**Study Protocol**

**Sequential compression alone for the prevention of deep venous thrombosis in operating theatres (SoCS-FREE-OT)**

**STUDY INVESTIGATOR(S)**

## Joint Chief Investigator

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1. **INTRODUCTION**

Venous thromboembolism (VTE) is a condition whereby a blood clot forms inappropriately in the veins. This clot may dislodge from its point of origin and be carried to the lung vasculature, which may be a fatal event. Thus, VTE incorporates both deep vein thrombosis (DVT) and pulmonary embolism (PE). It has been estimated that the Australian annual incidence of VTE is 0.83 per 1000 individuals and is associated with significant morbidity and health related economic costs1. In 2008, the estimated cost to the Australian economy was $1.7 billion dollars1. Venous thromboembolism may be provoked by major surgery, which is defined as surgery of at least 45 minutes duration. The risk of surgically provoked VTE may be mitigated by the combined use of both chemical and mechanical thromboprophylaxis, as recommended by the 2012 American College of Chest Physicians (ACCP) clinical practice guidelines and more recently, the 2019 American Society of Hematology (ASH) clinical practice guidelines2, 3. Despite this, there is no clear recommendation as to the timing of chemical thromboprophylaxis or the type of mechanical thromboprophylaxis that should be used.

The exact role of mechanical VTE prophylaxis is less well researched. The two common modalities used are graduated compression stockings (GCSs) and sequential calf compression devices (SCCDs). GCSs have commonly been used on patients in the ward setting whereas SCCDs require a pump and are generally only available in the operating theatre and recovery. Recent evidence suggests that the addition of GCSs to chemical thromboprophylaxis adds no benefit to VTE prevention, and may contribute to harm with pressure ulcers and a potential falls risk3, 4. There is also very weak evidence comparing both modalities, with one study demonstrating an advantage with SCCDs (a VTE rate of 2.5% with SCCDs vs 5.9% with GCSs)5. There is no evidence supporting combined use, although this is a common practice in the operating theatre.

We wish to perform a point prevalence study of all laparoscopic cholecystectomies (elective and emergency) with a standardized mechanical prophylaxis protocol, to determine if we can maintain a low rate of VTE on SCCDs alone compared with the historical cohort of patients managed with combined SCCDs and GCSs, whilst maintaining safety including the risk of bleeding.

1. **BACKGROUND**

Venous thromboembolism that has been provoked by major surgery is a modifiable risk factor that may be dependent upon the timing and type of chemical thromboprophylaxis, in addition to the type of mechanical thromboprophylaxis that is simultaneously used. Unfortunately, no gold standard exists, therefore it is impossible to compare the incidence of VTE not only between differing types of surgery, but even within the same surgical procedure.

A retrospective study, performed at many of the hospitals involved in this study, by Liu *et al*., of 1744 elective laparoscopic cholecystectomies revealed that the timing of chemical prophylaxis varied from early (either pre-operatively or intra-operatively), postoperatively, or in some cases was not given at all6. Mechanical thromboprophylaxis consisted of either a combination GCSs, SCCDs, or either GCSs or SCCDs alone. A combination of GCSs and SCCDs were used for 67.4% of the patients, GCSs only were used for 24.5% of patients, whilst SCCDs only were used for 3.8% of patients. The incidence of VTE was determined to be 0.3%, which compares with the overall annual surgical incidence of VTE at the primary investigative site for this study, Northern Health (NH), which has varied between 0.2 – 0.4% over the last 5 years (internal data).

Although many surgeons believe that early administration of chemical thromboprophylaxis reduces the incidence of VTE, this was not borne out in the study by Liu *et al*.6. Instead, harm was seen to be associated with this practice, as the incidence of surgical bleeding was determined to be 2.4% and in 50% of these patients, bleeding was determined to be a major event, requiring surgical control of the bleeding (11.9%), blood transfusion (21.4%), or a reduction in haemoglobin from baseline of > 20 g/L. There was one bleeding related mortality. Thus, intra-operative mechanical prophylaxis followed by post-operative chemical prophylaxis appears to offer both the best in VTE prevention and minimisation of complications. However, there is no consensus upon the ideal method or use of mechanical prophylaxis.

