Reducing the hospital burden of heparin-induced thrombocytopenia:

impact of an avoid-heparin program

Short Title – IMPACT OF AN AVOID-HEPARIN PROGRAM ON HIT

Authors: Kelly E. McGowan,1 Joy Makari,2 Artemis Diamantouros,2 Claudia Bucci,2 Peter Rempel,2 Rita Selby,1,3 and William Geerts1,4

Author Affiliations:
1Departments of Medicine, 2Pharmacy, and 3Clinical Pathology, and 4Centre for Patient Safety, University of Toronto, Toronto, Ontario, Canada

Corresponding Author: William Geerts, MD, Thromboembolism Program, Room D674, Sunnybrook Health Sciences Centre, 2075 Bayview Avenue, Toronto, ON, Canada, M4N 3M5; Phone: (416) 480-4427, Fax: (416) 480-4186, Email: william.geerts@sunnybrook.ca

Abstract word count: 206

Word Count (excluding abstract, references, tables, and figures): 3289

Figures: 3, Tables: 3, References: 36

Supplemental data – Figures: 1, Tables: 6

Key Words: heparin-induced thrombocytopenia, patient safety, quality improvement

Abbreviations: ELISA, enzyme-linked immunosorbent assay; HIT, heparin-induced thrombocytopenia; HITT, HIT with thrombosis; IQR, interquartile range; LMWH, low molecular weight heparin; OD, optical density; PF4, platelet factor 4; RRR, relative risk reduction; SRA, serotonin release assay; UFH, unfractionated heparin
KEY POINTS

- LMWH use is associated with a lower risk of HIT and HITT compared with use of UFH.
- An “Avoid-Heparin Initiative” resulted in a dramatic reduction in the burden of suspected HIT, adjudicated HIT, HITT, and associated costs.

ABSTRACT

Heparin-induced thrombocytopenia (HIT) is a serious complication of heparin, occurring in up to 5% of patients exposed to unfractionated heparin (UFH). We examined the impact of a hospital-wide, avoid-heparin strategy on the incidence of HIT, HIT with thrombosis and HIT-related costs. This “Avoid-Heparin Initiative”, implemented at a tertiary-care hospital in Toronto, Canada since 2006, involved replacing UFH with low molecular weight heparin (LMWH) for prophylactic and therapeutic indications. Consecutive cases with suspected HIT from 2003 through 2012 were reviewed. Rates of suspected HIT, adjudicated HIT, HIT with thrombosis, and HIT-related expenditures were compared in the pre-intervention (2003-2005) and the Avoid-Heparin (2007-2012) phases. The annual rate of suspected HIT decreased 42%, from 85.5 per 10,000 admissions in the pre-intervention phase to 49.0 per 10,000 admissions in the Avoid-Heparin phase (p<0.001). The annual rate of patients with a positive HIT assay decreased 63% from 16.5 to 6.1 per 10,000 admissions (p<0.001); adjudicated HIT decreased 79% from 10.7 to 2.2 per 10,000 admissions (p<0.001); and HIT with thrombosis decreased 91% from 4.6 to 0.4 per 10,000 admissions (p<0.001). Hospital HIT-related expenditures decreased by $266,938 per year in the Avoid-Heparin phase. To our knowledge, this is the first study demonstrating the success and feasibility of a hospital-wide HIT prevention strategy.
INTRODUCTION

Heparin-induced thrombocytopenia (HIT) is a transient, limb- and life-threatening, immune-mediated adverse drug reaction in patients exposed to heparin. HIT is characterised by immunoglobulin G antibodies against platelet factor 4 (PF4)-heparin complexes which trigger a highly prothrombotic state through intravascular platelet aggregation, intense platelet activation and excessive thrombin generation.\(^1\) The diagnosis of HIT is based on a significant fall in the platelet count with or without venous or arterial thrombosis combined with serologic evidence of HIT antibodies in patients exposed to unfractionated heparin (UFH) or low molecular weight heparin (LMWH).\(^2-4\) Treatment of HIT involves discontinuing all forms of heparin and administration of an alternative, non-heparin anticoagulant.\(^4\)

