low 0 (0%) Low 1-2 (0%) Moderate 3-4 (4.5%) High ≥5 (2.2%)	Prospective observational cohort	1269	31	2.4%	30 days postoperatively
Song et al (2019)[36]	Lung resection surgery	Low 0-4 (0%) Moderate 5-8 (12.3%) High ≥9 (40%)	Prospective observational cohort	262	30	11.5%	30 days postoperatively
Moss et al (2020)[23]	Adults admitted to children's hospital	Minimal 0 Low 1-2 Moderate 3-4 High ≥5	Case control	117	39	Not applicable	During admission
Hewes et al (2015)[18]	Esophagectomy	Very low 0 Low 1-2 Moderate 3-4 High 5-8 Highest ≥9	Retrospective cohort	70	10	14.3%	60 days postoperatively
Hazeltine et al (2021)[70]	Trauma	Low 0-4 Medium 5-6 High 5-8 Highest ≥9	Retrospective cohort	1279	33	2.6%	During admission
Bilgi et al (2016)[37]	Surgical inpatients	Low 0-1 (0%) Moderate 2 (0%) Higher 3-4 (0%) Highest ≥5 (17.3%)	Prospective observational cohort	301	22	7.3%	30 days postoperatively
Tian et al (2019)[71]	Thoracic surgery	Low 0-4 (1.6%) Moderate 5-8 (11.9%) High ≥9 (17.4%)	Retrospective cohort	533	45	8.4%	Postoperatively (not otherwise specified)

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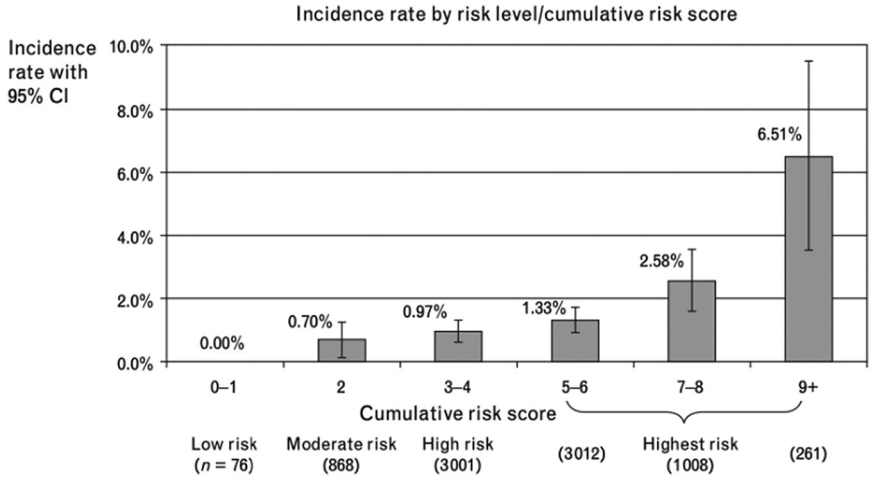
Supplementary Table III (online only). Continued.

