A systematic review of the management of acute limb ischemia in children

Johannes Meyer, MD,[a,b] Ulrich Rother, MD,[c] Frederico Bastos Goncalves, MD,[d,e,f] Willemien van de Water, MD,[g] Frank-Mattias Schäfer, MD,[h] Alexander Meyer, MD,[i,j] *and* Eliane von Klitzing, MD,[i,j] *Nürnberg, Germany; Erlangen, Germany; Lisboa, Portugal; Maastricht, Netherlands; Regensburg, Germany; and Berlin, Germany*

ABSTRACT

Objective: Literature on pediatric acute limb ischemia (PALI) is scarce with controversial management regarding diagnostics and treatment. The aim of this review was to evaluate the management of PALI.

Methods: A systematic literature search (PubMed, Embase, Cochrane Library) following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was performed (Prospero registration number CRD420251035570). All English full-text studies published in the past 30 years reporting on acute limb ischemia in children were included. Cases series and cohorts with fewer than 10 patients were excluded from the pooled analysis. Primary outcomes were treatment modalities and diagnostics used. Secondary outcomes were recorded mortality directly linked to PALI and the etiology of PALI, as well as long-term morbidity and amputation rates.

Results: In all, 17 studies (2484 children; 66.3% male; mean age, 2.14 years) were included in the quantitative synthesis. In 89.9%, PALI was caused by arterial cannulation. The most commonly affected location was the common femoral artery (49.8%). Ultrasound was the most commonly used diagnostic means. Conservative treatment of PALI was first-line treatment in 87% and was considered successful without the need for surgical intervention (65% of reports; 11/17). Surgery was reserved for failed conservative treatment with an amputation rate of 2.4%. Mortality directly related to PALI was low (0.01%).

Conclusions: Acute ischemia in pediatric patients most often occurred iatrogenically. Conservative treatment proved to be successful and should be considered as the treatment of choice. (J Vasc Surg 2026;■:1-11.)

Keywords: Acute limb ischemia; Children; Neonates; PALI; Pediatric

From the Department of Pediatric Surgery and Pediatric Urology, Diakoneo, Cnopfsche Kinderklinik, Nürnberg[a]; the Academic Teaching Hospital of the University Hospital Erlangen, Erlangen[b]; the Department of Vascular Surgery, University Hospital Erlangen, Erlangen[c]; the NOVA Medical School, Faculdade de Ciências Médicas, NMS|FCM, Universidade Nova de Lisboa, Lisboa[d]; the Hospital de Santa Marta, Unidade Local de Saúde São José, Centro Clínico Académico de Lisboa, Lisboa[e]; the Portugal Hospital CUF Tejo, Lisboa[f]; the Department of Vascular and Endovascular Surgery, Maastricht University Medical Center, Maastricht[g]; the Surgical Center for Children (Operatives Kinderzentrum, OKIZ), Department of Pediatric Surgery and Pediatric Traumatology, Hospital St. Hedwig of the Order of St. John of God, University Children's Hospital Regensburg (KUNO), Regensburg[h]; the Helios Klinikum Berlin-Buch, Clinic of Vascular and Endovascular Surgery, Berlin[i]; and the Medical School Berlin, Berlin.[j]

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Correspondence: Johannes Meyer, Department of Pediatric Surgery and Pediatric Urology, Diakoneo, Cnopfsche Kinderklinik, St.-Johannis Mühlgasse 19, Nürnberg 90419, Germany (e-mail: Johannes.meyer@diakoneo.de).

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Acute limb ischemia (ALI) in adults is not an uncommon event, potentially damaging nerve and muscle tissue, and may even lead to necrosis unless the limb is not revascularized in time, with damage present as early as 4 to 6 hours following arterial occlusion.[1] Contrarily, ALI in the pediatric population is considered an extremely rare entity, occurring with an incidence of only 26 per 100,000 pediatric hospitalizations.[2]

The rate of pediatric acute limb ischemia (PALI) is even reported to be under 1% of all patients with ALI.[3] Due to this rarity, there is a scarcity of literature, and management is heterogeneous, as evidenced by the low availability of PALI data, which often relies on recommendations for adult patients.[4] ALI in children not only differs in its frequency of occurrence compared with adults, but also in its etiology. PALI is often seen in post-traumatic events or iatrogenically and is only rarely secondary to an embolic event or an arterial occlusive disease, which is often the case in the adult cohort.[5] However, it is important to note that limb ischemia in children is not a single entity, as it contains different age groups with neonates or older children. Against this background, Lim et al have shown that etiologies, management, and outcomes differ depending on age.[2] Furthermore, ALI in children can lead to lifelong complications such as claudication and limb length discrepancies, which can also progress into severely limited range of motion.[6]

The purpose of this systematic review was to evaluate current approaches how ALI is diagnosed and treated in children and give an up-to-date overview of the management.

ARTICLE HIGHLIGHTS

- **Type of Research:** Systematic review article
- **Key Findings:** This systematic review represents the largest cohort of children (2484 patients) with pediatric acute limb ischemia (PALI) in literature so far. In 89.9%, PALI was caused by arterial cannulation. Conservative treatment of PALI was first-line treatment in 87%.
- **Take Home Message:** Conservative treatment proved to be successful and should be considered as treatment of choice. Surgery was reserved for failed conservative treatment, with an amputation rate of 2.4%. Acute ischemia in pediatric patients most often occurred iatrogenically.

METHODS

Information sources and search strategy. Two investigators (J.M., E.K.) independently screened all titles and abstracts collected from electronic databases. Literature search for the term “acute limb ischemia” was conducted in Medline (PubMed), Embase, Cochrane Library and Web of Science. Results were transferred to Rayyan online library. The following keywords were applied: “children,” “pediatric,” “paediatric,” “infant,” “newborn,” and “neonate.” The search followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[7] Titles and abstracts collected from the search strategy were screened for relevance. This systematic review has been registered in the PROSPERO public database (CRD420251035570).

