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ORIGINAL ARTICLE

Quality improvement approaches to heparin-induced thrombocytopenia: a scoping review

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Abstract

Background: Heparin-induced thrombocytopenia (HIT) is a relatively uncommon condition characterized by 2 exceedingly common phenomena in hospitalized patients: thrombocytopenia and heparin exposure. Consequently, HIT is frequently overdiagnosed and inappropriately treated. These issues are the focus of many quality improvement (QI) initiatives.

Objectives: In this scoping review, we identified and characterized all published QI studies on improving the diagnosis and management of HIT.

Methods: We conducted a systematic literature search through April 2022 for studies reporting on QI interventions regarding the diagnosis, treatment, and/or prevention of HIT.

Results: Thirty studies were included in the final review. Studies were separated into 5 groups based on the focus of the interventions: increasing HIT recognition, reducing HIT incidence, reducing HIT overdiagnosis, promoting safer HIT management, and creating HIT task forces. Nine studies focused on the implementation of 4Ts score calculator into electronic medical record orders for HIT testing, while only 1 evaluated the impact of reducing unfractionated heparin use in favor of low-molecular-weight heparin. Six studies focused on the implementation of direct thrombin inhibitor management protocols, while none evaluated the use of alternative anticoagulants in HIT management.

Conclusion: The bulk of published HIT QI research focused on reducing overdiagnosis and promoting safer direct thrombin inhibitor therapy, while minimal attention has been devoted to HIT prevention and the use of evidence-based alternative HIT therapies.

KEYWORDS
diagnostic errors, heparin, incidence, review literature as topic, thrombocytopenia

Essentials

- Overdiagnosis and inappropriate treatment of heparin-induced thrombocytopenia (HIT) are common.
- Quality improvement work can address drivers of HIT overdiagnosis and inappropriate treatment.
- Some topics are well researched (eg, electronic medical record–based 4Ts score calculators reduce rates of misdiagnosis).
- Others need more focus (eg, HIT prevention and increasing the use of oral factor Xa inhibitors and fondaparinux in HIT).

1 | INTRODUCTION

Heparin-induced thrombocytopenia (HIT) is a life-threatening prothrombotic disorder that occurs as a complication of heparin therapy. While HIT is relatively uncommon, heparin use and thrombocytopenia are common in hospitalized patients [1,2]. Consequently, HIT is often overdiagnosed and inappropriately treated [3,4]. This leads to misuse of laboratory resources [5,6], avoidable adverse drug events [7–9], and high costs to patients and healthcare systems [8].

Many of the drivers of HIT overdiagnosis and inappropriate treatment can be addressed through quality improvement (QI) efforts. The 4Ts score, a well-validated pretest prediction tool, is both underused and misused [10]. The numerous available immunoassays for detection of the antiheparin-platelet factor 4 antibody have varying performance characteristics and require nuanced interpretation [11]. Suspicion of HIT necessitates empiric treatment, which can involve intravenous anticoagulants that increase cost and may increase bleeding risk. QI interventions can promote appropriate use of diagnostic tools, restrict nonindicated test orders, and reduce medication errors. As healthcare systems seek to improve patient safety and reduce unnecessary expenditures, HIT will continue to be a common QI focus.

QI work is often performed within single institutions, which leads to multiple publications from different sites on the same topic. While this may verify the efficacy of a particular approach, it leaves other areas under-investigated. The purpose of this scoping review is to identify and characterize all published QI projects on the diagnosis and management of HIT. Our aim is to create a resource for hospitals and providers seeking strategies to improve the quality of their HIT care and to guide the focus of future QI efforts toward less-studied areas.

2 | METHODS

2.1 | Protocol and registration

We performed a scoping review—a comprehensive literature synthesis that aims to map the prior research on a particular topic, identify key concepts, and determine gaps—on QI approaches to the diagnosis and management of HIT. This review was conducted with guidance from the latest version of the Joanna Briggs Institute Manual for Evidence Syntheses [12] and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews and searches [13]. The protocol for this scoping review was preregistered and published on Open Science Framework prior to the literature search [14].