As shown in the recent Liu *et al.* study, the use of combined GCSs and SCCDs as mechanical prophylaxis is common6, however, there is no strong clinical evidence in the literature that the combined use during the surgical procedure offers any greater protection in terms of thrombo-prophylaxis than protection that is offered by the use of SCCDs alone. It is has been recognised that SCCDs are superior to the use of GCSs as a means of providing mechanical thromboprophylaxis, as is borne out in the 2012 ACCCP guidelines and confirmed in the 2019 ASH clinical practice guidelines2, 3. In the GAPS study, which was a non-inferior randomised controlled trial involving 1,858 surgical participants, the use of low molecular weight heparin (LMWH) alone was shown to be non-inferior in terms of the incidence of VTE when compared to the combined use of LMWH with GCSs7. This suggests that GCSs add nothing if chemical prophylaxis is used.

There is extensive data in the literature that the use of GCSs is associated with harm. In one study of 2,518 participants which compared GCSs to no prophylaxis for VTE prevention in surgical patients, the odds ratio (OR) for harm associated with the use of GCSs was 4.18 (2.4-7.27)3. Harm was defined as skin breaks, blisters, ulcers and necrosis. This was confirmed in the CLOTS study with a 5% vs 1% increase in ulceration and tissue necrosis with GCSs4. At NH, the primary investigative site, the incidence of Riskman reports associated with the use of GCSs on the wards, which included falls, varied from 15% - 24% for the years 2015 – June 2020 (internal data). Additionally, the cost of GCSs is quite significant. The annual cost of the purchase and application of GCSs for surgical patients has been estimated at £63.1 million in England alone7.

We wish to determine if a standardised protocol with respect to the type of mechanical thromboprophylaxis is effective with respect to the incidence of VTE, using a standardised surgical procedure (laparoscopic cholecystectomy). If this demonstrates no difference when compared with data, including the recent Liu et al. study, this will be used to justify a surgery wide multicentre study (with appropriate grant funding).

1. **AIM(S) OF STUDY**

This study aims to determine if a standardized approach to the intra-operative use of SCCDs only will result in a non-inferior incidence of 30 day symptomatic VTE in patients undergoing either elective or emergency laparoscopic cholecystectomies compared to a reference published study.

1. **OBJECTIVES**

There are 2 main objectives of this prospective point prevalence study

1. To determine that the structured approach of VTE prophylaxis using SCCDs alone is non-inferior with respect to the incidence of symptomatic VTE by day 30 post-operatively when compared to the historical control of the Liu *et* *al*. study amongst others.
2. To determine that the safety of the structured approach of VTE prophylaxis results in a reduction in the incidence of surgical bleeding and GCSs related complications.
3. **HYPOTHESIS**

**5a. Primary Hypothesis**

H0: The incidence of symptomatic VTE at day 30 post-operatively is more than the comparison figure of 0.30%. (An estimated 95% CI of the incidence of VTE will indicate a non-inferior comparison to a threshold of 0.45%)

HA: The incidence of symptomatic VTE at day 30 post-operatively is less than the estimated 95% CI of 0.45%.

**5b. Secondary Hypotheses**

HO: The incidence of surgical bleeding is not associated with the exclusive use of SCCDs intra-operatively

HA: The incidence of surgical bleeding is associated with the exclusive use of SCCDs intra-operatively

1. **STUDY DESIGN**

This is a prospective point prevalence, surgical comparative effectiveness study of patients undergoing either an emergency or elective laparoscopic cholecystectomy. The incidence of symptomatic VTE at day 30 post-surgical procedure will be compared to a previously obtained incidence of VTE at 0.3%, which was obtained for elective laparoscopic cholecystectomies only, when there was no standardization of timing of chemical thrombo-prophylaxis or the type of mechanical thromboprophlyaxis used.