Article	Population	Category of Risk (VTE rate if reported)	Study design	No. of patients	No. of events	VTE rate	Follow-up duration
Barber et al (2016)[24]	Gynecological oncology	Low 0 (0%) Moderate 1-2 (0%) High 3-4 (2.5%) Highest ≥5 (1.8%)	Retrospective cohort	17,713	313	1.8%	30 days postoperatively
McAlpine et al (2017)[25]	Major abdominal or pelvic urological surgery	Very low 0 (0%) Low 1-2 (0.9%) Moderate 3-4 (1%) High ≥5 (1.5%)	Retrospective cohort	65,100	956	1.5%	30 days postoperatively
Bo et al (2020)[48]	Bedridden inpatients	Low 0-1 (0.2%) Moderate 2 (0.4%) High 3-4 (0.7%) Highest ≥5 (2.0%)	Prospective observational cohort	24,525	221	0.90%	During admission
Macht et al (2017)[38]	Thyroid and parathyroid surgery	Low 0-2 (0%) Moderate 3-4 (0%) High 5-8 (0%) Highest ≥9 (5.8%)	Retrospective cohort	1012	1	0.10%	30 days postoperatively
Vasilakis et al (2020)[49]	Abdominal body contouring surgery	Low ≤ 4 Medium 5-6 High ≥9	Prospective interventional cohort	195	1	0.51%	90 days postoperatively
Taengsakul et al (2021)[26]	Major abdomino-pelvic surgery	Very low 0 (0%) Low 1-2 (0%) Moderate 3-4 (0.1%) High ≥5 (0.8%)	Retrospective cohort	2,462	12	0.49%	180 days postoperatively
Feng et al (2021)[72]	PICC-related venous thrombosis in lung cancer	Very low 0 Low 1-2 Moderate 3-4 High ≥5	Prospective cohort	237	32	13.5% (not split up)	21 days postoperatively
Ohta et al (2019)[73]	Inflammatory bowel disease inpatients	Low 0-1 Medium 2 High 3-4 Extremely high ≥5	Retrospective cohort	72	6	8.3%	60 days after admission
Paz Rios et al (2021)[19]	Severe coronavirus infection	Very low 0-2 Moderate 3-4 High 5-6 Very high 7-8 Highest ≥8	Retrospective cohort	184	14	7.6%	During admission
Chen et al (2021)[74]	Elderly (≥65 years old) intensive care unit patients	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Case-control	434	200	Not applicable	Before admittance to ICU or <2 days into ICU stay
Weber et al (2016)[75]	Posterior lumbar spinal fusion	Low 0-1 Moderate 2 High 3-4 Highest ≥5	Retrospective cohort	107	4	3.7%	90 days postoperatively
Levi et al (2021)[41]	Head and neck surgery	Very low ≤2 (0.8%) Low 3-4 (0%) Moderate 5-7 (0%) High ≥8 (0%)	Prospective cohort	508	1	0.20%	90 days postoperatively
Feng et al (2021)[27]	PICC-related venous thrombosis in lung cancer	Very low 0 Low 1-2 Moderate 3-4 High ≥5	Prospective cohort	468	82	17.5%	21 days postoperatively
Ulrych et al (2016)[28]	Surgery for benign disease	Very low 0 Low 1-2 Moderate 3-4 High ≥5	Prospective cohort	216	1	0.46%	30 days postoperatively

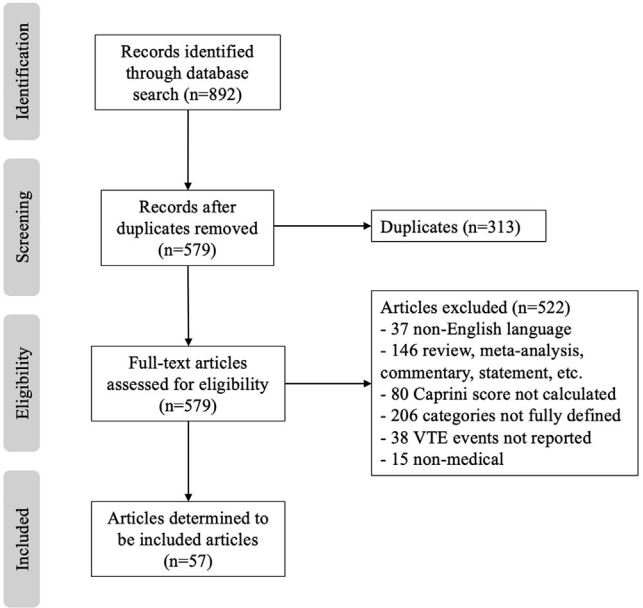
Supplementary Table III (online only). Continued.

Article	Population	Category of Risk (VTE rate if reported)	Study design	No. of patients	No. of events	VTE rate	Follow-up duration
Pittelkow et al (2021)[29]	Microsurgical breast reconstruction	Very low 0 Low 1-2 Moderate 3-4 High ≥5	Prospective cohort	103	2	1.9%	120 days postoperatively
Abdel-Razeq et al (2010)[39]	Cancer inpatients	Low ≤2 (0%) Moderate 3-4 (3.4%) High ≥5 (4.2%)	Prospective cohort	606	21	3.5%	60 days after discharge

ICU, Intensive care unit; *n/a*, not available; *PICC*, peripherally inserted central catheter; *VTE*, venous thromboembolism.



Supplementary Fig 1 (online only). Incidence rate of venous thromboembolism (VTE) for various risk categories using the Caprini risk assessment model (RAM) 2010. (Reproduced with permission from Joseph Caprini, MD.)



Supplementary Fig 2 (online only). Flow chart according to the PRISMA statement. *VTE*, venous thromboembolism.