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Venous thromboembolism in children with lower limb fractures: A systematic review and meta-analysis

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ABSTRACT

Objectives: There is limited evidence regarding Venous Thromboembolism (VTE) in children with lower limb fractures. Our primary objective was to assess the rate, risk factors, mortality and role of pharmacological prophylaxis of VTE in children with lower limb fractures.

Methods: Systematic review and meta-analysis. PubMed, CINAHL, and Cochrane CENTRAL were searched. Full published studies reporting on the rate of venous thromboembolism and/or on the efficacy of chemical thromboprophylaxis in children with lower limb fractures. Data extraction and quality appraisal were performed. Meta-analysis was conducted using a random effects model. The protocol was prospectively registered with PROSPERO (CRD42021278566).

Results: Literature search identified 8342 articles of which 8 were included. All included studies were retrospective and studied paediatric populations in the USA and China. Meta-analysis of 5 studies reporting on children aged equal to or less than 18 years showed an overall estimated VTE rate of 0.53% (95%CI 0.20–1.38). There was sparse evidence related to risk factors for VTE and mortality rates in this patient population, and no evidence related to the impact of VTE prophylaxis.

Conclusions: VTE is a recognised occurrence in children with lower limb fractures, but it is estimated to be infrequent. There is a need for high-quality research to further evaluate the rates of VTE in subgroups of paediatric patients as well as to determine the risk factors, mortality and efficacy of pharmacological prophylaxis. Individualised assessment and management is recommended in the meantime.

Level of Evidence: Level III, systematic review of Level III retrospective studies

Introduction

Venous thromboembolism (VTE) including symptomatic or asymptomatic deep vein thrombosis (DVT) and pulmonary thromboembolism (PE) are well recognised complications of lower limb fractures in adults. VTE has been reported in 4.3% to 40% of adults with a leg injury immobilized in a plaster or a brace, without prophylaxis. Comparable rates have been reported in operated versus non-operated patients, and in patients with fractures versus soft-tissue injuries.[1] Factors associated with an increased risk of VTE in adults include previous VTE, heart failure, smoking, hypertension, hyperlipidaemia, diabetes mellitus, obesity, multiple fractures, prolonged operation time and prolonged bed rest. The VTE rate is substantially reduced with VTE prophylaxis such as Low Molecular Weight Heparin (LMWH) [2].

Despite a substantial body of evidence surrounding VTE in adults with lower limb fractures there remains limited evidence in children, yet lower limb injuries are common in this group. One in three children in the United States of America (USA) will sustain a fracture before the age of 16 years, and nearly one of every four paediatric visits is for a lower extremity musculoskeletal complaint [3]. In England between 2012 and

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2019, 85 737 children were admitted to the National Health Service (NHS) hospitals with lower limb fractures, accounting for almost 25% of all paediatric hospital admissions due to injury. The majority occurred in older children with 37,622 (44%) in 10–15-year-olds and 18,326 (22%) in 16–18-year-olds [4].

Given the limitation of current knowledge, we undertook a systematic review and meta-analysis of VTE in children with lower limb fractures. The aim was to establish the rate, risk factors, associated mortality and effectiveness of pharmacological prophylaxis in this patient cohort. Such information is vital in guiding clinical care and helping clinicians as well as patients and their carers make informed decisions.

Methods

Cochrane methodology was utilised for this systematic review. Literature search of PubMed, CINAHL and Cochrane CENTRAL electronic databases was conducted on 8th September 2025, from the date of the databases' inception. The search strategy was compiled of key words entered into all databases including: "children", "paediatric", "pediatric", "adolescent", "venous", "vein", "fracture", and "trauma". The protocol of the study was prospectively registered with PROSPERO (CRD42021278566).

Inclusion / exclusion criteria

Published studies were included if they reported on the rate of VTE in children with lower limb fractures and/or efficacy of chemical thromboprophylaxis. There was no language restriction. The primary cohort of patients included were children $\leq$ 18 years old. However, during our search it became apparent that studies from the USA referred to children as under the age of 21, hence we also included these studies for a further sub-analysis. We excluded systematic reviews, meta-analyses and case series with $<$ 5 cases. The titles of studies identified by the searches were reviewed and screened by 3 researchers independently and duplicates were removed. Abstracts were screened and where appropriate full manuscripts were reviewed for inclusion. The reviewers also examined the reference lists of all selected studies to include articles missed by the library search.