2.2 | Eligibility criteria

Studies eligible for inclusion were abstracts or published manuscripts evaluating QI interventions focused on the diagnosis, treatment, and/or prevention of HIT. QI efforts aim to standardize processes and structure to reduce variation, achieve predictable results, and improve outcomes for patients and healthcare systems [15]. Studies with preintervention and postintervention data were eligible for inclusion. Projects included, but were not limited to, formal QI projects, hospital-sanctioned initiatives, and department- or specialty-driven endeavors. Papers reporting on HIT pathogenesis, diagnostic test development, treatment development and outcomes, and clinical trials were excluded. Review articles, case reports, and guidelines were also excluded.

2.3 | SEARCH STRATEGY

An information specialist (M.M.M.) developed and conducted comprehensive searches in Medline (Ovid), Embase (embase.com), Cumulative Index to Nursing and Allied Health Literature (CINAHL) Complete (EBSCOhost), Cochrane Central Register of Controlled Trials (CENTRAL, wiley.com), and Web of Science Core Collection (Clarivate Analytics) on June 2 and 3, 2022. Search terms included database subject terms and keywords identified from sentinel articles and team feedback. As HIT is not a Medical Subject Heading term, several keyword synonyms for HIT were determined. These keywords were then combined with thrombocytopenia keywords, as well as broader Medical Subject Heading terms (eg, anticoagulation, blood platelet disorders, etc.) to ensure sensitivity. Additionally, concepts related to QI (such as safety, disease management, and health professionals sets) were combined with the HIT keywords as well. EndNote (Clarivate) was used to manage citations and remove duplicates, with Covidence (Veritas Health Innovation) providing a second means for duplicate removal. We also searched specifically for conference abstracts from the American Society of Hematology (2004-2021) and the International Society on Thrombosis and Haemostasis (2003-2021) as abstracts from these conferences may not

have been captured in the databases. The search strategies used for each database and source are detailed in the Supplementary Material.

2.4 | Study selection

Covidence (Veritas Health Innovation), a web-based systematic review platform, was used to screen and select studies. After duplicates were removed, all titles and abstracts of the literature search results were screened by 2 authors (J.C.C. and M.Y.L.) based on the eligibility criteria to determine if the study should receive more in-depth review. All potentially eligible studies were independently reviewed by both the authors. Any disagreements were planned to be resolved by consultation with a third author (J.E.M.); there were no conflicts.

2.5 | Data collection and outcomes

Data extraction was performed by 2 authors (J.C.C. and M.Y.L.) using a standardized data extraction form, which was designed in advance in Microsoft Excel. Any discrepancies in interpretation between the reviewers were resolved through a discussion of the text of the original articles. The following data were extracted from all included studies: author names, year of publication, site of study, population and sample size, intervention type, intervention duration, outcomes, and key findings related to the focus of the scoping review. Outcome variables (if reported) included HIT enzyme-linked immunosorbent assay (ELISA) and/or functional assay positivity rates, HIT ELISA and/or functional assay test order quantities, number of inappropriate HIT ELISA and/or functional assay orders, number of patients started on direct thrombin inhibitor (DTI), heparin administration during HIT testing, heparin allergy documentation, cost savings related to testing intervention, cost savings related to drug use intervention, and cost savings related to preventative intervention.

3 | RESULTS

A total of 6419 citations were identified (Figure). After removal of duplicates, 3993 references were screened by title and abstract review. All studies that did not meet the inclusion criteria based on the study title or abstract were excluded. Subsequently, there were 107 full-text articles and 26 conference abstracts that were then reviewed in depth for inclusion. Ultimately, 30 studies (24 studies and 6 conference abstracts) met inclusion criteria and were included in the final analysis.

3.1 | Increasing HIT recognition

Three studies focused on promoting early detection of HIT, all using interventions to alert clinicians to a fall in platelet counts in patients receiving heparin products (Table 1). Two studies evaluated an electronic medical record (EMR) alert triggered by a significant platelet count decrease [16,17], while another involved direct pharmacy surveillance of platelet count trends in patients on heparin [18]. All 3 studies reported increases in HIT testing as a result of these interventions. One study reported a nonsignificant reduction in rate of thrombosis from 50% to 29% ($P = .39$) during surveillance [18]. Others noted no difference in time from platelet fall to HIT testing and treatment [17], or in rates of HIT ELISA or serotonin release assay (SRA) positivity [16,17].