HIT occurs in up to 5% of patients exposed to UFH, one of the drugs most commonly prescribed to hospital patients.\(^5-7\) The recognition and evaluation of suspected HIT is often delayed.\(^4,6,8,9\) Even with prompt cessation of heparin and implementation of a HIT-safe anticoagulant, thromboembolic complications occur in 20-50% of patients, and death or limb amputation occurs in approximately 5-10%.\(^4,8,10-14\) In addition to the significant disease burden, HIT is associated with substantial resource use. An economic analysis study from our center reported that the direct costs to the hospital for HIT were $456,787 over a one-year period.\(^15\)

Although improved surveillance and management may reduce the burden of HIT, comprehensive initiatives to prevent HIT are likely to be more effective in decreasing the morbidity, mortality and costs associated with HIT. It is well-established that LMWH is associated with a five to 10-fold lower risk of HIT than UFH.\(^16-21\) Furthermore, thrombosis is less likely to occur when HIT is triggered by LMWH than by UFH.\(^21\) Therefore, reducing patient exposure to UFH and substitution of UFH with LMWH may improve patient safety.
related to HIT. The aim of this quality improvement study was to evaluate the impact of an Avoid-Heparin intervention on the incidence of HIT, its clinical consequences and associated costs over a 10-year period.

METHODS

Study Setting

In 2005, a multidisciplinary committee was created to develop strategies to reduce the burden of HIT at Sunnybrook Health Sciences Centre in Toronto, Canada. Sunnybrook is a tertiary-care, university-affiliated hospital with over 450 adult acute care beds, a large Cardiac Surgery program and a Thromboembolism service that manages all cases of established HIT. The intervention selected was an institution-wide, Avoid-Heparin program that was implemented during 2006. The components of this program included:

- Systematic replacement of most intravenous and subcutaneous UFH with subcutaneous LMWH in prophylactic or therapeutic doses. The remaining uses of UFH were hemodialysis, intraoperative for cardiovascular surgery and some patients with acute coronary syndrome
- Replacement of heparinized saline in arterial and central venous lines with saline flushes
- Modification of order sets to exclude UFH options
- Removal of UFH stores from most nursing units

Most care providers were not aware that heparin was being replaced by LMWH as part of an Avoid-Heparin initiative and none were aware that this practice change was being studied. There were also no efforts to educate staff about HIT nor were there any changes in the approach to its diagnosis.
Consecutive inpatients with a clinical suspicion of HIT who underwent enzyme-linked immunosorbent assay (ELISA) testing for PF4-heparin antibodies from January 1, 2003 to December 31, 2012, were identified through the Special Coagulation Laboratory database. A confirmatory serotonin release assay (SRA), which was performed at McMaster University, was ordered at the discretion of the patient’s attending or consultant service. Electronic and paper medical records were reviewed for demographic and clinical data in all patients with a positive HIT ELISA. The incidence and complications of HIT, and associated costs were compared in the pre-intervention phase (2003-2005) and the Avoid-Heparin phase (2007-2012). Since the Avoid-Heparin intervention was implemented over the year 2006, cases during this year were excluded from all comparisons. This study was approved by the research ethics board of Sunnybrook Health Sciences Centre.

Case Definitions

Explicit definitions of the various study groups were established a priori (Table S1).

**Suspected HIT** was defined as a clinical suspicion of HIT with a HIT ELISA performed. A **positive HIT ELISA** was defined as a HIT ELISA optical density (OD) $\geq 0.4$. Patients with a positive HIT ELISA who were excluded were those who underwent follow-up testing for a previously positive HIT assay, those whose heparin exposure occurred exclusively as an outpatient or at another hospital, and those who had no documented heparin exposure despite an extensive search. The following data were abstracted: demographic information, admitting service, duration and type of heparin exposures, date of suspected HIT, presence of HIT-related complications, and length of hospital stay.
All patients with a positive HIT ELISA were adjudicated by the investigators using information available in the medical record. **Adjudicated HIT** was defined as suspected HIT with:

1. positive SRA or
2. positive HIT ELISA, SRA not done, and diagnosed and treated as HIT by the Thromboembolism service at the time of the suspected HIT and confirmed at the independent adjudication review using standardized criteria outlined in Table S1.

**HIT negative** was defined as suspected HIT with:

1. negative HIT ELISA,
2. negative SRA or
3. positive HIT ELISA, SRA not done, but not diagnosed with or treated as HIT by the Thromboembolism service at the time of suspected HIT and also classified as HIT negative during adjudication review.