The full texts of all relevant articles were obtained and reviewed for suitability independently by both reviewers. Any disagreement in study inclusion was resolved by consensus (Supplementary Appendix, online only).

Eligibility criteria. All English full-text studies published in the past 30 years reporting on PALI were included. Case reports, poster articles, or case series with fewer than 10 patients were excluded. Additionally, the methodology of articles had to be of retraceable design as well as data of patients with PALI. Studies with a mixed population (adults and children) were excluded. Primary outcomes included the systematic collection of treatment modalities and their success, as well as the diagnostic methods applied in the studies. Secondary outcomes were mortality directly linked to ALI and the etiology of PALI, as well as long-term morbidity, limb function, and amputation rates.

Study records. The same two reviewers (J.M., E.K.) independently extracted data using standardized Excel sheets. This was done in duplicate to increase accuracy and to reduce measurement bias. Any disagreement in data collection was resolved by consensus (third party with majority decision).

Data items. Data extracted included study characteristics (origin and year of publication, study design, number of cases) and patient characteristics (age, gender, clinical presentation, invasive and noninvasive diagnostics, treatment options and their success, amputation rates, and follow-up). Subgroup analysis was carried out for neonatal patients regarding treatment and outcome (amputation rates).

Quality analysis of included studies. Study quality was classified using the recommended level of evidence rating by Sackett.[8] Lowest level (IV) was indexed as small patient series and Level I as high-quality randomized controlled trials. Risk of bias was assessed with the Revised Cochrane risk-of-bias tool (RoB 2).[9]

Statistical analysis. For descriptive statistics, numerical data were presented as the median and mean value and categorical data as counts and percentages. Further analysis in terms of comparison of treatment and patients' age was not deemed appropriate due to the mostly small study samples and the great heterogeneity.

RESULTS

Literature search

The literature search yielded 276 articles according to predefined search terms. Thirty-one records were assessed for eligibility. Finally, 17 studies met the inclusion criteria and were included in the review (Fig 1 and Table).[2,3,5,6,10-22] Of these, 15 were single-center retrospective studies, one retrospective analysis of registry data, and one systematic review (studies in the one systematic review were not included twice). Sample size ranged from 10 to 1576 (registry data) patients. Year of publication ranged from 2001 to 2024 (Fig 2). The majority of published articles were from the United States (47%) (Fig 3).

Quality of reports

With 16 articles, the overall majority of reports included in the analysis were of a retrospective nature containing case series with low evidence level (IV). There was one systematic review of retrospective case series graded as evidence level IIIa. One partly prospective report was included. In total, the level of analyzed studies was poor. Risk of bias judgment was assessed on basis of

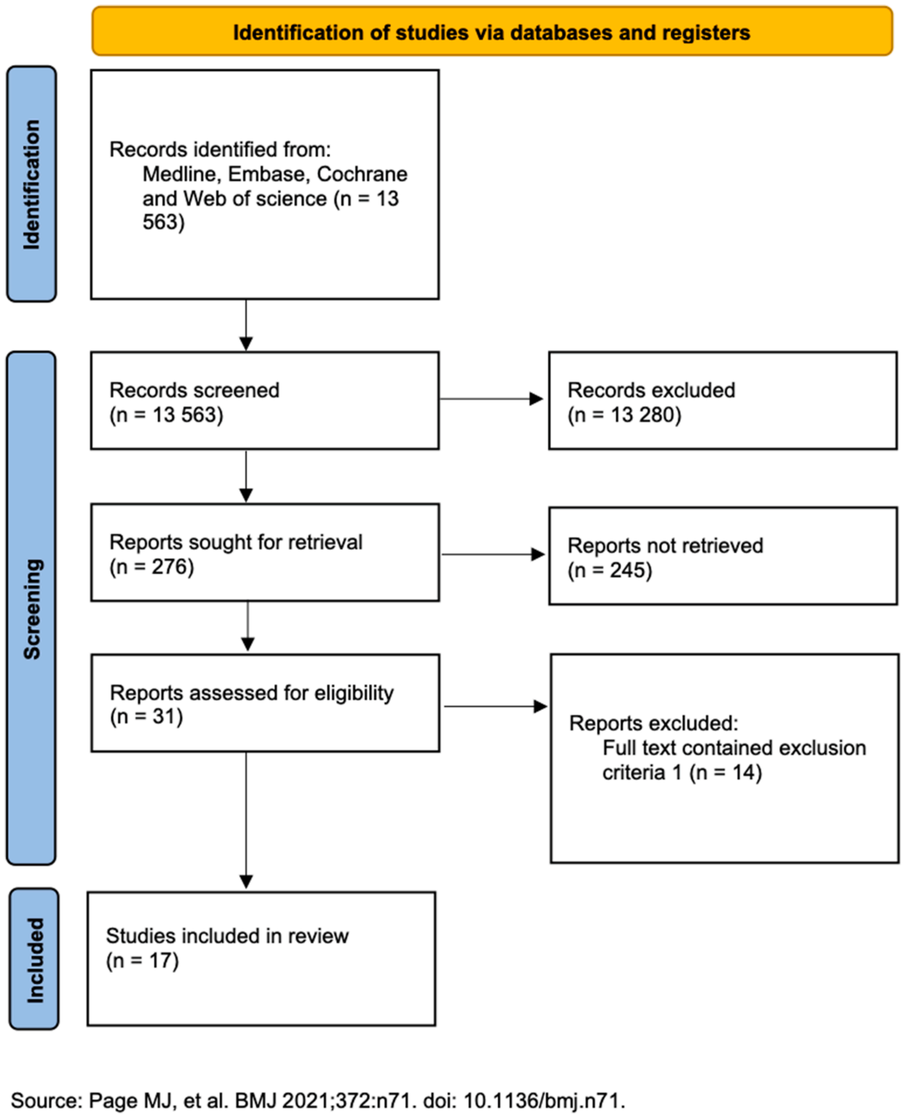

Fig 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. Seventeen studies met inclusion criteria and were included in the review.

the RoB 2 tool. Every report in analysis was assessed with some concerns in the tool. Data presented in the reports were heterogenous, and not all articles gave information on analyzed items.