3.2 | Reducing HIT incidence

One study reported the impact of systematically replacing unfractionated heparin (UFH) with low-molecular-weight heparin at a single medical center [19] (Table 2), given the estimates of a 0.2% incidence of HIT with low-molecular-weight heparin, versus 2.6% with UFH [20,21]. In this study, order sets were modified to exclude UFH options and efforts were made to prevent unnecessary UFH exposure (removal of UFH stores from nursing units and replacement of heparinized saline flushes with regular saline flushes). The authors evaluated the impact of these interventions on rates of suspected and diagnosed HIT as well as HIT-related expenses. Findings included a 42% decrease in the annual rate of suspected HIT, a 63% decrease in positive HIT assays, a 79% decrease in diagnosed HIT, and a 91% decrease in cases of HIT with thrombosis ($P < .001$ in all instances). This intervention was associated with over $250,000 in decreased HIT-related expenditures per year.

3.3 | Reducing HIT overdiagnosis

Thirteen studies focused on promoting the proper use of HIT testing and reducing overdiagnosis (Table 3). Across these studies, overdiagnosis is driven, at least in part, by provider misutilization of the 4Ts score (lack of use, improper use, etc.). Despite efforts to educate providers about the appropriate use of the 4Ts score, high rates of HIT testing sent on patients with a calculated low probability score were still observed [22].

To tackle this issue, 9 studies reported on the addition of 4Ts score calculator to EMR orders for HIT screening assays [23–31]. Authors quantified HIT diagnostic assay orders and the percentage of appropriate orders based on 4Ts scores before and after score calculator implementation. Most studies demonstrated reductions in inappropriate HIT testing (ie, the proportion of tests ordered on patients with a 4Ts score of 3 points or fewer) [25–27,29–31]. Five studies also showed a decrease in total HIT diagnostic assays ordered [24–27,31], and 3 studies noted more frequent discontinuation of heparin products in cases with at least intermediate probability 4Ts scores [25–27]. Two additional studies had pharmacists or laboratory personnel review all HIT test orders, calculate 4Ts scores, and make recommendations to the ordering providers based on calculated scores [32,33]. These interventions reduced the total quantities of HIT

TABLE 1 Interventions to increase heparin-induced thrombocytopenia recognition.

Intervention type	Author	Year	Country	Intervention details	Preintervention group	Postintervention group	Findings
Platelet fall alert							
	Andreescu et al. [18]	2000	USA	Pharmacy-based surveillance of platelet count in patients on heparin, with HIT testing ordered on patients with platelet decline.	Historical controls over 10 y	8672 patients over 3 y	• Increase in HIT testing (5 tests/y vs 26 tests/y) • Reduction in thrombosis rates in cases of confirmed HIT (50% vs 29%, P = .39)
	Riggio et al. [17]	2009	USA	EMR alert when a patient with an active order for heparin experienced a 50% platelet count decrease (or 30% if absolute platelet count was <150,000/μL) over a 3-wk time period	32,152 patients	33,452 patients	• Increase in SRA testing (610 orders vs 826 orders, P < .0001) • No impact on time from fall in platelet count to HIT testing (2.3 d vs 3.0 d, P = .30) • No impact on time to therapy (19.3 d vs 15.0 d, P = .45)
	Austrian et al. [16]	2011	USA	EMR alert when platelet count decreased by 50% or to < 100,000/μL after recent heparin exposure	1006 patients	1081 patients	• Increase in HIT ELISA orders (17.1% vs 24.6%, P = < .01) • More DTI orders in the postintervention group (2.6% vs 4.4%, P = .03) • No difference in rates of HIT antibody positivity between groups (2.8% vs 2.7%, P = .99) • No difference in LOS (49.7 vs 50.3 d, P = .94) or 90-d mortality (29.0 vs 34.2 d, P = .98)

DTI, direct thrombin inhibitor; ELISA, enzyme-linked immunosorbent assay; EMR, electronic medical record; HIT, heparin-induced thrombocytopenia; LOS, length of stay; SRA, serotonin release assay.

TABLE 2 Interventions to reduce heparin-induced thrombocytopenia incidence.