Cases were labeled **HIT uncertain** if the HIT ELISA was positive but the diagnosis could not be confirmed or ruled out at adjudication. In the small number of cases with a positive HIT ELISA that were not seen by the Thromboembolism service or when the adjudication process yielded a different HIT status for a patient than that made at the time of clinical suspicion, the case was re-reviewed and consensus among investigators was used based on the diagnostic criteria in Table S1. **HIT with thrombosis (HITT)** was defined as HIT positive with proven venous and/or arterial thrombosis less than seven days before or up to 30 days after the date of suspected HIT. For thrombotic events that occurred less than seven days before the date of suspected HIT, each case was carefully reviewed to determine the probable sequence of events. Patients with thromboembolism prior to heparin exposure who subsequently developed HIT were not labelled as HITT. **Major bleeding** was defined as overt bleeding in a
patient receiving a HIT-safe anticoagulant and meeting at least one of the following criteria: requiring two or more units of packed red blood cells, prolonging hospital admission, fatal or life-threatening bleeding at a critical site such as intracranial or retroperitoneal, or bleeding requiring an intervention such as endoscopic or endovascular treatment or surgery.\textsuperscript{22}

\textbf{Anti-PF4-Heparin HIT ELISA}

Throughout the study period, the Special Coagulation Laboratory detected polyspecific PF4-heparin antibodies using the Genetic Testing Institute PF4 ELISA (GTI Diagnostics, Waukesha, WI).\textsuperscript{23} An OD value of $\geq0.4$ was used as the threshold for a positive test as suggested by the manufacturer and locally validated by the laboratory.

\textbf{Outcomes}

The rates of suspected HIT, positive HIT ELISA, adjudicated HIT, and HITT in the pre-intervention and the Avoid-Heparin phases were compared. Annual rates per 10,000 admissions were determined using admission data from the Health Data Resources Department. The additional costs for suspected HIT, adjudicated HIT and HITT were based on a published cost-analysis done at our institution and the observed events in the present study.\textsuperscript{15} HIT-related costs in the pre-intervention phase were compared to those in the Avoid-Heparin phase.

\textbf{Statistical Analyses}

Statistical analyses were performed with SPSS 16.0 (SPSS, Chicago, IL). Continuous variables were summarized as medians with interquartile ranges (IQR), because of non-normal distributions. The Mann-Whitney $U$ test was used to detect differences in continuous
variables and the Pearson chi-square test, or Fisher’s exact test, were used to detect differences between categorical variables. All tests were two sided and \( P<0.05 \) was accepted as statistically significant.

RESULTS

Suspected HIT, Positive HIT ELISA, Adjudicated HIT, and HITT

From 2003 to 2012, there were 1,118 cases of suspected HIT. Among these, 175 patients (16%) had a positive HIT ELISA. An additional 16 patients with a positive HIT ELISA were excluded because they received heparin exclusively as an outpatient or at another institution (10), there was no documented heparin exposure (2), the HIT assay was ordered for a clinical trial (2) or was performed in error (1) or for previous HIT (1). Among the 175 patients with a positive HIT ELISA, 89 (51%) were adjudicated HIT positive, 84 (48%) HIT negative and, in two cases, the HIT status remained uncertain after adjudication. An SRA was performed in 40% (70/175) of patients with a positive HIT ELISA (Table S2). Among the 84 patients adjudicated as HIT negative, 46 (55%) had a negative SRA, 37 (44%) did not have a SRA performed, one had a SRA reported as “equivocal”, and none had a positive SRA. Among the 37 patients adjudicated HIT negative who did not have a SRA performed, only 5 had a HIT ELISA OD >1.0. A HIT ELISA OD \( \geq 1.0 \) was observed in 75 (84%) patients with adjudicated HIT, compared to 16 (19%) patients with a positive HIT ELISA who were adjudicated HIT negative \( (p<0.001) \). Over the 10-year period, 31 (35%) patients with adjudicated HIT developed HITT. In ten of these patients, the thromboembolic event occurred 1-5 days before the diagnosis of HIT and four were diagnosed with thromboembolism and HIT on the same day.
Comparison of the Pre- and Post-Intervention Periods