Due to the low incidence of VTE, we are unable to perform a randomized controlled trial as the number of patients that are required to power this study to determine a 20% reduction in the incidence of symptomatic VTE from 0.3 to 0.24, would require 234,828 participants.

1. **STUDY SETTING/LOCATION**

This is designed as a multi-centre study of surgical patients undergoing a laparoscopic cholecystectomy (either as an elective or an emergency procedure) across eleven hospital campuses, which includes the Victorian hospitals Northern Health, Western Health (Sunshine Hospital and Footscray Hospital), Royal Melbourne Hospital, Monash Health, and Barwon Health in Geelong; Nepean Hospital and Hunter New England Health in New South Wales; and Flinders Medical Centre and Royal Adelaide Hospital in South Australia. The Northern Hospital will be the lead hospital for this study. These hospitals have been selected as they have either already adopted the study protocol or are in the process of either adopting or trialing the study protocol irrespective of this research study.

This study will utilise the WestSURG collaborative, a surgical registrar-run research collaborative based at Western Health, to maintain contact with the multiple sites and continue recruitment of registrars who will act as data collectors for the study.

1. **STUDY POPULATION**

The study population includes all patients undergoing either an emergency or an elective laparoscopic cholecystectomy at one of the hospital campuses listed above. The total number of surgical participants is 5,190 and there is no minimum requirement from each of the various hospital campuses, nor is there any stratification of any of the various hospital campuses.

1. **ELIGIBILITY CRITERIA**

**9a. Inclusion criteria**

All patients who undergo a laparoscopic cholecystectomy either as an emergency or elective procedure at each of the hospital campuses are eligible for inclusion in this study. There is no gold standard approach for chemical and mechanical thromboprophylaxis and the proposed intervention is one of the accepted surgical techniques for the prevention of VTE. All of the involved hospitals have either already adopted SCCDs alone, or are in the process of either permanently adopting or performing an internal trial using this study’s protocols. It is a requirement of this study that all involved hospitals have adopted this protocol prior to the commencement of data collection, in order that this study is a true cohort study.

**9b. Exclusion criteria**

Participants will be excluded for the following criteria:

* If they are fitted with GCSs exclusively, combined GCSs and SCCDs, or no mechanical prophylaxis is used intra-operatively.
* A planned or unplanned conversion to open cholecystectomy.
* Under the age of 18 years

1. **STUDY OUTCOMES**

**10a. Primary Outcome**

The primary outcome is the incidence of symptomatic VTE by day 30 post-operatively, which is proven by any imaging technique.

**10b. Secondary Outcome(s)**

The secondary outcome is the incidence of surgical bleeding, in particular, bleeding that is defined as a major bleeding event as defined by the need for radiological or surgical control, a blood transfusion or a drop in the baseline haemoglobin of > 20 g/L.

1. **STUDY PROCEDURES**

**11a. Recruitment of participants**

All patients who require a laparoscopic cholecystectomy, either as an emergency or elective procedure are eligible for the study. It is anticipated that by combining the resources of multiple hospital campuses that we will be able to recruit 5,190 surgical participants within 18 months from the commencement of the study.

**11b. Study procedure**

It is a requirement of the study that any participating hospital has already adopted or is trialing the protocol of routine SCCDs alone for laparoscopic cholecystectomy prior to data collection, and that this decision is made on clinical grounds and not for the purposes of research. All patients requiring either an elective or an emergency laparoscopic cholecystectomy will be recruited into this study.