Intervention Type	Author	Year	Country	Intervention details	Preintervention group	Postintervention group	Findings
Replace UFH with LMWH							
	McGowan et al. [19]	2016	Canada	Institution-wide "avoid heparin" program, including: • Replacement of most UFH with LMWH in prophylactic or therapeutic doses. • Replacement of heparinized saline in arterial and central venous lines with saline flushes. • Modifications of order sets to exclude UFH options. • Removal of UFH stores from most nursing units.	Historical controls	1118 patients with suspected HIT	• 42% decrease in annual rate of suspected HIT (85.5 vs 49.0 per 10,000 admissions, $P < .001$) • 63% decrease in positive HIT assays (16.5 vs 6.1 per 10,000 admissions, $P < .001$) • 79% decrease in adjudicated HIT (10.7 vs 2.2 per 10,000 admissions, $P < .001$) • 91% decrease in HITT (4.6 vs 0.4 per 10,000 admissions, $P < .001$) • $266,938 decrease in HIT-related expenditures per year in post-intervention phase.

HIT, heparin-induced thrombocytopenia; HITT, heparin-induced thrombocytopenia with thrombosis; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

TABLE 3 Interventions to reduce heparin-induced thrombocytopenia overdiagnosis.

Intervention type	Author	Year	Country	Intervention details	Preintervention time frame	Postintervention time frame	Findings
4Ts score calculator							
	Samuelson et al. [31]	2015	USA	Mandatory 4Ts score calculator implemented into HIT ELISA EMR order.	8 mo	8 mo	• Reduction in aggregate testing (43 tests/mo vs 22 tests/mo, $P < .001$). • Reduction in proportion of tested patients with low probability 4Ts scores (66% vs 56%, $P = .07$). • Increase in average 4Ts score of tested patients (3.0 vs 3.4, $P = .01$).
	Schaffner et al. [24][a]	2017	USA	• Mandatory 4Ts score calculator implemented into HIT ELISA EMR order.	8 mo	8 mo	• 161 HIT ELISA orders pre-intervention (81% negative) vs 105 postintervention (82% negative). • Reduction in HIT ELISA ordering in patients with low probability 4Ts scores (67% vs 57%, $P = .13$). • 4Ts score discordant between ordering provider and hematologist in 67% of cases.
	Tsui et al. [25][a]	2017	USA	• Mandatory 4Ts score calculator implemented into HIT ELISA EMR order.	24 mo	24 mo	• 213 HIT ELISA orders before intervention vs 189 after intervention. • Fewer tests sent on patients with low probability 4Ts scores (54% vs 30%, $P < .001$). • More frequent discontinuation of heparin in patients with intermediate probability (66% vs 74%, $P < .001$). • Higher rates of HIT diagnosis (5.6% vs 11.1%, $P < .05$).
	Arshad et al. [29]	2018	USA	• Educational sessions for providers • Optional 4Ts score calculator incorporated HIT ELISA EMR order	18 mo	7 mo	• Reduction in inappropriate HIT ELISA orders (86.2% vs 56.4%, $P < .001$). • Increased documentation of 4Ts score (3.3% vs 30.8%, $P < .001$). • Increase in proportion of positive ELISA results (4.9% vs 10.3%, $P = .22$).

(Continues)

TABLE 3 (Continued)

Intervention type	Author	Year	Country	Intervention details	Preintervention time frame	Postintervention time frame	Findings
	Swarup et al. [27][a]/ Ball et al. [26][a,b]	2018/ 2019	USA	Mandatory 4Ts score calculator implemented into HIT ELISA EMR order	12 mo	6 mo	• 170 HIT ELISA orders pre-intervention vs 69 postintervention. • Increased 4Ts score documentation (3% vs 100%). • Reduced proportion of patients with low probability 4Ts scores receiving testing (66.4% vs 47.8%). • Increase in number of patients with intermediate or high probability 4Ts scores receiving alternative anticoagulant during testing period (71% vs 88%).
	Baumann Kreuziger et al. [23][a]	2019	USA	Mandatory 4Ts score calculator implemented into HIT ELISA EMR order.	6 mo	6 mo	• 104 HIT ELISA orders pre-intervention vs 112 orders postintervention. • Increase in the number of appropriately ordered tests (54% vs 80%, $P < .001$).
	Zayac et al. [28]	2020	USA	Mandatory 4Ts score calculator implemented into HIT ELISA EMR order.	7 mo	7 mo	• No difference in rates of inappropriate HIT ELISA orders (68.8% vs 66.3%). • No significant difference in rates of 4Ts score documentation
	Obadina et al. [30]	2022	USA	Mandatory 4Ts score calculator implemented into HIT ELISA EMR order; if score ≤3, a clinical reason for testing must be manually entered.	12 mo	12 mo	• 4.1% decrease in number of HIT ELISAs performed. • Similar rates of positive HIT ELISAs in preintervention and post-intervention (13.6% vs 14.7%). • Fewer tests sent in patients with low probability 4Ts scores (74.5% vs 10.6%).
4Ts score calculated by nonclinicians							
	Burnett et al. [32]	2016	USA	Reference laboratory contacts AMS when a HIT ELISA is received; AMS calculates 4Ts score and contacts ordering provider to recommend for or against	12 mo	12 mo	• Reduction in HIT ELISA orders (176 vs 107, $P < .001$) • 41% reduction in total HIT ELISAs processed by laboratories (176 vs 63, $P < .001$)