There were 424 and 576 patients with suspected HIT in the pre-intervention and Avoid-Heparin phases, respectively. The annual incidence of suspected HIT cases per 10,000 admissions decreased from 85.5 in the pre-intervention phase to 49.0 in the Avoid-Heparin phase (relative risk reduction [RRR]=41.7%, \(p<0.001\), Figure 1). The annual incidence of patients with a positive HIT ELISA decreased from 16.5 to 6.1 per 10,000 admissions in the pre-intervention and Avoid-Heparin phase, respectively (RRR=62.9%, \(p<0.001\), Figure 1) and corresponding rates of patients with a HIT ELISA >1.0 decreased from 10.1 to 2.5 per 10,000 admissions (RRR=75.1%, \(p<0.001\)). The annual incidence of adjudicated HIT cases decreased from 10.7 to 2.2 per 10,000 admissions in the pre-intervention and Avoid-Heparin phase (RRR=79.0%, \(p<0.001\)), and HITT decreased from 4.6 to 0.4 per 10,000 admissions (RRR=90.7%, \(p<0.001\), Figure 1). The annual rates of HIT and HITT over the study period are shown in Figure 2.

Demographic and clinical characteristics of HIT positive patients in the pre-intervention phase (n=53) and the Avoid-Heparin phase (n=26) were similar (Table 1). Approximately 60% of patients with HIT in both phases were admitted under the cardiovascular surgery service. The durations of UFH/LMWH exposure and median lengths of hospital stay were similar between the groups. The median HIT ELISA OD among patients with HIT was significantly higher in the Avoid-Heparin phase (2.79, IQR 1.76-2.89) compared with the pre-intervention phase (2.07, IQR 1.21-2.40, \(p=0.001\)). While the overall use of LMWH increased 4-fold (based on doses purchased) over the study period, the annual rate of HIT associated with LMWH remained constant at 0.9 cases per 10,000 admissions in the pre-intervention and Avoid-Heparin phases (\(p=0.78\), Figure 3). There were no significant differences in patient age, gender, duration of UFH/LMWH exposure, or length of hospital stay among patients with
HIT exposed to UFH compared with LMWH (Table S3). HIT was reduced 77% in cardiovascular surgery, 77% in other surgery, 75% in cardiology patients, and 62% in medical patients (Figure S1).

Comparison of HIT with and without Thrombosis

Patients with HIT in the pre-intervention phase more frequently developed HITT (43%) than patients with HIT in the Avoid-Heparin phase (19%, \( p=0.035 \), Table 2). The most frequently observed HIT complication in both phases was venous thromboembolism. The median length of stay from date of suspected HIT to discharge among patients with HITT was 22 days (IQR 13-44) compared to 8 days (IQR 6-14) for patients with HIT without thrombosis (\( p<0.001 \)). Over the entire study period, the HIT ELISA OD values among patients with HIT without thrombosis and those with HITT were similar (median OD 1.96; IQR 1.24-2.74 and 2.34; IQR 1.86-2.70, respectively, \( p=0.157 \)). Patient age, gender, admitting service, exposure to LMWH only, duration of heparin exposure, and alternative anticoagulant use were similar among patients with HITT and those with HIT without thrombosis (Table S4).

HIT-Related Treatment & Costs

The mean number of suspected HIT cases per year decreased from 141.3 in the pre-intervention phase to 96.0 in the Avoid-Heparin phase (Table S5). The mean number of patients per year with a positive HIT ELISA, adjudicated HIT and HITT per year decreased from 27.3 to 11.8, 17.7 to 4.3, and 7.7 to 0.8, respectively, in the pre-intervention and Avoid-Heparin phases. HIT was treated with lepirudin and danaparoid more frequently in the pre-intervention phase while fondaparinux and argatroban were used more frequently in the Avoid-Heparin phase (Table S6). Based on a published study from our institution\(^{15}\), the
average estimated costs of HIT care per year were reduced by $266,938, from $322,321 in the pre-intervention phase to $55,383 in the Avoid-Heparin phase, using 2007 Canadian dollars (Table 3).

DISCUSSION
Following the implementation of a hospital-wide quality improvement program based on replacing UFH with LMWH, we observed a dramatic reduction in the burden of HIT with a 42% decrease in suspected HIT, 63% decrease in patients with positive HIT ELISA, 79% decrease in adjudicated HIT, 91% decrease in HITT, and 83% decrease in HIT-related costs of care. Although the greatest overall impact of the program was in cardiac surgery, the HIT burden was also reduced in other surgical and medical patients. The heparin avoidance strategy that we utilized was not complex or costly, and would be feasible in other centers.