Data extraction

Data was extracted from the final list of studies using a predesigned

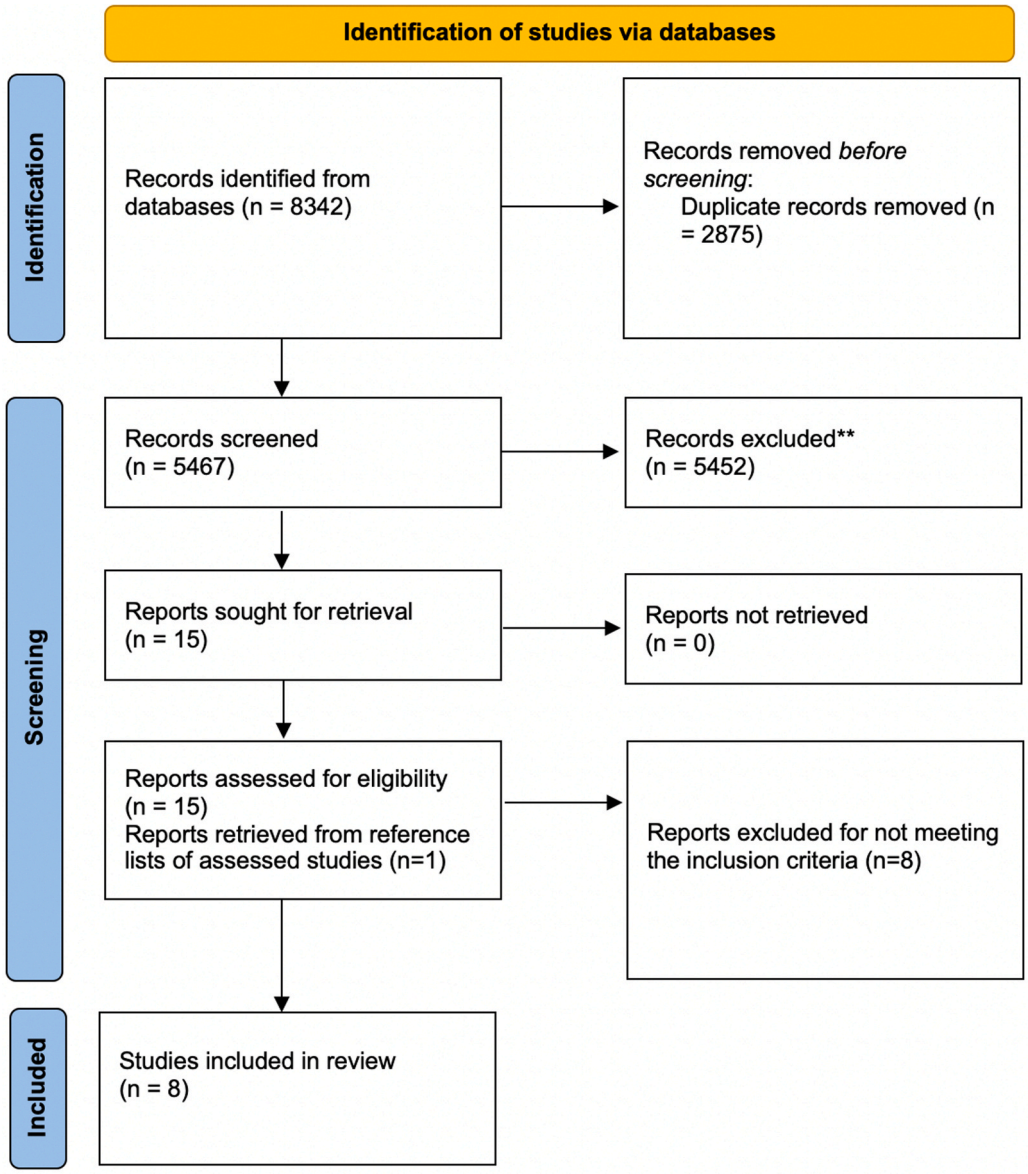

Fig. 1. Literature search results flowchart.

proforma. Clarification was sought from the primary authors of the selected studies as required. Data points of interest included patient demographics, occurrence or absence of VTE, use of thromboprophylaxis, clinical outcomes, and mortality.

Bias assessment

Two researchers independently assessed the risk of bias using the MINORS tool for observational studies [5].