(Continues)

TABLE 3 (Continued)

Intervention type	Author	Year	Country	Intervention details	Preintervention time frame	Postintervention time frame	Findings
				processing and reporting of laboratory results.			• Reduction in inappropriate HIT ELISAs processed (72.2% vs 52.4%, P = 0.004). • Reduction in major bleeding events (10.2% vs 6.5%, P = .279). • Cost savings of 62% per patient exposed to heparin ($19.58 vs $7.51)
	Condon et al. [33]	2020	USA	• HIT ELISA orders trigger page to clinical pharmacist to calculate 4Ts score and determine assay appropriateness. • Order set guiding providers to calculate a 4Ts score with HIT ELISA order along with recommendations based on the score.	12 mo	12 mo	• 279 HIT ELISA/SRA orders pre-intervention (23/mo) vs 177 post-intervention (15/mo) • 303 pages received by pharmacists, 109 missed due to unavailability of pharmacist at time of page; 194 pages reviewed, 134 intervened on. • 107 scored as low risk by 4Ts score, 70 as intermediate risk, 9 as high risk. • 64 HIT ELISAs and 11 SRA discontinued due to pharmacist intervention.
Provider education							
	Malalur et al. [22]	2019	USA	Implementation of an HIT education program involving lectures to providers and individual feedback from hematology consultants to ordering clinicians.	Not stated	3 mo	• 83.3% of HIT ELISA orders were sent on low-risk cases, 12.5% on intermediate-risk, and 4.2% on high-risk cases.
Laboratory stewardship of SRA testing							
	Cusick et al. [34]	2022	USA	SRA test completion controlled by laboratory; SRA only sent for analysis if HIT ELISA returned with OD ≥ 0.400 units	23 mo	28 mo	• Reduction in SRA results per 1000 admissions (3.7 vs 0.6). • Reduction in number of 50-mL argatroban bags used per 1000 admissions (18.8 vs 14.3).

AMS, anticoagulation management service; ELISA, enzyme-linked immunosorbent assay; EMR, electronic medical record; HIT, heparin-induced thrombocytopenia; OD, optical density; SRA, serotonin release assay.

[a]Conference abstract

[b]Multiple publications on same data.

TABLE 4 Interventions to promote safer heparin-induced thrombocytopenia management.

Intervention type	Author	Year	Country	Intervention details	Preintervention group or time frame	Postintervention group or time frame	Findings
DTI protocol implementation							•
	Kennedy et al. [37]	2011	USA	Implementation of protocol for the use of argatroban or lepirudin in the management of HIT.	19 patients	10 patients	• More subtherapeutic aPTTs after protocol implementation (14.2% vs 22%, P = .03). • Reduction in time to therapeutic aPTT (15 h vs 8.1 h, P = .677).
	Kiser et al. [36]	2011	USA	Implementation of a dosing and titration protocol for argatroban and bivalirudin use.	83 patients	47 patients	• Shorter median time to goal aPTT (13 h vs 5 h, $P < .0001$). • Shorter median time to dose stabilization (22 h vs 10 h, $P < .0001$). • Higher median percentage of aPTT values at goal (53% vs 67%, P = .027).
	Gilmore et al. [35]	2015	USA	Implementation of guidelines for bivalirudin and argatroban use, with dosing and titration guidance for 3 aPTT goal ranges, based on age, organ function, and clinical condition.	50 patients	50 patients	• Higher rate of therapeutic aPTT achievement (72% vs 92%, $P < .01$). • Higher rates of therapeutic aPTT with initial dose (16% vs 44%, $P < .02$). • Fewer number of DTI titrations to therapeutic aPTT (3.14 ± 3.02 vs 1.85 ± 2.78, $P < .05$).
Pharmacist-driven DTI management							
	Lobo et al. [39]	2010	USA	Pharmacist oversight of all argatroban and lepirudin management based on pre-established protocols.	18 patients	17 patients	• Less common dosing errors (38% vs 9%, P = .0376). • Less heparin re-exposure after HIT diagnosis (39% vs 6%, P = .041).