For those participants who are booked for an elective laparoscopic cholecystectomy, they will be admitted to the hospital on the day of their surgery. A sequential calf compressor device will be fitted as per manufacturer’s specifications, immediately prior to the commencement of surgery and will be used for the duration of surgery. At the completion of surgery and immediately before the patient is transferred to the post anaesthetic care unit (PACU), the SCCDs will be removed. Chemical thromboprophylaxis will be initiated by the subcutaneous injection of 40 mg of enoxaparin, 5,000 IU of dalteparin or 5,000 IU of heparin at any time at the discretion of the treating team. Subsequent does of enoxaparin and dalteparin (if required) are given 24 hours later following the initial dose. The dosing of enoxaparin is to be based on BMI and renal function only. For those patients whose BMI is < 40, use 40 mg once daily (OD), for those patients whose BMI is ≥ 40, use 40 mg twice daily, with the second dose being given 12 hours after the initial dose. For those patients with chronic renal disease, with a creatinine clearance <3o mL/minute, a renal adjusted dose will be given. For those patients receiving heparin, the second dose will be given 12 hours post the initial dose. No participant undergoing an elective operation is to have GCSs fitted either pre- or post-operatively. Participants may be discharged home on the day of their surgery, or after an overnight hospital stay, at the discretion of their treating surgeon. During the operation, positioning of the patient and the intra-abdominal insufflation pressure will be at the discretion of the treating surgeon.

For those participants who are undergoing an emergency laparoscopic cholecystectomy, access to theatre may differ across the various hospital campuses. This will be controlled for by the acquisition of data pertaining to the length of time of admission to the hospital, relative to the timing of their actual surgery. For these patients, it is anticipated that they will have received chemical thromboprophylaxis prior to their operation. This data will be collected and analysed separately as a sub-analysis. There will be no restrictions on the type and timing of chemical thromboprophylaxis used. These patients are allowed to have GCSs fitted pre-operatively. However, these GCSs will be removed when the patient presents to the operating theatre and the use of GCSs post-operatively is contraindicated. Demographic and operative data will be collected at the end of the operation by the surgical fellow/registrar/resident who has been recruited to the study and trained under the auspices of the WestSURG collaborative. This process will also be supervised by the PI from each institution.

All participants may be seen post-operatively in surgical outpatient clinics at the discretion of the treating surgeons. This clinic appointment may be face to face, or conducted via telephone or telehealth. At this visit, symptoms of VTE may be enquired about, and if suggestive of a VTE, image confirmation may be obtained. As part of this study, all patients will be contacted between day 30 and 35 post-operatively via telephone to enquire about symptoms that may be suggestive of the development of VTE, irrespective of the clinical follow-up. At this time, verbal consent will be obtained to proceed with a pro forma telephone questionnaire and this process will occupy approximately 2 – 5 minutes of their time. For those participants who have symptoms suggestive of a VTE, they will be invited back to their treating hospital for image confirmation of VTE and if this is confirmed, then an anticoagulation regime will be commenced at the discretion of the clinical team, the duration of which is guided by the latest guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand (Tran *et al*., 2019).

**11c. Measurement tools used**

All data will be transcribed into a central REDCap database accessible electronically and maintained at Northern Health. All data that are to be captured are data that are already generated and used by the various hospitals as part of National Safety Standards and good clinical practice (GCP) guidelines and may be obtained from medical charts, anaesthetic charts, surgical operation reports and electronic pathology reports. Data may be obtained during the participant’s hospital admission up to and including the day of discharge from hospital. The defined time point for data collection will be between day 30 and 35 post-operatively, by a telephone consultation with a pro-forma of specific questions to ask to determine if a participant has symptomatic VTE present. If the participant’s symptoms are suggestive of a VTE, the participant will be invited back to the treating hospital to confirm this via imaging techniques and to commence anticoagulation. This data will also be captured.

It is anticipated that several people from each of the various hospital campuses will be involved with the entering of data into the central REDCap database. All people entering the data will have a medical background and will include various members from the surgical team involved with the participant’s operation, thus having access to the patients’ files in the course of their clinical duties. Data collectors will be recruited and trained either by WestSURG or by the PI from the institution. The database will be regularly checked by WestSURG for data completeness and a contact person for each of the study participant’s data will be nominated, to ensure that missing data is provided. Every 6 months, the PIs at the institutions will perform 3 random checks in conjunction with WestSURG to ensure accurate data collection.