Characteristics of patients

Overall, a total of 2484 patients were analyzed. Of the patients, 66.3% were male, and 33.7% were female. The mean patient age was 2.14 years (median, 0.46 years; range, 0-17 years). The right extremity was affected in 60% of cases, the left extremity in 35.4%, and both in 4.6%. In 592 patients, the localization of the affected artery was reported. Most commonly, the location was the common femoral artery (49.8%), followed by the brachial artery in 16.3%, the radial artery in 12.7%, the external iliac artery in 11.9%, and the superficial femoral artery in 3.9%.

Etiology was reported in 859 patients. In 89.9%, iatrogenic arterial cannulation or catheterization (intensive care patients) was the most common cause, followed by traumatic genesis in 10%. In 8.7% of overall cases and in 87% of all traumatic cases accordingly, PALI was due to supracondylar humeral fracture. Accidental intraoperative damage was reported in 0.5%, congenital causes in 0.2%, and coagulation disorders were the reason for PALI in 0.2%.

Symptoms

Extracted data regarding clinical presentation of ALI in children were scarce, as most studies did not focus on the symptoms. Five of 17 studies reported cyanosis in 17 of 141 children (12.1%[1,10-12,17]). Pain as a symptom was reported in 68 of 79 patients (86.1%; 2 of 17 reports[10,12]).

Table. Study characteristics

Author, year	Reference number	Type of study/no, patients	Mean age	Etiology of ischemia	Type of therapy (%)	Main outcomes	Limitations
Liu, 2022	1	Prospective observational cohort study/125	3.21 days	Cannulation of radial artery	Conservative (100)	Changes in PPI after peripheral artery cannulation in newborns is a feasible indicator of ALI	Regional bias
Warner, 2022	2	Retrospective observational study/76	3.5 years	Arterial catheterization	Anticoagulation (100)	Pediatric lower limb arterial thrombosis results in low distal PSV and no short-term limb loss or mortality. Recanalization rate is 57%.	Retrospective data analysis, no long-term data
Ade-Ayaji, 2008	3	Single-center retrospective observational study/10	35.5 weeks	Arterial catheterization, compression, polycythemia	Systemic thrombolysis (80); thrombectomy (20)	Systemic thrombolysis and selective surgery lead to good tissue function	Retrospective data, small number of patients
Al Hinai, 2024	4	Single-center retrospective observational study/13	n/d	Arterial catheterization, trauma, unclear	Conservative (61.5), endovascular (7.7), surgery (15.4)	15.38% mortality rate. A multidisciplinary approach is necessary for most favorable outcomes	Retrospective data, small number of patients
Andraska, 2017	5	Single-center retrospective observational study/74	1.4 years	Arterial catheterization	Heparinization (92), surgical revascularization (10,8)	7.5% limb-related early complications in patients managed medically, 88% limb salvage following revascularization	Only 58% of medically managed patients received surveillance duplex
Kara, 2024	6	Single-center case series/11	13.4 days	Arterial catheterization	Heparinization (100)	100% limb salvage after conservative treatment	Retrospective data, small number of patients
Kayssi, 2014	7	Single-center retrospective observational study/151	1.51 years	Arterial catheterization	Heparinization/thrombolysis/oral anticoagulation (94), surgery (6.6), initial amputation (0.7)	15% complications related to ALI or anticoagulation. ALI in children can generally be managed with anticoagulation	44% lost to follow-up, retrospective data of patients identified through an imaging database
Lim, 2018	8	Retrospective analysis of prospective collected registry data/1576	9.9 years	Any etiology of ALI	Conservative (83.3), operative revascularization (16.7)	Conservative management leads to similar low amputation rates and mortality rates compared to operative management. Infants (<2 years) are at higher risk of in-hospital mortality	Use of administrative database with no assessment of cause of ALI, symptoms and indications for further management

Table. Continued.

Author, year	Reference number	Type of study/no, patients	Mean age	Etiology of ischemia	Type of therapy (%)	Main outcomes	Limitations
Lin, 2001	9	Single-center case series/14	4.1 years	Arterial catheterization	Operative revascularization	100% limb salvage, 84% of children with ALI gained normal circulation	Retrospective data, small number of patients
Louahem, 2016	10	Single-center case series/68	7.5 years	Supracondylar humeral fracture	Conservative (92,6), surgery (7.4)	Conservative management in pink, pulseless hands results in good outcomes	Retrospective study, no objective vascular evaluation (angio-MRI) in follow-up
Matos, 2011	11	Single-center case series/12	3 months	Arterial catheterization	Heparinization (83,3), operative revascularization (8.3)	Surgical intervention only for cases with tissue loss	Retrospective data, small number of patients
Naga, 2022	12	Single-center case series/11	5.4 years	Blunt trauma to the brachial artery	Conservative (100)	Patients with warm pulseless hands can be managed conservatively, 18.2% required operative revascularization after not regaining pulse after 48 hours of conservative treatment	Retrospective data, small number of patients
Ramirez, 2020	13	Single-center case series/50	9.9 weeks	Arterial catheterization	Heparinization (90), operative revascularization (2)	64% of patients treated with anticoagulation had a complete resolution of thrombus after 30 days	Retrospective study, only patients with surveillance imaging available were selected
Rizzi, 2018	14	Systematic review/ 52	5.8 months	Arterial catheterization	Heparinization (97), systemic thrombolysis (87), surgery (3.8)	82% complete resolution rate of catheter-related arterial thrombosis	No direct data, systematic review
Silverberg, 2023	15	Single-center retrospective observational study/78	3.8 months	Arterial catheterization	Anticoagulation (100), operative revascularization after failure of anticoagulation (2.6)	No major amputation, no deaths related to limb ischemia	Retrospective data, 14% loss to follow-up
Vaughn, 2023	16	Single-center retrospective observational study/236	65 days	97.5% arterial catheterization	Conservative (93,5), endovascular (0.8), operative revascularization (3)	98.7% limb salvage, anticoagulation does not increase the need for surgical intervention or long-term complications	Retrospective data
Wang, 2018	17	Single-center retrospective observational study/25	3.6 months	88% arterial catheterization	Conservative (100), heparinization (80)	96% limb salvage after ALI managed with anticoagulation	Retrospective data