(Continues)

TABLE 4 (Continued)

Intervention type	Author	Year	Country	Intervention details	Preintervention group or time frame	Postintervention group or time frame	Findings
	To et al. [40]	2011	USA	PDAS automatically consulted when argatroban or lepirudin ordered; PDAS selects appropriate DTI, orders initial dosing, and performs relevant lab monitoring and dosing adjustments.	95 patients	98 patients	• 32% increase in time spent in therapeutic aPTT range (64.4% vs 84.7%, $P < .001$). • Reduction in time to therapeutic aPTT (18.9 h vs 6.4 h, $P < .001$). • Less bleeding events (8 vs 3, $P = .130$).
	Cooper et al. [38]	2012	USA	Institutional protocol where pharmacists monitor and adjust dosing of argatroban and bivalirudin infusions.	25 patients	25 patient	• Faster attainment of therapeutic aPTT (7.7 h vs 3.4 h, $P = .009$). • Similar rates of bleeding (12% vs 20%, $P = .702$) and mortality (20% vs 24%, $P = .496$). • Less frequent medication errors documented (40% vs. 12%, $P = .05$).
Reduce heparin administration during testing/ promote heparin allergy documentation							
	Northam et al. [41]	2021	USA	Multidisciplinary workflow involving an EMR order set triggering pharmacist and nursing consultations.	14 mo	12 mo	• Reduction in heparin product administration while HIT testing results were pending (54.2% vs 20.0%, $P < .001$). • Increase appropriate heparin allergy documentation (95% vs 100%, $P < .001$).

aPTT, activated partial thromboplastin time; DTI, direct thrombin inhibitor; EMR, electronic medical record; HIT, heparin-induced thrombocytopenia; PDAS, pharmacist-directed anticoagulation service.

diagnostic assays ordered and the proportion of inappropriate tests ordered.

Additionally, one study reported on laboratory-controlled SRA testing [34]. Laboratory personnel would review all HIT ELISA tests sent and subsequently send SRAs only on cases with optical density units ≥0.400. This study showed reductions in SRA results per 1000 admissions as well as reductions in the unnecessary use of argatroban.

3.4 | Promoting safer HIT management

Seven studies described efforts to improve the safety of HIT management (Table 4). The majority focused on improving DTI stewardship, primarily through the implementation of hospital-wide and pharmacist-driven DTI protocols. Three studies reported the impact of DTI management protocols, with 2 studies showing significantly greater rates of therapeutic levels (measured by activated partial thromboplastin time [aPTT] in patients receiving DTIs after intervention) [35,36]. However, 1 study showed no significant difference in time to therapeutic aPTT but significantly more subtherapeutic aPTTs after protocol implementation [37].

Three additional studies reported on pharmacist-driven DTI management interventions [38–40]. Results included significantly shorter time to therapeutic aPTT, more time spent in the therapeutic aPTT range, fewer dosing errors and less frequent heparin re-exposure. Two studies noted no significant difference in rates of bleeding despite these interventions [38,40].

Finally, 1 study attempted to reduce heparin administration during active HIT testing and to promote heparin allergy documentation via a multidisciplinary workflow [41]. This intervention involved an EMR order set for HIT testing that triggered pharmacist and nursing consultations. This intervention successfully reduced heparin administration during HIT testing and increased rates of heparin allergy documentation.

3.5 | Creating HIT task forces

Six studies describe the development of HIT task forces designed to improve multiple aspects of the diagnosis and management of HIT [42–46] (Table 5). Task forces were multidisciplinary and worked to coordinate multiple interventions, including several of those described above (eg, 4Ts score calculators, DTI guidelines, etc.). Most studies showed changes in DTI use patterns (reductions in overall use, reductions in median duration of use, and increased rates of discontinuation within 24 hours of negative test results) [42–45]. One abstract reported significant reductions in new thrombotic and ischemic events after HIT diagnosis [47]. Finally, 1 study reported initial reductions in HIT diagnostic assay use [42]. Over subsequent years, testing rates began to increase again due to changes in the EMR ordering system. Through the continued activity of this task force, however, these changes were detected and interventions were implemented.