A lower risk of HIT and its thrombotic complications among patients exposed to LMWH compared to UFH has been previously demonstrated.7,16-21 LMWH is thought to induce a less robust antibody response when complexed to PF4 than observed with UFH-PF4 due to stoichiometric differences of heparin-PF4 complexes.24 Despite the four-fold increase in LMWH use over the study period, the incidence of HIT in patients who received LMWH was low and remained stable over the 10-year study period. Others have also demonstrated stable rates of HIT despite substantial increases in LMWH use.7,25 Our results expand on observations from studies with limited target groups and focused interventions. Replacement of UFH with LMWH in orthopedic surgery has been shown to reduce both venous thromboembolism and HIT.26

The literature has emphasized early recognition and treatment of HIT, while its prevention has been largely overlooked.27 Guidelines recommend platelet count monitoring
for patients receiving heparin who have a HIT risk greater than 1%. 4 However, adherence to platelet count monitoring, testing for HIT antibodies if thrombocytopenia develops and switching to HIT-safe anticoagulation when HIT is suspected is challenging, resource intensive and may not reduce the adverse consequences of HIT. 6,9,28-30 Previous studies have demonstrated that over half of the thrombotic events in HIT occur following the cessation of heparin without additional treatment of HIT. 8,11 In our study, we observed that more than half of the HITT cases [17/31] had the thromboembolic event diagnosed after the diagnosis of HIT and while on HIT-safe anticoagulation, emphasising not only the need for early recognition and treatment, but also the need to prevent HIT. We observed that patients with HIT in the Avoid-Heparin phase were two times less likely to develop HITT. A previous study from our center demonstrated that the incremental hospital cost of suspected and confirmed cases of HIT was $456,787 over a one-year period and 90% of these costs were attributed to HITT. 15 Together, these findings suggest that a hospital-wide, Avoid-Heparin program leads to a substantial reduction in the morbidity, mortality and institutional costs associated with HIT.

Consistent with published literature, the positive predictive value of the HIT assay was 51% (89/175) over the entire study period. 31,32 Among the 84 patients with a HIT ELISA OD between 0.4 and 1.0, only 17% were found to have HIT. False positive HIT assays were found with OD values as high as 2.4, emphasizing that HIT cannot be diagnosed by laboratory evidence alone. 4,33 The median HIT ELISA OD in patients with HIT was higher in the Avoid-Heparin phase than the pre-intervention phase (2.79 vs 2.07, respectively, Table 1). Because the likelihood of true HIT increases with increasing OD, this could suggest that there were more false-positive diagnoses in the pre-intervention phase. Recently, Chan et al 34 reported that the HIT ELISA OD cut-off could be increased from 0.4 to 1.00 to improve the positive predictive value without losing sensitivity.
This study has limitations that warrant consideration. It was conducted at a single tertiary care hospital whose HIT-related practices may differ from other centers. Since there is no reference standard for the diagnosis of HIT and only 40% of patients with a positive HIT ELISA had an SRA, we cannot determine the accuracy of our case allocation in all patients. However, the observations in this study were based on a review of all cases with suspected HIT over a 10-year period and therefore reflect routine clinical practice. We attempted to minimise potential bias in adjudication of HIT by establishing case definitions \textit{a priori}. In only 5 cases did the final case allocation after adjudication differ from that made by the clinical team at the time of suspected HIT. Although this study’s findings are based on a prospective quality improvement project, patient data were abstracted and cases were adjudicated retrospectively. This could have led to possible bias in case definition by the investigators. We were unable to calculate the 4Ts score for patients with suspected HIT retrospectively.\textsuperscript{35,36} However, patient characteristics in the pre-intervention and Avoid-Heparin phases were similar, and we were unable to identify any other factors that could have accounted for the dramatic reductions in suspected HIT, adjudicated HIT and HITT during the study period. The long duration of observation showing a sudden and sustained reduction in HIT after implementation of the Avoid-Heparin strategy was designed to demonstrate that this was not a random observation. Finally, we were unable to determine hospital-wide, patient-level data on exposures to UFH and LMWH; however, LMWH use increased more than four-fold based on overall changes in drug utilization over the study period. Clearly, the cost reductions we observed are specific to our center and will differ in other centers depending on overall HIT burden and the local costs of investigating and treating HIT.