ALI, Acute limb-threatening ischemia; *MRI*, magnetic resonance imaging; *n/d*, no data; *PPI*, peripheral perfusion index; PSV, peak systolic velocity.

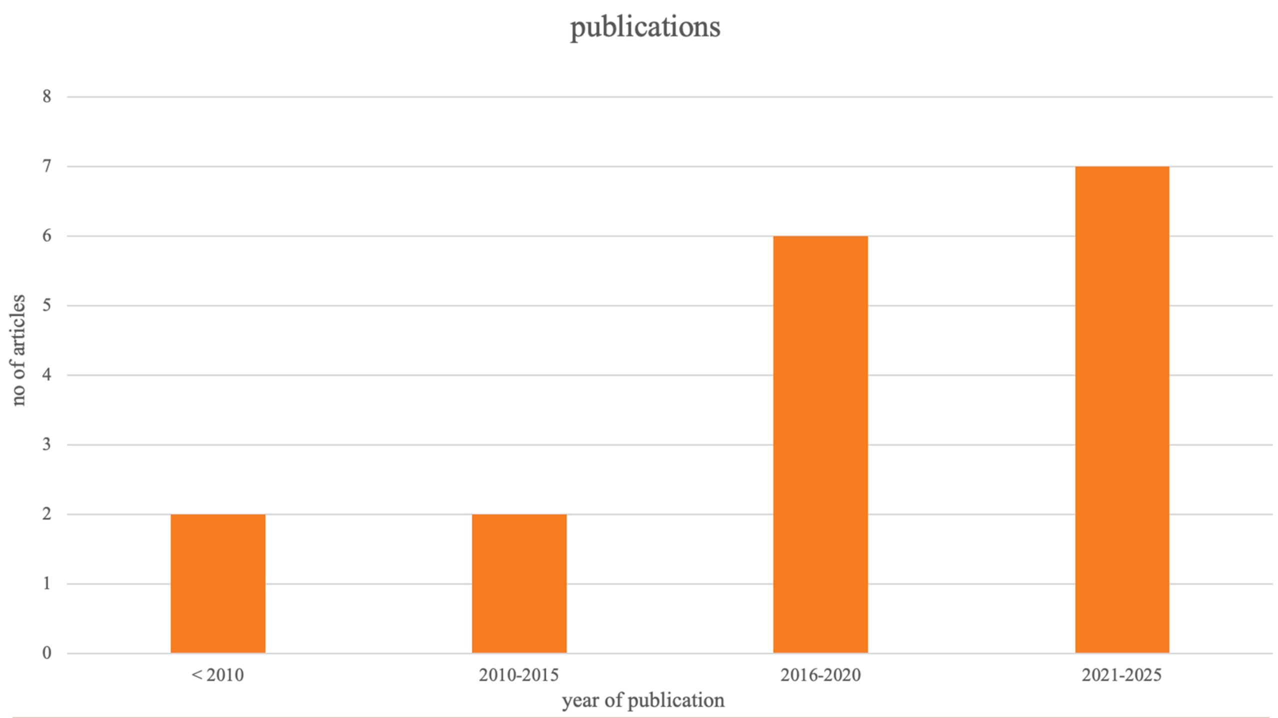

Fig 2. Publications over the years. The number of published articles was rising over the years, with a peak in 2021 to 2025.

Diagnostics

In seven studies, information on the pulse status was documented with either complete absent or reduced pulse.[10-13,15-17] The most commonly used diagnostic modality was duplex sonography in 87.9% of children (14/17 studies). Sonography was even performed initially or as follow-up diagnostic tool. Angio-magnetic resonance imaging was not carried out in any study. Angio-computed tomography and digital subtraction angiography or imaging were not used as primary diagnostic methods. In the pooled data computed angiography was reported in only three cases and digital subtraction imaging in five patients.

Treatment

Conservative treatment. PALI was initially managed conservatively in 87.3% of patients (16 of 17 studies, whereas one study specifically focused on PALI treated surgically). Conservative treatment modalities comprised removal of catheter, closed reposition in fractures, systemic thrombolysis, anti-platelet therapy, or watchful waiting with no medication or systemic heparinization (unfractionated heparin [UFH]/low molecular weight heparin [LMWH]).

Eleven of 16 studies managed PALI with primary conservative treatment.[5-8,10-13,15-17] Anticoagulation with heparin (UFH or LMHW) was explicitly documented as a treatment intervention in 11 studies. Specific heparin dosing protocols were detailed only in three studies. An initial bolus of 100 units was given,[11] followed by continuous infusion ranging from 10 to 20 IU/kg/h.[3,11] Monitoring of therapeutic dosage was documented in two studies by either maintaining activated partial thromboplastin time (aPTT) at 1.5 to 2 times above baseline values[15] or achieving anti-factor Xa levels within the range of 0.35 and 0.7 U/mL.[15]