4 | DISCUSSION

In this scoping review, we have identified and categorized the published QI initiatives focused on the diagnosis and management of HIT. Overdiagnosis and inappropriate treatment of HIT lead to overuse of hospital resources and avoidable adverse events. This endeavor enables us to highlight well-researched interventions (eg, the use of an EMR 4Ts score calculator, creation of DTI management protocols) available for hospital systems seeking to improve HIT care to implement. We are also able to identify relative gaps in the literature (eg, reducing the use of UFH and increasing the use of non-DTI anticoagulants) deserving of more attention in future QI efforts.

Among the more promising QI efforts, there is an imbalance of attention to different aspects of HIT care. While 11 studies reduced over-testing through the implementation of 4Ts score calculator into HIT EMR order sets, only 1 study evaluated the impact of reducing UFH use overall on the incidence of HIT. A large proportion of hospitalized patients receive pharmacologic venous thromboembolism prophylaxis. Thus, while the importance of mandating 4Ts score calculation prior to HIT testing is well documented, more attention could be devoted toward interventions to help healthcare systems move away from the use of UFH.

Similarly, while substantial attention has been devoted to improving the quality of DTI use, there are no published efforts that we could identify regarding the use of alternative treatments for HIT. Six studies evaluated the impact of implementing DTI management protocols, with 3 studies directly incorporating pharmacists into day-to-day titration of DTIs. While DTIs are an important management option for HIT, they are very costly and, as evidenced by these studies, require complex and intensive monitoring. Fondaparinux, another therapeutic option for HIT, is both cheaper than DTIs and associated with fewer adverse events [48]. Further, oral inhibitors of factor IIa (eg, dabigatran) and factor Xa (eg, apixaban and rivaroxaban) are appropriate management options as well [49]. Some clinicians prefer factor Xa inhibitors (parenteral or oral) over DTIs for the management of suspected and confirmed HIT [50]. Efforts could be directed toward utilization of alternative management strategies, particularly in intermediate-risk cases in stable patients.

When evaluating the interventions in this review, it is important to consider the era in which each study was performed. For instance, platelet fall alerts were effective in raising awareness of HIT during the time period in which HIT was underrecognized [18]. As the pendulum has shifted toward higher rates of HIT overdiagnosis and inappropriate treatment, the role of the platelet fall alert—which appears to consistently increase the volume of HIT testing without concordant increases in test positivity [16,17]—is less clear. In order to make this type of intervention more specific to HIT, future alerts should account for the timing of platelet fall in relation to more immediately proximate heparin exposure.

HIT is a complex condition to diagnose and treat. As a result, several centers formed HIT task forces, which were able to meaningfully address the variety of aspects of HIT care that can be improved. The categories of published interventions described in this

TABLE 5 Heparin-induced thrombocytopenia task force creation.

Intervention Type	Author	Year	Country	Intervention details	Preintervention group or time frame	Postintervention group or time frame	Findings
Task force with multiple goals							
	Davis et al. [47][a]	2005	USA	Formation of an HIT task force with a focus on reducing heparin exposure and developing aids for HIT diagnosis and treatment.	232 patients	204 patients	• Decreased adverse outcomes after HIT diagnosis: thrombotic/ischemic events (15.5% vs 8.3%, P = .022). • Increased warfarin initiation upon platelet recovery (80.4% vs 89.1%, P = .03). • Decrease in presentations with thrombosis (46.1% vs 37.8%, P = .08), and all-cause mortality (21.1% vs 16.7%, P = .243). • No difference in rates of DTI use within 1 d of suspicion of HIT (64.9% vs 67.5%, P = .593).
	Smythe et al. [45]/ Smythe et al. [46][b]	2012	USA	Implementation of a protocol for HIT recognition and management; guidelines for DTI use; refinement of ordering and documentation of HIT ELISA results in the EMR; and multidisciplinary education.	61 patients	46 patients	• Increase in DTI discontinuation within 12 h (19.4% vs 40%, P = .058) and 24 h (30.4% vs 61.5%, $P < .05$) of negative ELISA. • Higher rate of DTI initiation within 12 h of HIT ELISA ordering (25.8% vs 77.4%, $P < .0001$). • Reduced rate of thrombotic events (34.4% vs 13.0%, P = .01).