Table 1
Methodology characteristics of the inlcuded studies

Citation	Age (years)	Sex of patients	Population Information	Setting	Source of Data
Vavilala et al., 2002 Vavilala MS, Nathens AB, Jurkovich GJ, Mackenzie E, Rivara FP. Risk factors for venous thromboembolism in pediatric trauma. *J Trauma*. 2002;52(5):922–927.	Age < 16	Male (66.7%) Female (33.3%)	Patients entered over one-year 1997/1998 to the discharge database for numerous American states.	Numerous American states Hospital Discharge database merged with American Hospital Association annual survey	Numerous American states Hospital Discharge database merged with American Hospital Association annual survey
Candrilli et al., 2009 Candrilli SD, Balkrishnan R, O'Brien SH. Effect of injury severity on the incidence and utilization-related outcomes of venous thromboembolism in pediatric trauma inpatients. *Pediatr Crit Care Med*. 2009;10(5):554–557.	Age < 20 years No minimum age threshold	62% male, 38% female	Pediatric and adolescent trauma inpatients identified through ICD−9 trauma codes (n = 240 387 admissions)	Nationwide U.S. sample — 3 438 acute-care hospitals represented in the 2003 HCUP Kids' Inpatient Database.	Healthcare Cost and Utilisation Project HCUP KID 2003
O'Brien & Candrilli, 2011 O'Brien SH, Candrilli SD. In the absence of a central venous catheter, risk of venous thromboembolism is low in critically injured children, adolescents, and young adults: Evidence from the National Trauma Data Bank. *Pediatr Crit Care Med*. 2011;12(3):251–256.	≤ 21 years	Male 69.8% Female 30.2%	Critically injured trauma patients admitted to ICU; subgroup with lower-extremity fractures analysed (n = 11,075)	Multicentre trauma centres (Level I–IV) in the USA	National Trauma Data Bank (NTDB), USA (2001–2005)
Guzman et al., 2017 Guzman D, Sabharwal S, Zhao C, Sabharwal S. Venous thromboembolism among pediatric orthopaedic trauma patients: A database analysis. *J Pediatr Orthop*. 2017;37(7):e449–e455.	Age < 21	Male (67%) Female (33%)	Admissions to paediatric hospitals across the USA in 2012.	Paediatric Hospitals in the USA from Kids Inpatient Database.	2012 Kids Inpatient Database – includes national estimates of hospital inpatient stays by children
Labuz et al., 2021 Labuz DF, Cunningham A, Tobias J, Dixon A, Dewey E, et al. Venous thromboembolic risk stratification in pediatric trauma: A Pediatric Trauma Society Research Committee multicenter analysis. *J Trauma Acute Care Surg*. 2021;91(3): e84–e91.	Age < 18 (Patients younger than 30 days excluded)	Male (63%) Female (37%)	Inpatient admissions to 10 trauma centres in the USA from 2009 - 2018	10 trauma centres in the USA	Data attained from 10 multicentre trauma registries
Mets et al., 2022 Mets EJ, Pathak N, Galivanche AR, McLynn RP, Frumberg DB, Grauer JN. Risk factors for venous thromboembolism in children undergoing orthopedic surgery. *Orthopedics*. 2022;45(1):31–37.	< 18 years No minimum threshold for age	50% male / 50% female	81,490 paediatric orthopaedic surgeries (3099 femur fractures analysed separately)	Multi-centre (U.S.; >100 hospitals)	NSQIP-Pediatric database (2012–2017)
Hou et al., 2024 Hou W, Kong J, Liu L, Han Y, Ren F, Yin S, et al. Incidence of acute deep vein thrombosis in pediatric and adolescent orthopedic trauma hospitalized patients and effect of rivaroxaban treatment. *Injury*. 2024;55(8):111710.	≤ 18 years (children and adolescents) Minimum age threshold 1 (1−18)	Male: 85.1% Female: 14.9%	Pediatric and adolescent orthopedic trauma inpatients admitted between September 2017 and December 2023; includes fractures, dislocations, soft-tissue injuries, acetabular fractures, and polytrauma requiring surgery; study focuses on patients with ultrasound-confirmed acute DVT	Single-centre, tertiary trauma hospital (Tianjin Hospital, China)	Hospital electronic medical records **and** ultrasound registry database
Mittal et al., 2025 Mittal MM, Acevedo KV, Hosseinzadeh P. Risk of venous thromboembolism in pediatric patients with surgically treated lower-extremity fractures: A propensity-matched cohort study. *J Bone Joint Surg Am*. 2025;107 (11):1171–1179.	Age < 18 years No minimum age threshold	52% male, 48% female	Pediatric patients (≤ 18 y) undergoing surgery for lower-extremity fracture (femur, tibia/ fibula, ankle) identified in a national administrative dataset; matched 1:1 with children with upper-extremity fractures.	Multicentre, nationwide U.S. — PearlDiver Mariner database aggregates data from > 80 participating health-care systems and hospitals across all U.S. regions.	PearlDiver Mariner claims database (2010–2023)

Statistical analysis

A summary of patient demographics, study characteristics and quality assessments were constructed. Meta-analysis was performed on homogenous studies using a random effects model for analyses involving 3 or more studies. Estimated rates of VTE were calculated, with heterogeneity assessed using I^2, tau^2 and Q values. Comprehensive Meta-analysis version 2 (Biostat, Englewood, NJ, USA) was used for the analysis.

Results

Our initial search identified 8342 articles of which 8 were included for analysis. (Fig. 1).

All selected studies were retrospective, seven were from the USA and one from China, mainly children presenting to paediatric or trauma centres (Table 1). The age of the paediatric populations studied varied amongst studies, with 5 reporting on cohorts aged 18 or less (4 <18, 1 ≤18), which includes one on a cohort aged less than 16. There was also one study on a cohort aged less than 20, and two on cohorts aged less than 21 years old. (Table 1) The 7 studies and cohorts from America reviewed children admitted and treated in a variety of paediatric and trauma centres, and the single cohort from China focused on children suffering trauma that required operative intervention.

The rate of VTE varied from 0.25% to 3.08% (Table 2). Meta-analysis of 5 studies reporting on children equal to or less than 18 years with lower limb fractures in isolation showed an overall estimated VTE rate of 0.53% (95% CI 0.20–1.38) (heterogeneity: $tau^2 = 1.18$; $I^2 = 98.21\%$; $Q = 223.05$; $df = 4$; $p < 0.001$) Fig. 2.

Analysis of studies looking at lower limb fractures which included older patients up to the age of 21 years gave an estimated rate of 0.65% (95% CI 0.40–1.06) (heterogeneity: $tau^2 = 0.47$; $I^2 = 98.03\%$; $Q = 356.14$; $df = 7$; $p < 0.001$). Fig. 3.

Sensitivity analyses looking only at studies reporting on cohorts from the USA showed similar low VTE rates of 0.34% (95% CI 0.19–0.61) for those equal to or less than 18 years old, and 0.53% (95% Ci 0.35–0.80) when studies reporting on older patients up to the age of 21 years were included.