Our findings cannot be explained by an overall reduction in the number of admissions or length of stay over the study period. In fact, total patient admissions increased 21% while the
mean length of stay decreased only 9% over the study period. The decision to test each patient was at the discretion of the patient’s clinical service and was not influenced by the investigators or the Thromboembolism team. Moreover, the greater reduction in cases of HIT (79%) and HITT (91%) than in suspected HIT (42%) suggests a decrease in the actual disease burden rather than a biased increase in diagnostic threshold (Figure 1). The temporal pattern of this study’s findings show that the reduction in HIT was not gradual but occurred in 2006 and was maintained beyond the intervention year (Figure 2), suggesting it is unlikely that secular trends in decreased UFH utilisation could explain these findings. The study’s observations can also not be accounted for by use of direct oral anticoagulants since rivaroxaban was approved only for hip and knee arthroplasty thromboprophylaxis in 2009 and dabigatran was approved for atrial fibrillation in 2011.

Conclusions

The introduction of a hospital-wide, Avoid-Heparin program led to a dramatic decrease in the burden of suspected HIT, diagnosed HIT and HITT, as well as in the costs of HIT care. To our knowledge, this is the first study demonstrating the success of a HIT prevention strategy. Our findings suggest that a highly feasible heparin avoidance intervention can improve patient safety and reduce hospital costs.
Authorship

Contribution: W.G. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis; W.G., K.E.McG., J.M., C.B., and A.D. contributed equally to this work; W.G., C.B., A.D., and R.S. developed the study concept and design; W.G., K.E.McG., J.M., A.D., C.B., and P.R. acquired the data; W.G., K.E.McG., J.M., A.D., C.B., and R. S. analysed and interpreted the data; W.G., K.E.McG., J.M., A.D., and C.B. drafted the manuscript; all authors critically revised the manuscript; and W.G., J.M., A.D., C.B., and R.S. provided administrative, technical and material support.

Conflict of Interest Disclosure: K.E.McG. has no conflicts of interest to report. J.M. reports holding an institutional fellowship that received financial support from Bayer Healthcare. A.D. reports receiving salary support from a hospital fund that had contributions from the Canadian Patient Safety Institute and Sanofi, consulting for Leo Pharma and Sanofi, serving on an advisory board for Sanofi and receiving payment for educational activities from Bayer Healthcare, Leo Pharma, Pfizer, and Sanofi. C.B. reports receiving payment for educational activities from Astra Zeneca and Bayer Healthcare, consulting for Astra Zeneca, Bayer Healthcare, BMS, and Pfizer and serving on an advisory board for Astra Zeneca, BMS and Pfizer. P.R. received a studentship that received financial support from an unrestricted educational grant from Bayer Healthcare. R.S. reports receiving grant support from Boehringer-Ingelheim, consulting for Instrumentation Laboratories and receiving payment for educational activities from BMS/Pfizer. W.G. reports receiving partial salary support from a hospital fund that had contributions from Sanofi, consulting for Bayer Healthcare, Boehringer-Ingelheim, Leo Pharma, Pfizer, Jansen, Bristol-Myers Squibb and Sanofi, and receiving payment for educational activities from Bayer Healthcare, Boehringer-Ingelheim, Leo Pharma, Pfizer, GlaxoSmithKline and Sanofi. No other disclosures were reported.
Funding/Support: No external funding was used to support this study.
REFERENCES


20


McGOWAN et al. IMPACT OF AN AVOID-HEPARIN PROGRAM ON HIT


Figure 1. Annual incidence of suspected HIT, patients with a positive HIT assay, adjudicated HIT, and HITT per 10,000 admissions, 2003-2005 and 2007-2012.

*p<0.001 for each comparison

Abbreviations: HIT, heparin-induced thrombocytopenia; HITT, heparin-induced thrombocytopenia with thrombosis
Figure 2. Annual incidence of adjudicated HIT and HITT, 2003-2012.

Abbreviations: HIT, heparin-induced thrombocytopenia; HITT, heparin-induced thrombocytopenia with thrombosis
Figure 3. Incidence of UFH- and LMWH-associated HIT cases per 10,000 admissions per year, 2003-2012.

$p<0.001$ for UFH-associated HIT time trends and $p=0.78$ for LMWH-associated HIT time trends.