(Continues)

TABLE 5 (Continued)

Intervention Type	Author	Year	Country	Intervention details	Preintervention group or time frame	Postintervention group or time frame	Findings
							• Reduction in major bleeding (13.1% vs 6.5%, P = .26). • Annual cost savings > $450,000.
	Reardon et al. [43]/ Ritchie et al. [44]	2015/2016	USA	Hemostatic and Antithrombotic Stewardship task force created to provide clinical surveillance of HIT diagnostic workups and management of DTI therapy.	332 patients	259 patients	• Reduced median duration of DTI therapy (6.64 d vs 5.17 d, P = .01). • Reduced duration of DTI use for patients with suspected HIT (4.07 d vs 2.86 d, P = .01). • Annual cost reduction of $248,500.
	Lim et al. [42]	2018	USA	Implementation of multidisciplinary HIT task force; mandatory 4Ts score calculation prior to HIT ELISA ordering; treatment algorithm with automatic hematology consultation for intermediate-to-high risk patients; SRA ordering at discretion of hematology consultants; and widespread education to clinical staff.	2010	2013	• Reductions in HIT ELISA orders (600 in 2010 vs 374 in 2013, 13.5% decrease) and SRA (202 orders vs 29 orders, 85% decrease). • 78% reduction in DTI use.

DTI, direct thrombin inhibitor; ELISA, enzyme-linked immunosorbent assay; EMR, electronic medical record; HIT, heparin-induced thrombocytopenia; SRA, serotonin release assay.
[a]Conference abstract.
[b]Multiple publications on same data.

scoping review can serve as a template in the development of future HIT task forces. A HIT QI "bundle" could include interventions to reduce the incidence of HIT by promoting the use of an alternative to UFH wherever possible, reduce overdiagnosis through mandatory 4Ts score calculation prior to assay ordering, enhance the safety of HIT treatment through developing institutional DTI treatment protocols, and address other details of HIT care, such as discontinuation of heparin pending laboratory confirmation and documentation of heparin allergy in confirmed HIT. Institutional investment in task force sustainability is important in creating lasting change in healthcare systems [42].

Research to improve HIT care is not limited to QI efforts. For instance, testing for HIT takes time, with HIT ELISA testing generally performed at most once daily [51,52], and ELISA results are often challenging for providers to interpret. In response, rapid tests have been developed to provide faster serological input and hopefully remove the need for extended empiric treatment [53]. Additionally, new diagnostic algorithms and decision support systems have been created and validated [49,54,55]. Incorporation of these tools into practice, along with ongoing QI interventions to bridge the inevitable gaps in recognition and appropriate management, will hopefully lead to better HIT care.

This study has several limitations. While efforts were made to include all relevant literature, it is possible that studies were missed due to limitations of the electronic databases used. We attempted to overcome this by performing a dedicated search for conference abstracts from 2 prominent hematology organizations (the American Society of Hematology and the International Society on Thrombosis and Haemostasis) via review of their websites and associated journals. Further, only studies published in English were included. As this is a scoping review, we did not perform a formal assessment of publication bias or study quality. QI efforts that were unsuccessful may not have been submitted or accepted for publication, thus it is possible that our results do not represent the current state of QI initiatives in the field of HIT. Finally, patient-level demographic information was not available, and thus, our conclusions may not fully account for important sociocultural determinants of health.

In conclusion, this scoping review highlights that the bulk of the published HIT QI research focuses on reducing overdiagnosis and promoting safer DTI therapy. Comparatively less attention has been devoted to efforts to prevent the development of HIT and to promote alternative anticoagulation therapies for suspected and/or confirmed HIT. Interdisciplinary collaboration is key to the effective diagnosis and management of HIT, and the establishment of HIT task forces has proven successful. This review serves as a resource for healthcare systems looking to deliver better HIT care and reduce misuse of related resources and for investigators seeking underresearched topics for improving the diagnosis and management of HIT.

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AUTHOR CONTRIBUTIONS

J.C.C. and M.Y.L. designed the study, analyzed the data, and wrote the manuscript. M.M.M. performed the literature search. M.M.M. and J.E.M. reviewed and edited the manuscript. All authors approved the final version of the manuscript.

RELATIONSHIP DISCLOSURE

J.C.C., M.M.M., and J.E.M. declare no competing financial interests. M.Y.L. reports receiving honoraria for participation on the following advisory boards: Sobi, Takeda, and Alexion.

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SUPPLEMENTARY MATERIAL

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