Most studies evaluated VTE risk across broader paediatric trauma or orthopaedic populations rather than exclusively in children with lower-limb fractures, examining fracture location (particularly femur and pelvis) alongside clinical and treatment-related factors such as surgery, immobilisation, critical illness, obesity, older adolescent age, and chemoprophylaxis use (Table 3). One included study demonstrated variation in VTE risk according to fracture location, with higher rates observed in proximal lower-extremity fractures such as the femur and lower rates in distal fractures including the foot and ankle. [6].

VTE-related mortality was low across included studies reporting on this parameter. No deaths were observed in paediatric patients with VTE in two studies. [6,7] In one study, mortality was higher in patients with VTE than those without (0.8% vs 0.4%), although absolute rates remained low.[8] (Table 2).

Reporting on pharmacological VTE prophylaxis was limited and inconsistent. Mets et al. [9], Guzman et al. [8] and Hou et al. [10] reported prophylaxis use, although in Hou et al. this was confined to patients who developed DVT. Prophylaxis mainly involved LMWH or aspirin and was used in only a minority of patients. No study assessed prophylaxis effectiveness or reported bleeding or other adverse events, limiting evaluation of its clinical benefit in paediatric lower-limb fracture patients.

Bias assessment

Critical appraisal of the included studies using the MINORS criteria is summarised in Table 4. Of the 8 studies included; the lowest MINORS score was 10. 1 scored 11, 4 scored 12, 1 scored 15 and the highest scored 17. A score of 9–12 is considered indicative of moderate quality [5]. A clearly stated aim was observed with adequate statistical analysis in all studies, with adequate follow up of patients. All studies were however retrospective in nature (Table 4).

Discussion

This meta-analysis reveals a low VTE rate of 0.53% in patients with lower limb fractures aged equal to or less than 18 years old. When cohorts reporting on patients aged 18 to the age of 21 were included in our analysis the VTE rate was higher at 0.65% [6–13]. None of the included studies specifically assessed risk factors for VTE in children with lower limb fractures, apart from the effect of fracture location. One study reported a higher mortality in children with lower limb fracture that developed VTE [8]. We could not identify any published data on the effectiveness of VTE pharmacological prophylaxis in children with lower limb fracture.

Our observed VTE rates in children are lower than those in adults with lower limb fractures who have reported rates of 4.3% to 40% [1]. Higher rates of VTE in adults following a lower limb fracture are seen in those with co-morbidities and additional risk factors contributing to thrombus formation including venous stasis, endothelial injury, and hypercoagulability [14,15]. Children may have increased coagulant factors such as factor VIII, and lower levels of anticoagulants such as protein C. However, children have higher levels of α2 macroglobulin, a glycoprotein which has anti-thrombin activity and may play a role in the protection against thrombosis in children [16].

The overall incidence of VTE in paediatric populations in developed countries is variably reported, ranging from 0.0007% to 0.0049% and is higher in hospitalised children (0.05% to 0.22%).[17] There is a bimodal distribution with a peak in early infancy and adolescence, with a substantial proportion of renal VTE and central venous catheter related VTE in neonates due to venous stasis and endothelial damage.[17,18] Immobilisation, trauma, and surgery are also considered risk factors for VTE in children.[19] In a systematic review of 105 studies in 20,718,294 children, the prevalence of hospital-acquired VTE was 4.1% (95% CI, 2.9%−5.2%) and was associated with central venous catheterisation, age > 10 years, surgery, infection, obesity, mechanical ventilation, blood transfusion, malignancy, coagulation and haemorrhagic disorders, as well as length of hospitalisation [20].

The American Paediatric Surgical Association Outcomes and Evidence-Based Practice Committee systematic review on VTE in children identified an incidence of VTE in paediatric surgical populations of 0.29% (range 0.1%−0.48%). This was correlated with surgery type, transfusion, prolonged anaesthesia, malignancy, congenital heart disease, inflammatory bowel disease, infection, and female sex. Similarly, the incidence of VTE in their paediatric trauma population was 0.25% (range 0.1%−0.8%) and correlated with injury severity, major surgery, central line placement, body mass index, spinal cord injury and length-of-stay [21].

A systematic review by Mulpuri et al. [22] included 30 studies in paediatric orthopaedic surgery and reported a pooled VTE incidence of 0.2% (95% CI 0.11% to 0.37%). Studies with less than 10,000 patients, and those involving trauma had the highest incidence of VTE. Increased risk of VTE was attributed to age, sex, obesity, type of surgery, and central venous catheterisation [22].

Several studies assessed risk factors for VTE in children in our analysis, but none assessed it in children with lower risk fractures in isolation, apart from the effect of fracture location. Obesity and immobility are recognised as risk factors for VTE. The Non-Communicable Disease (NCD) Risk Factor Collaboration found an 8-fold increase in obesity in 5–19-year-olds over the last 40 years, and the United Nations Children's Fund (UNICEF) found a doubling of obesity rates in 2–4-year-olds between 1975–2022 [23,24] The increasing prevalence of childhood obesity may contribute to rising rates of VTE in paediatric trauma populations. Previous studies have demonstrated a 2- to 3-fold increased