Duration of anticoagulation was reported in six of 11 studies, primarily employing conservative management for PALI.[7,12,13,15-17] Treatment durations varied considerably. One study (n = 142) reported a mean anticoagulation duration of 2.5 ± 3.9 months, with extended treatment determined by coexisting conditions requiring prolonged anticoagulation.[7] Another study found significant variability depending on the managing specialty team, with a median treatment duration of 28 days.[16] Three studies employed ultrasound-guided treatment protocols.[13,15,17] One study recommended biweekly duplex ultrasound surveillance to guide anticoagulation, with approximately one-third of patients achieving thrombus resolution every 2 weeks.[13] Another study (n = 78) utilized early clinical reassessment at 2 hours, continuing anticoagulation for 2 to 5 days if ischemia resolved or prolonging treatment based on ultrasound findings with a median UFH duration of 5 days. LMWH was continued for a median of 28 days.[15] A third study treated patients with UFH and transitioned to enoxaparin or warfarin for 4 weeks with repeat duplex ultrasound assessment, extending to 12 weeks if needed,

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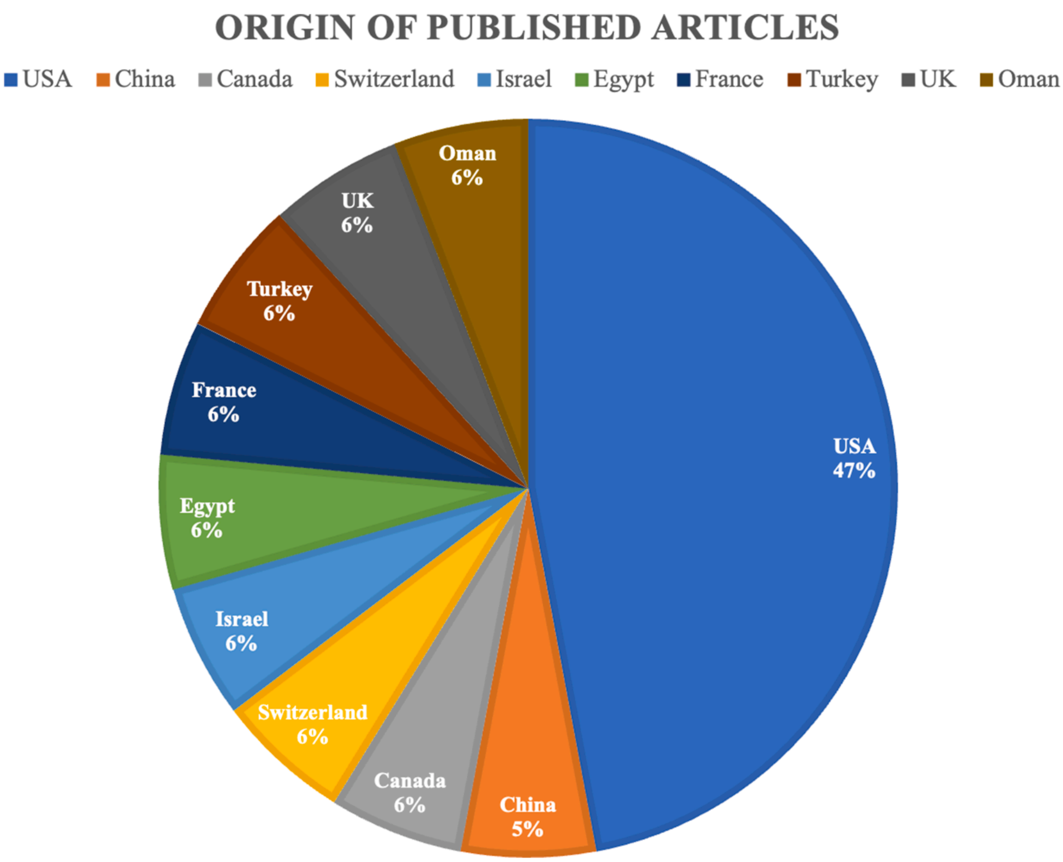

Fig 3. Origin of published reports. *UK*, United Kingdom; *USA*, United States.

but no treatment beyond 3 months.[17] One study (n = 11) of blunt brachial artery trauma continued anticoagulation for at least 48 hours after fracture stabilization, proceeding to surgical exploration if no clinical improvement occurred.[12]

A total of five studies reported on systemic thrombolysis as conservative treatment modality,[3,7,8,14,15] partially performing systemic thrombolysis secondary in heparin non-responders.[7,15] The dosage of recombinant tissue plasminogen activator ranged from 0.25 to 0.5 mg/kg/h, for a mean duration ranging from 6 to 7.1 hours.[3,14]

Catheter-directed thrombolysis was only documented in three patients and did not play a major role in treatment of PALI. One study compared the duration of anticoagulation and found no significant difference in patients anticoagulated for <28 vs >28 days in regards to tissue loss or limb-length discrepancy.[20]

Invasive treatment. Initial surgical treatment was performed in 12.7%. Thrombectomy represented the most common performed surgical intervention, accounting for 36 specifically listed cases. Due to absence of procedural specifications in one major study representing 263 surgical cases, the proportional contribution of embolectomy procedures cannot be calculated. Further arterial reconstruction comprised of patchplasty, vein interposition, bypass grafts, and managing complications on puncture sites, such as ligation of arteriovenous fistulas or pseudoaneurysms. Apart from arterial reconstruction, surgical procedures consisted of fasciotomy and major amputation. Primary amputation was only performed in four patients. Endovascular treatment, such as percutaneous thrombectomy or catheter-directed thrombolysis, was only mentioned in three studies and performed in individual cases. Surgical treatment was performed initially due to contraindications to anticoagulation, severe cases of ischemia, or also secondarily after failed medical treatment.