Abbreviations: HIT, heparin-induced thrombocytopenia; LMWH, low molecular weight heparin; UFH, unfractionated heparin.
Table 1. Characteristics of patients with HIT in the pre-intervention and avoid-heparin phases.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>68 (60-74)</td>
<td>72 (61-78)</td>
<td>0.280</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>30 (57)</td>
<td>10 (38)</td>
<td>0.130</td>
</tr>
<tr>
<td>Primary admitting service, n (%)</td>
<td></td>
<td></td>
<td>0.950</td>
</tr>
<tr>
<td>Cardiovascular surgery</td>
<td>32 (60)</td>
<td>15 (58)</td>
<td></td>
</tr>
<tr>
<td>Other surgical service</td>
<td>13 (24)</td>
<td>6 (23)</td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>4 (8)</td>
<td>2 (8)</td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>4 (8)</td>
<td>3 (11)</td>
<td></td>
</tr>
<tr>
<td>Duration of UFH or LMWH exposure before the diagnosis of HIT, median (IQR), days</td>
<td>10 (8-12)</td>
<td>11 (8-13)</td>
<td>0.526</td>
</tr>
<tr>
<td>HIT ELISA OD, median (IQR)</td>
<td>2.07 (1.21-2.40)</td>
<td>2.79 (1.76-2.89)</td>
<td>0.001</td>
</tr>
<tr>
<td>HIT ELISA OD, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1.0</td>
<td>11</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>1.0-2.0</td>
<td>15</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>27</td>
<td>18</td>
<td>0.123</td>
</tr>
<tr>
<td>Total length of stay*, days median (IQR)</td>
<td>24 (17-42)</td>
<td>21 (14-28)</td>
<td>0.224</td>
</tr>
<tr>
<td>Length of stay after HIT suspected**, days, median (IQR)</td>
<td>14 (7-26)</td>
<td>9 (6-20)</td>
<td>0.198</td>
</tr>
</tbody>
</table>

* Date of admission to date of discharge

** Date HIT first suspected to date of discharge

Abbreviations: HIT, heparin-induced thrombocytopenia; IQR, interquartile range; OD, optical density
Table 2. HITT and other complications associated with HIT in pre-intervention and avoid-heparin phases.

<table>
<thead>
<tr>
<th>Specific complications*</th>
<th>Pre-intervention n=53</th>
<th>Avoid-heparin n=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>HITT**, n (%)</td>
<td>23 (43.4%)</td>
<td>5 (19.2%)</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>DVT or PE</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Adrenal vein thrombosis</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Arterial thromboembolism</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Leg ischemia</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Leg ischemia with amputation</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Acute bowel ischemia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Transient global amnesia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Death related to HIT</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Major bleeding on treatment for HITT</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*4 patients in the pre-intervention phase and no patients in the Avoid-Heparin phase had more than one thromboembolic complication

**p=0.035

Abbreviations: DVT, deep vein thrombosis; HITT, heparin-induced thrombocytopenia with thrombosis; PE, pulmonary embolism
**Table 3. Estimated costs* associated with HIT care in the pre-intervention and avoid-heparin phases.**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases/year</td>
<td>Cost/year</td>
<td>Cases/year</td>
</tr>
<tr>
<td>HIT negative</td>
<td>$119</td>
<td>123.7</td>
<td>$14,716</td>
</tr>
<tr>
<td>HIT without thrombosis</td>
<td>$4,575</td>
<td>10.0</td>
<td>$45,750</td>
</tr>
<tr>
<td>HITT</td>
<td>$34,155</td>
<td>7.7</td>
<td>$261,855</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td><strong>$322,321</strong></td>
</tr>
</tbody>
</table>

*2007 Canadian dollars

#From a cost-of-illness study performed at Sunnybrook Health Sciences Centre

Abbreviations: HIT, heparin-induced thrombocytopenia; HITT, heparin-induced thrombocytopenia with thrombosis
Figure 1

For personal use only.

From October 24, 2017, by guest

www.bloodjournal.org
Figure 2

Avoid-Heparin Program Implementation – 2006

Patients/10,000 Admissions

Year

• HITT  ▪ HIT

Figure 3

Avoid Heparin Program Implementation – 2006

Cases/10,000 Admissions

- HIT with Exposure to UFH
- HIT with Exposure to Both UFH & LMWH
- HIT with Exposure to LMWH

Reducing the hospital burden of heparin-induced thrombocytopenia: impact of an avoid-heparin program

Kelly E. McGowan, Joy Makari, Artemis Diamantouros, Claudia Bucci, Peter Rempel, Rita Selby and William Geerts