Table 2
Venous thromboembolism demographics and outcomes in the included studies

Citation	Number of lower limb fracture cases	Types of fracture	Bones	VTE Prophylaxis	VTE Definition	VTE Incidence in lower limb fractures	Types of VTE	Diagnostic method	VTE related mortality
Vavilala et al., 2002 Vavilala MS, Nathens AB, Jurkovich GJ, Mackenzie E, Rivara FP. Risk factors for venous thromboembolism in pediatric trauma. *J Trauma*. 2002;52 (5):922–927.	3640	Long bone fractures of Lower Limb fractures	Long bones of lower limb	Not specified	ICD−9 definition of VTE	Lower Limb – 9/ 3640 (0.25%)	Not specified	Not specified	Mortality rate reported in cases with VTE= 0
Candrilli et al., 2009 Candrilli SD, Balkrishnan R, O'Brien SH. Effect of injury severity on the incidence and utilization-related outcomes of venous thromboembolism in pediatric trauma inpatients. *Pediatr Crit Care Med*. 2009;10(5):554–557.	35640	Lower Limb Fracture and Pelvis Fractures coded and analysed separately	Lower Limb = Femur, Tibia, Foot Pelvis	Not reported	ICD−9 diagnosis codes for DVT or PE recorded during hospitalization	212 / 35 640 = 0.60%	DVT 73%, PE 23%, both 5%	Administrative diagnosis codes from the Healthcare Cost and Utilization Project – Nationwide Inpatient Sample (HCUP-NIS)	Not reported
O'Brien & Candrilli, 2011 O'Brien SH, Candrilli SD. In the absence of a central venous catheter, risk of venous thromboembolism is low in critically injured children, adolescents, and young adults: Evidence from the National Trauma Data Bank. *Pediatr Crit Care Med*. 2011;12(3):251–256.	11,075 (within ICU trauma cohort)	Lower limb fractures and pelvic fractures coded and analysed separately	Lower limb fractures: femur, tibia, fibula, ankle, foot	Not reported	ICD−9 diagnosis codes for DVT or PE recorded during hospital admission (NTDB registry-defined)	187 / 11,075 = 1.69% Incidence for lower limb fractures in ICU cohort	DVT and PE reported (fracture-specific breakdown not reported) Overall ICU cohort: DVT predominant over PE	Administrative diagnosis codes from the National Trauma Data Bank (registry-defined reporting)	Not reported
Guzman et al., 2017 Guzman D, Sabharwal S, Zhao C, Sabharwal S. Venous thromboembolism among pediatric orthopaedic trauma patients: A database analysis. *J Pediatr Orthop*. 2017;37(7):e449–e455.	21238	Fractures of the upper limb, lower limb, spine, pelvis, and multiple locations (where fracture occurred in at least 2 locations)	Not specified	Not specified	Not specified	128/21238 (0.6%) – lower limb fractures	Not specified	Not specified	Mortality reported for population of children with lower limb fractures Mortality in Lower limb fracture cases with VTE= 0.8% Mortality in Lower Limb fracture cases without VTE= 0.4%
Labuz et al., 2021 Labuz DF, Cunningham A, Tobias J, Dixon A, Dewey E, et al. Venous thromboembolic risk stratification in pediatric trauma: A Pediatric Trauma	5994	Lower limb and pelvic fractures	Lower limb fractures defined as from the femur to the level of the metatarsals.	Not specified	VTE defined according to the American College of Surgeons' National Trauma Data Standards definitions and determined based on registry-defined	17/5994 Lower Limb fractures (0.28%)	Not specified	Diagnosis inferred from patient notes	No reports on rates of mortality directly associated with VTE

(*continued on next page*)

Table 2 (*continued*)

Citation	Number of lower limb fracture cases	Types of fracture	Bones	VTE Prophylaxis	VTE Definition	VTE Incidence in lower limb fractures	Types of VTE	Diagnostic method	VTE related mortality
Society Research Committee multicenter analysis. *J Trauma Acute Care Surg*. 2021;91(3): e84–e91.					reporting or an ICD−9/10 code.				
Mets et al., 2022 Mets EJ, Pathak N, Galivanche AR, McLynn RP, Frumberg DB, Grauer JN. Risk factors for venous thromboembolism in children undergoing orthopedic surgery. *Orthopedics*. 2022;45(1):31–37.	3099 (femur fracture cases only)	Orthopedic surgical	Femur	Pharmacologic prophylaxis in 6% (aspirin or LMWH)	Clinically detected DVT/PE within 30 days post-op	8/3099 (0.26%) Femur fracture VTE incidence	DVT > PE (unspecified ratio)	Administrative diagnosis codes from a large U.S. pediatric hospital database	Not reported
Hou et al., 2024 Hou W, Kong J, Liu L, Han Y, Ren F, Yin S, et al. Incidence of acute deep vein thrombosis in pediatric and adolescent orthopedic trauma hospitalized patients and effect of rivaroxaban treatment. *Injury*. 2024;55(8):111710.	2823	Orthopaedic trauma–related lower-extremity fractures	Femur, tibia/fibula, ankle, foot	Reported for VTE cohort 42.6% of patients received prophylaxis prior to diagnosis	Acute DVT defined on Doppler ultrasound as non-compressible vein and/or absent flow.	87 / 2823 = 3.08% 87 cases of DVT in lower extremity fracture cohort confirmed by authors	DVT (primary outcome). PE was not routinely screened; among those with lower-extremity DVT (n = 90), 1 had coexistent PE.	Doppler ultrasonography; PE work-up not systematic, only if PE suspected (CT pulmonary angiography).	Not reported
Mittal et al., 2025 Mittal MM, Acevedo KV, Hosseinzadeh P. Risk of venous thromboembolism in pediatric patients with surgically treated lower-extremity fractures: A propensity-matched cohort study. *J Bone Joint Surg Am*. 2025;107(11):1171–1179.	51036	Surgically treated lower-extremity fractures (pelvis/hip excluded by deduction from tabulated data)	Femur/knee; tibia/fibula/ankle; foot/toes	Not reported	ICD−10 codes for DVT or PE within 90 days of surgery	0.61% (311/51036) in lower extremity cohort	DVT ≈ 286 (estimated); PE ≈ 118 (estimated) — *derived using overall pediatric proportions; fracture-site–specific counts not reported.*	Administrative diagnosis codes from a large multicenter U.S. database (TriNetX)	Not reported for pediatric subgroup