PALI caused by trauma. Two of the 17 studies[10,12] specifically focused on the treatment regime in ALI and type III supracondylar humeral fractures, where the distal humerus is completely displaced. Fractures were the most common cause in the traumatic PALI group (87%). Louahem et al[10] reported on 68 patients with acute vascular injury and no pulse palpable. Sixty-three patients with pulseless and well-perfused hand (pink hand) underwent reposition. A palpable radial pulse was restored in 42 patients immediately, whereas in 18 patients, no immediate return of pulse, but a perfused hand was present. In these 18 patients, pulse returned in all cases within a few hours up to 11 days postoperatively. No secondary changes with need of reoperation occurred in all pink hands with successful reposition,

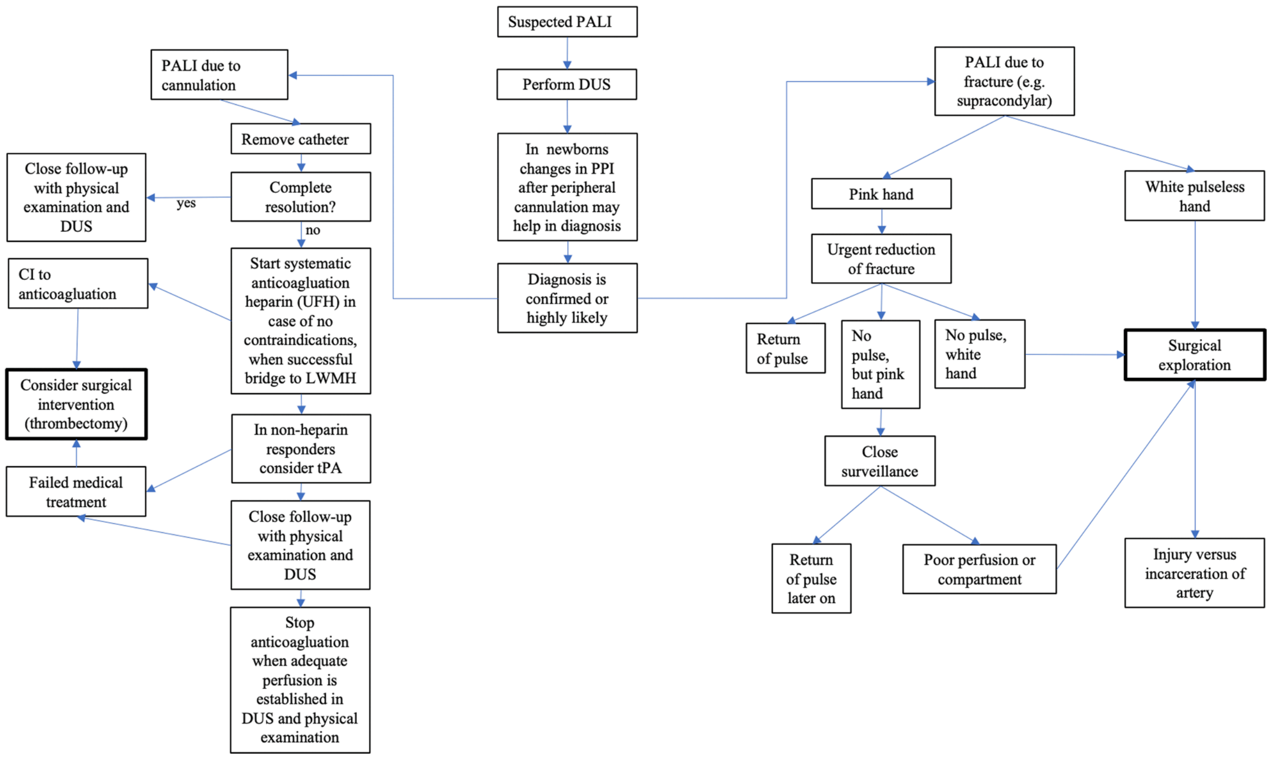

Fig 4. Suggested flowchart of management in pediatric acute limb ischemia (*PALI*). Pathways are given for the two most common causes of PALI. The pathway is based on suggested flowcharts of Louahem et al, Ade-Ajayi et al, and Andraska et al. *DUS*, Duplex ultrasound; *LMWH*, low molecular weight heparin; *PPI*, peripheral perfusion index; *tPA*, tissue plasminogen activator; *UFH*, unfractionated heparin.

and no vascular exploration was needed. Three patients of the 63 patients with pink hand had unsuccessful reposition and therefore required immediate intra-operative surgical exploration due to incarceration of brachial artery. Of the 68 patients in their report, five patients had primary ischemia with no pulse-white hand and needed immediate vascular repair. Their data showed that a pulseless, but well-perfused warm hand ("pink hand") can successfully be treated conservatively with watchful waiting and monitoring under the premise of an adequate orthopedic reposition.

Outcome and complications

Sixteen of 17 studies (908 patients) reported on mortality rates as well as causes of death. Mortality directly linked to PALI could be detected in one patient (0.01%). Overall amputation rate was 2.4% in all studies (range, 0-30%). All 11 reports[5-8,10-13,15-17] highlighting treatment in PALI stated conservative treatment was successful. Four studies[5,6,16,17] recommended surgery to be reserved only for failed medical treatment. PALI caused by trauma showed overall good results without amputation or death. Two articles[8,9] reported on children under the age of 2 years having a higher risk of in-hospital mortality and less satisfactory outcome. The 17 studies reported on 120 deaths (4.8%), but only one could directly be related to PALI. Fifteen of the 17 reports gave information about further adverse events. Twenty-eight patients experienced complications related to anticoagulation, and 11 patients (7/17 studies[5,7,10-12,16,17]) exhibited limb growth discrepancies in follow-up. Bleeding complications after thrombolytic therapy were not consistently recorded. In total, there were 18 patients with bleeding complications after thrombolytic therapy.[3,7,14] In 17 patients, bleeding was limited to the puncture site,[7,14] and one patient experienced extension of the pre-existing intracranial hemorrhage.[3]

Other rare complications were skin contractures after surgery (2), recurrence (1), hemorrhage one week after interposition graft (1), persistent occlusion (1), chronic deep vein thrombosis (2), and fasciotomy (3).