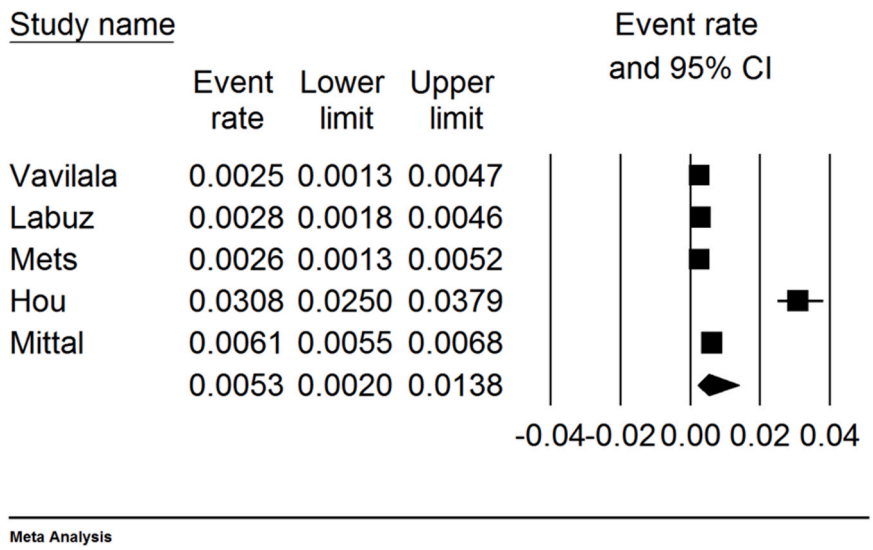

Fig. 2. Forest plot of studies assessing VTE rates in children ≤ 18 years old with lower limb fractures.

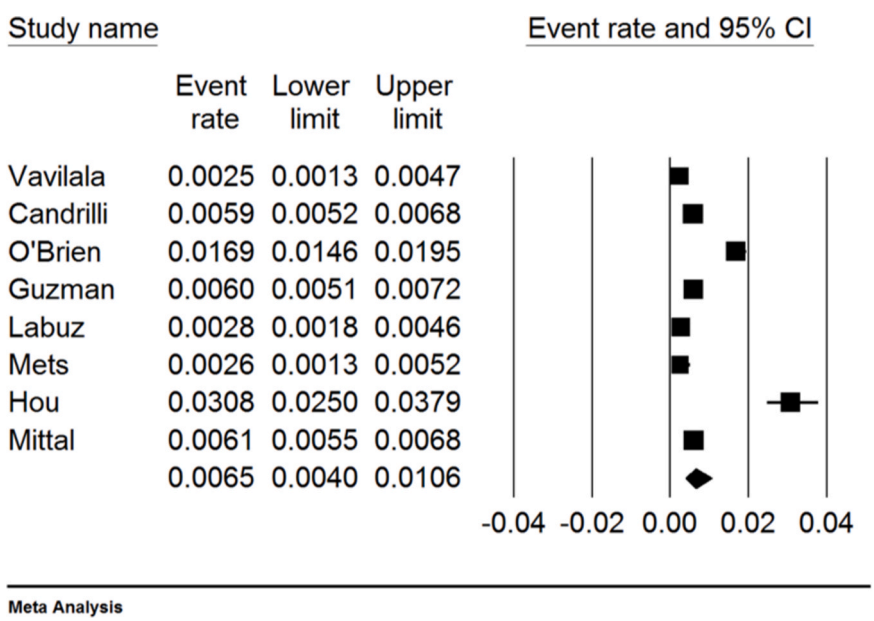

Fig. 3. Forest plot of studies assessing VTE rates in patients ≤ 21 years old with lower limb fractures.

risk of VTE in obese hospitalised children compared with normal-weight children, whilst obesity has also been associated with recurrent thromboembolic events [25,26]. In addition, increasing numbers of physiologically adult-sized adolescents are being managed in adult trauma centres, yet evidence guiding thromboprophylaxis indications and dosing strategies in this higher-risk subgroup remains limited. Further prospective research evaluating the interaction between obesity, injury severity, and thromboprophylaxis practice in adolescent fracture patients is required.

There is also a trend towards more invasive management of paediatric fractures. In the USA between 1997 and 2012 the rate of operative treatment in patients under the age of 20 years with tibial fractures rose from 57.3% to 74.3% [27]. These rising rates of surgical treatment in children with fractures may also influence the risk of VTE.

It is notable that the highest reported VTE rate in this review (3.08%) occurred in a cohort limited to children undergoing surgical management of lower-limb fractures, compared with lower rates in studies including both surgically and non-surgically treated patients [10]. In addition, VTE rates varied by fracture location, with higher rates reported in proximal fractures such as the femur compared with distal fractures [6]. Finally, one included study reported outcomes in a critically injured ICU trauma cohort which may partly account for higher observed VTE rates compared with non-ICU paediatric fracture populations [12].

Whilst younger children have a low incidence of VTE, mortality may be associated with VTE in this patient population [28]. In our review most studies did not directly report on mortality in our desired cohort, however Guzman et al. found a 2-fold increase in mortality in those with VTE compared to those without (0.8% versus 0.4%) [8].

A retrospective study of VTE at Johns Hopkins hospital, between 1992 and 2013, found a VTE-attributable mortality of 0.8%, with the majority of VTE-attributable deaths occurring within 30 days of VTE diagnosis [29]. Furthermore, in a large Canadian population-based cohort of children aged 1–17 years, the incidence of VTE was approximately 0.29 VTE per 10 000 person-years (95% CI 0.26–0.31). Although all-cause mortality was low at 11.4 per 1000 children-years, younger

Table 3
Risk factors for venous thromboembolism in the included studies - most studies evaluated VTE risk across broader paediatric trauma or orthopaedic populations rather than exclusively in lower-limb fractures

Citation	Risk Factors for VTE
Vavilala et al., 2002 Vavilala MS, Nathens AB, Jurkovich GJ, Mackenzie E, Rivara FP. Risk factors for venous thromboembolism in pediatric trauma. *J Trauma*. 2002;52 (5):922–927.	- Major vessel injury - Pelvic fractures - Spinal cord injuries - Central venous catheter (CVC)
Candrilli et al., 2009 Candrilli SD, Balkrishnan R, O'Brien SH. Effect of injury severity on the incidence and utilization-related outcomes of venous thromboembolism in pediatric trauma inpatients. *Pediatr Crit Care Med*. 2009;10 (5):554–557.	- Lower extremity fractures - Pelvic Fractures - Higher injury severity score
O'Brien & Candrilli, 2011 O'Brien SH, Candrilli SD. In the absence of a central venous catheter, risk of venous thromboembolism is low in critically injured children, adolescents, and young adults: Evidence from the National Trauma Data Bank. *Pediatr Crit Care Med*. 2011;12(3):251–256.	- Central venous catheter (CVC) - Lower extremity fracture - Pelvic fracture - Spinal cord injury - Major vessel injury - Higher injury severity score - Older age - Mechanical ventilation / intubation - Blood transfusion
Guzman et al., 2017 Guzman D, Sabharwal S, Zhao C, Sabharwal S. Venous thromboembolism among pediatric orthopaedic trauma patients: A database analysis. *J Pediatr Orthop*. 2017;37(7): e449–e455.	- Central venous catheter (CVC) - Coagulopathy - Spinal cord injury - Blood loss anaemia - Osteomyelitis - External fixation - Obesity - Longer Hospital Length of stay
Labuz et al., 2021 Labuz DF, Cunningham A, Tobias J, Dixon A, Dewey E, et al. Venous thromboembolic risk stratification in pediatric trauma: A Pediatric Trauma Society Research Committee multicenter analysis. *J Trauma Acute Care Surg*. 2021;91 (3):e84–e91.	- Intubation - Admission to ICU - Blood transfusion - Central venous catheter (CVC) - Pelvic fracture - Lower extremity fracture - Major surgery
Mets et al., 2022 Mets EJ, Pathak N, Galivanche AR, McLynn RP, Frumberg DB, Grauer JN. Risk factors for venous thromboembolism in children undergoing orthopedic surgery. *Orthopedics*. 2022;45(1):31–37.	- Femur fracture - Arthrotomy procedures - Older age (16−18 years) - Higher ASA class(III-V) - Pre-operative blood transfusion
Mittal et al., 2025 Mittal MM, Acevedo KV, Hosseinzadeh P. Risk of venous thromboembolism in pediatric patients with surgically treated lower-extremity fractures: A propensity-matched cohort study. *J Bone Joint Surg Am*. 2025;107(11):1171–1179.	- Fractures site: (highest risk with femur and pelvis/hip fractures)

children aged 1–5 years had a nearly seven-fold higher mortality risk compared with adolescents aged 15–17 years [30].

There are extensive guidelines on VTE prevention in adults, but sparse guidance for children [31,32]. In our review none of the studies assessed the effectiveness of VTE prophylaxis. Previous studies have shown that anticoagulation may reduce VTE events in children undergoing central venous catheterisation and in those with multisystem inflammatory syndrome caused by COVID−19 [33,34]. The American Paediatric Surgical Association Outcomes and Evidence-Based Practice Committee recommended using sequential compression devices in at-risk, non-mobile, paediatric surgical patients, and to consider mechanical prophylaxis alone or with pharmacological prophylaxis in children over the age of 15 years, as well as in post-pubertal children younger than 15 with injury severity scores of more than 25, with a preference for LMWH [21]. The Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI) recommended VTE prophylaxis in paediatric trauma patients only in those over the age of 13 years, based on a study from Stony Brook University Hospital Suffolk County NY, which recorded no VTE cases in children < 13 years [35]. However, a study included in our analysis, reported a 22.3% VTE rate in children between the age of 0–9 years suffering with generalised trauma [7]. Although evidence for VTE prophylaxis in children is limited, a recent systematic review of 10 studies reported a lower incidence of VTE in children receiving pharmacological thromboprophylaxis compared with no prophylaxis. This was reported for patients in the intensive care unit admitted after trauma and considered at a very high risk of VTE [36]. An interesting study published in 2023 reported a predictive machine learning algorithm that was developed from the Trauma Quality Improvement Program (TQIP) database of 383,814 injured children. This tool predicted the risk of VTE in injured children and may guide VTE prophylaxis [37].