Follow-up

Follow-up was reported irregularly. In only 13 of 17 studies, follow-up was reported either in part or complete ranging from 0 to a maximum of 15.7 years. The median value of follow-up time was 2.4 years (mean, 3.2 years).

PALI in neonates

Subgroup analysis was carried out regarding neonatal patients as they represent an especially vulnerable patient cohort.

Four studies[1,3,6,7] were included focusing on neonates including 103 patients. Localization of ischemia was radial (71.4%; 25 patients), brachial (11.4%; four patients), femoral (5.7%; two patients), iliac (5.7%; two patients), subclavian (2.8%; one patient) and popliteal (2.8%; one patient); the rest did not clarify. Three studies (46 patients)[1,3,6] disclosed the etiology of PALI; all were due to arterial catheterization. Conservative management was primarily performed in 101 neonates; in two patients, initial surgical treatment was performed by thrombectomy. One neonate required surgical revascularization and four patients amputation in the following due to failed medical treatment. In total, seven of 103 neonates were treated surgically with thrombectomy or amputation (primary or in the follow-up) implying a success rate of 93.2% of conservative treatment. Four neonates required amputation (mean, 3.9%; median, 0.5%). Amputation rate in neonates was slightly higher compared with the overall cohort (3.9% vs 2.4%). All neonates who required amputation were treated medically before. The three patients treated with thrombectomy (two due to contraindications of thrombolysis and one due to failed medical treatment) recovered and did not need amputation in the follow-up.

DISCUSSION

The present research represents a contemporary systematic review of PALI. Although clinical guidelines for the diagnosis and treatment of ALI in adult patients exist at both national and international levels, clear high-quality guidelines based on prospective studies for physicians managing this rare condition in pediatric populations are lacking. Apart from specialized pediatric centers, considerable uncertainty persists among vascular surgeons.[23]

As iatrogenic vascular injuries represent the most frequent cause of PALI, the common femoral artery was most commonly affected, followed by the brachial artery—both frequent sites for arterial access procedures.[17-19] Trauma-related vascular occlusions rarely led to ischemia (10% of cases).[15,16]

In 87.9% of cases, duplex sonography was performed initially or during follow-up after suspected PALI. However, vascular ultrasound can be challenging especially in neonates due to small vessel caliber and patient movement artifacts.[24] As demonstrated in our review, contrary to ALI in adults, computed tomography angiography played a minor role in PALI.

Conservative treatment represented the first-line treatment modality in 87.3% of patients. Due to incomplete dosage documentation in our dataset specific recommendations for UFH dosing in PALI cannot be established based on our analysis.

However, Matos et al recommend an initial UFH bolus of 100 units/kg followed by continuous infusion at 20 units/kg/h in infants with ALI.[3] A systematic review examining anticoagulation protocols in pediatric patients with venous thromboembolism suggested an initial bolus of 75 U/kg, followed by age-stratified continuous infusion rates: 28 U/kg/h for children under 1 year and 20 U/kg/h for children over 1 year, with dosage adjustments to maintain aPTT between 55 and 85 seconds.[25] The American College of Chest Physicians' clinical practice guidelines for antithrombotic therapy in neonates and children recommend limiting UFH bolus doses to 75 to 100 U/kg.[4] Therapeutic monitoring of maintenance doses should be performed using either anti-factor Xa activity levels (target range, 0.35-0.7 units/mL) or aPTT values maintained at 1.5 to 2.0 times above baseline.[4,19] Because long-term use of therapeutic UFH in children should be avoided, anticoagulation can be continued with LMWH after ending of UFH.[4,19]

Whereas systemic thrombolysis is obsolete in treatment of adult patients with ALI, this treatment modality was reported in five pediatric studies.[2,5,11,18,19] In a recent study regarding the outcome of 78 patients with PALI in pediatric intensive care units, tissue plasminogen activator was intravenously administered in five patients who did not respond after treatment with UFH.[19] Given the critically ill status and predominant involvement of preterm infants in PALI cases, intracranial hemorrhage may represent a significant risk factor and relative contraindication for systemic thrombolytic therapy.[11] There are several case series addressing systemic thrombolysis in children presenting with thrombosis following cardiac interventions, including both surgical and catheter-based procedures. High rates of successful thrombolytic therapy with effective clot resolution were demonstrated.[14,26-29] The overall occurrence of bleeding complications seemed to be low, mainly associated to bleeding on puncture sites, but ranged to major hemorrhagic complications occurring in individual cases.[26,27,30-32]

In the authors' view, due to reported incidence of severe complications, systemic thrombolysis for PALI might not be applied as first-line treatment for puncture-related femoral artery occlusions.

Based on our dataset, initial surgical intervention plays a secondary role in treatment of PALI, with thrombectomy being the most common procedure, suggesting that surgical interventions are reserved for specific indications.

In a recent retrospective study including 236 children with iliofemoral arterial thrombosis, only eight patients underwent surgical intervention, with the median age being relevantly higher than of the whole cohort (8.2 years vs 65 days).[20] Similar to Vaughn et al, the patients undergoing surgical revascularization demonstrated significantly higher mean age compared with those treated conservatively. Furthermore, traumatic etiology was more frequently observed in patients undergoing revascularization.[2] In the other most recent cohort study, only two required surgical revascularization after failure of anticoagulation therapy.[19] These findings suggest conservative management as first-line therapy in PALI.

Possible complications subsequent to PALI include an impaired length growth; nevertheless, with 8%, the prevalence is reportedly low.[33] This potential complication alone should not prompt primary surgical revascularization, as patients can also be followed by close clinical controls and, if need be, two-stage surgical reconstruction.[34] In general, the authors feel that indication for surgical treatment of puncture-associated PALI might be the more liberal with increasing age of affected children or when conservative treatment fails.

Both traumatic studies demonstrated concordant findings regarding the safety of conservative management in cases presenting with warm, pulseless hands, showing no impaired growth or function in the affected limb.[15,16]

Age-stratified analysis indicates that children older than 2 years are more likely to have PALI associated with musculoskeletal injury and subsequent operative revascularization of the affected limb, marking age-related differences in collateral circulation capacity and injury mechanisms in this population.[2] This goes in line with a recent systematic review comparing close observation strategy and the surgical exploration.[35]

Based on our dataset, mortality directly linked to PALI was low. The overall amputation rate was 2.4%, indicating favorable limb salvage outcomes in the majority of cases. Vascular recanalization rates after conservative treatment were incompletely documented in the majority of studies. However, Warner et al performed systemic duplex ultrasound surveillance and reported 57% recanalization rate within half a year following conservative treatment in pediatric lower limb arterial thrombosis.[22]

Based on our analyzed data as well as recommendations from Louahem et al, Ade-Ajayi et al, and Andraska et al, we suggest a diagnostic and therapeutic algorithm for PALI secondary to arterial cannulation or trauma (Fig 4).

There are several limitations in this study. Keeping in mind that no prospective studies exist on this subject and the general quality of evidence is low, results must be interpreted with caution. Furthermore, the existing literature is characterized by a significant heterogeneity among the mostly retrospective single-center cohort studies with substantial variability in documented clinical parameters and outcome measures, presenting considerable challenges in establishing coherent, generalizable conclusions from existent data.

CONCLUSIONS

Despite these methodical limitations, our dataset analysis demonstrates that physical examination together with duplex ultrasound are the optimal diagnostic approach for children with suspected PALI. Conservative management, predominantly consisting of anticoagulation therapy with heparinization, can safely be implemented as first-line treatment under close clinical surveillance. Systemic thrombolysis and surgical revascularization should be reserved for cases with failure of anticoagulation therapy or specific clinical indications requiring aggressive intervention. Trauma-induced PALI and children of higher age may require more extensive surgical reconstruction procedures, reflecting different pathophysiology and anatomical circumstances in these populations.

AUTHOR CONTRIBUTIONS

Conception and design: JM, UR, AM, EK
Analysis and interpretation: JM, UR, FBG, AM, WW, FS, EK
Data collection: JM, EK
Writing the article: JM, UR, AM, EK
Critical revision of the article: FBG, WW, FS
Final approval of the article: JM, UR, FBG, AM, WW, FS, EK
Statistical analysis: JM, UR, AM, EK
Obtained funding: Not applicable
Overall responsibility: JM

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DISCLOSURES

None.

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APPENDIX (online only)

Electronic search strategy. From March 1, 2025, until April 1, 2025, two investigators independently screened all titles and abstracts collected from electronic databases. Literature search for the term "acute limb ischemia" was conducted in Medline (PubMed), Embase, Cochrane Library and Web of Science. Results were transferred to Rayyan online library. From April 1, 2025 until May 15, 2025, the following keywords were applied in Rayyan: "children," "pediatric," "paediatric," "infant," "newborn," and "neonate."

The search followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two investigators independently screened all titles and abstracts collected from the search strategy for relevance and according to previously defined inclusion criteria (see main body text, from May 16, 2025 until May 30, 2025).

The full texts of all relevant articles were obtained and reviewed for suitability independently by both reviewers. Any disagreement in study inclusion was resolved by consensus.

This systematic review has been registered in the PROSPERO public database (CRD420251035570).

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist - abstract

Section and topic	Item #	Checklist item	Reported (yes/no)
Title			
Title	1	Identify the report as a systematic review.	Yes
Background			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
Methods			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (eg, databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	No
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
Results			
Included studies	7	Give the total number of included studies and participants and summarize relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (ie, which group is favored).	Yes
Discussion			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (eg, study risk of bias, inconsistency and imprecision).	No
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
Other			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. doi: 10.1136/bmj.n71.

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist - manuscript

Section and Topic	Item #	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	P 1, l.3-4
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	reported
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P 4, l.3-21
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P 4, l.20-21
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P 5, l.14-22
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	P 5, l.3-10
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	P 5, l.2-13
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	P 5, l.14- P6, l.3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	P 6, l.4-9/supplements S1
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (eg, for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P 5, l.18-22
	10b	List and define all other variables for which data were sought (eg, participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P 5, l.20-22
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	P 6, l.15-18
Effect measures	12	Specify for each outcome the effect measure(s) (eg risk ratio, mean difference) used in the synthesis or presentation of results.	P 6 15-18
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (eg, tabulating the study intervention characteristics and comparing against the planned groups for each synthesis [item #5]).	P 5, l.14-22
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	P 6, l.15-18

Journal of Vascular Surgery
Volume ■, Number ■

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Section and Topic	Item #	Checklist item	Location where item is reported
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	P 6, l.15-18
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	P 6, l.5-9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (eg, subgroup analysis, meta-regression).	P 6, l.8-9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	P 6, l.15-18
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	P 6, l.10-13
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	P 7, l.3-12
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	P 7, l.4-7
Study characteristics	17	Cite each included study and present its characteristics.	P 7, l.7/Table
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	P 7, l.18-19
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (eg, confidence/credible interval), ideally using structured tables or plots.	Table I
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	Table
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (eg, confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P 7, l.23- p 12, l. 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	P 7, l.14-21
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	P 7, l.18-21
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	P 7, l.15- 21
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P 12, l.21-p 16, l.16

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Section and Topic	Item #	Checklist item	Location where item is reported
	23b	Discuss any limitations of the evidence included in the review.	P 16, l. 19-24
	23c	Discuss any limitations of the review processes used.	P 16, l.19-24
	23d	Discuss implications of the results for practice, policy, and future research.	P 17, l. 6 - 14
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	P 5,l.9-10
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	P 5, l.9-10
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	P 5, l.9-10
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Stated in submission process
Competing interests	26	Declare any competing interests of review authors.	Stated in submission process
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Key findings of each study in Table and search strategy in supplements

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. doi: 10.1136/bmj.n71.