We could identify no published data on the effectiveness of VTE prophylaxis in children with lower limb fracture, and similarly there is a paucity of data on the adverse effects of VTE prophylaxis in children. The systematic review on the use of VTE prophylaxis in children admitted to intensive care after trauma found no increased bleeding risk, whilst achieving a lower incidence of VTE [36]. Heparin-induced thrombocytopenia is a recognised and heterogenous disorder in adults, though its incidence in children is low in comparison and LMWH is considered safe in this group [38]. Given the rarity of VTE events in paediatric lower limb fracture patients, future progress in this field will likely require prospective multicentre collaboration with standardised reporting of fracture characteristics, thromboprophylaxis practices, diagnostic pathways, and clinical outcomes. Development of evidence-based paediatric thromboprophylaxis guidelines and incorporation of paediatric VTE outcomes into trauma registries may improve risk stratification and standardise practice across paediatric and adult trauma centres caring for injured children.

We recognise that there are several limitations to our study. We acknowledge the inclusion of only a small number of observational studies which utilised multicentre registries or administrative databases to collect data not specifically for research and which may have partial overlap of their included patient populations. There was heterogeneity in patient age. Our initial protocol definition of children was less than18 years of age, in line with the United Nations Educational and Scientific and Cultural Organisation (UNESCO) definition for children [39]. However, in the USA the American Academy of Paediatrics advocates an upper limit of 21 years [40]. In contrast, in Europe some countries define a child to be up to 18-years, whilst some use the 14 and 16-year cut-off [41]. There was heterogeneity in the VTE definition, with 4 studies, retrospectively using the International classification of Disease 9 (ICD−9) code to define VTE, which may lead to underreporting [42]. There was also no standardised way of evaluating VTE occurrence. Diagnosis of VTE and pulmonary embolism in children may be particularly challenging, as clinical presentation is often subtle or non-specific and adult diagnostic prediction tools have not been validated in paediatric populations. Furthermore, several included studies relied on retrospective administrative coding or registry-based data rather than standardised diagnostic pathways, which may have contributed to under-recognition of asymptomatic or clinically occult VTE events [43].

Despite our study limitations we believe that VTE in children with lower limb fractures is a relevant condition which may contribute to morbidity or mortality in this group and our study aims to draw attention to the evidence that is available. With these data clinical decisions and treatment protocols for this group can be informed and the data may also be used to guide further research.

Table 4
Bias assessment using the methodological index for non-randomised studies (MINORS) tool

MINORS CRITERIA	Vavilala et al., 2002	Candrilli et al., 2009	O'Brien & Candrilli, 2011	Guzman et al., 2017	Labuz et al., 2021	Mets et al., 2022	Hou et al., 2024	Mittal et al., 2025
Aim	2	2	2	2	2	2	2	2
Inclusion of consecutive patients	0	1	0	0	0	1	2	1
Prospective Collection of Data	0	0	0	0	0	0	0	0
End Point appropriate to the aim of the study	2	2	2	2	2	2	2	2
Un-bias assessment of the study endpoint	1	1	1	1	1	1	2	1
Follow up period appropriate to the aim of the study	2	2	1	1	1	2	2	2
Lost to follow up < 5%	2	2	2	2	2	2	0	1
Prospective calculation of study size	1	0	0	1	2	0	0	0
Adequate control group	0	0	0	0	0	0	1	2
Contemporary Groups	0	0	0	0	0	0	1	2
Baseline equivalence of Groups	0	0	0	0	0	0	1	2
Adequate statistical analysis	2	2	2	2	2	2	2	2
Total Score	**12**	**12**	**10**	**11**	**12**	**12**	**15**	**17**

Conclusions

Overall, there seems to be a low prevalence of VTE in children with lower limb fractures, but the data is insufficient to assess rates of VTE in subgroups who may be considered at higher risk. There is a need for high-quality research to determine the risk factors, mortality and efficacy of pharmacological prophylaxis for VTE in children with lower limb fractures. In the meantime, individualised assessment and management is recommended. Collaborative prospective research and development of evidence-based paediatric thromboprophylaxis pathways are needed to better define optimal management strategies in this patient population.

CRediT authorship contribution statement

Zain Habib: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Emadeldin M. Ahmed:** Visualization, Validation, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Christos S. Zipitis:** Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Paul M. Sutton:** Writing – original draft, Project administration, Methodology, Conceptualization. **Rayaz A. Malik:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Charalambos P. Charalambous:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Ethics statement

Ethical approval was not required for this study as it involved analysis of previously published data and did not involve identifiable patient information.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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