**11d. Safety considerations/Patient safety**

Data to be collected are data that are generated and captured already by the various hospitals as part of National Safety Standards and on-going GCP guidelines. Risks that are associated with this study are the inherent anaesthetic and surgical risks associated with the laparoscopic cholecystectomy. As part of GCP guidelines, protocols already exist for the reporting and management of any adverse events. The only data that are not routinely collected are the 30 day post-operative follow up telephone call for the determination of symptoms that are consistent with the development of VTE, which will then require further investigations and the possibility of an anticoagulation regime. As this increases participants safety and overall quality of surgical experience, we feel that there is no negative impact to patient safety due to this study.

1. **STATISTICAL CONSIDERATIONS AND DATA ANALYSIS**

**12a. Sample size and statistical power**

This is a prospective non-inferior surgical comparative effectiveness study with a sample size of 5,190 patients. This sample size will provide 95% confidence intervals of 0.12% to 0.40% for a point estimate of 0.23% in the observed rate of VTE, a 20% reduction in the observed VTE incident rate observed by Liu et al (2020). This expected rate of 0.23% reflects 12 of the 5,190 patients that will be symptomatic VTE by day 30 post-operatively. The estimated confidence interval is based on an exact binomial estimation, with a Wald estimation providing an upper bound of the 95% confidence interval of 0.36% and a Wilson (Score) approximation upper bound of 0.40%.

**12b. Statistical methods**

Descriptive statistics will be prepared to provide a summary of the cohort. The incidence rate of VTE and surgical bleeding will be calculated. If the sample size allows, associations between patient and surgical factors with the primary and secondary outcomes will be performed using appropriate continuous or categorical statistical tests. Given the expected low incident rate of VTE, multivariable analysis is likely to be limited to the inclusion of two variables to assess potential confounding effects. The potential higher incident rate of surgical bleeding will allow up to 10 variables to be included, according to sample size calculations indicated by Peduzzi et al8.

1. **ETHICAL CONSIDERATIONS**

This study will be conducted in full conformance with principles of the “Declaration of Helsinki”, Good Clinical Practice (GCP) and within the laws and regulations of the states of Victoria, New South Wales and South Australia.

Retrospective data that has already been generated at each of the various contributory hospital campuses will be utilized as part of National Safety Standards and good clinical practice guidelines governance. There are no restrictions placed upon participants from culturally and language diverse backgrounds and all participants are automatically eligible for inclusion into this study, irrespective of the nature of their operation (elective or emergency laparoscopic cholecystectomy), or the time of day that the operation is performed. Ethics approval will be sought through a National Mutual Acceptance scheme authorized committee.

Data will be obtained from various sources including paper based admission notes, anaesthetic charts, surgical reports and electronic pathology reports. Data collected are shown in the REDCap pdf attachments and include:

* Age
* Gender
* Patient height
* Patient weight
* Risk factors for VTE (smoking, family history, medications)
* Operative details (time taken, intraoperative pressure used, operative surgeon)
* Caprini VTE Risk Score

For the 30 day post-operative telephone follow-up, some survey questions will be asked to determine the likelihood that a symptomatic DVT has formed, since discharge from the hospital. This data will then be entered into a central REDCap database that is protected electronically by the use of electronic signatures and security level access rights to the data. At the same time, hospital records will also be accessed to confirm:

* 30 day morbidity, in particular regarding VTE

Data will initially be obtained in a re-identifiable manner (hospital and UR number are recorded). This is required to enter the 30 day survey and audit of the 30 day morbidity to the patient dataset. This will also ensure data completeness, by the request of missing data from the person involved with the inputting of that particular participant’s data into the database, and also allowing 6 monthly random data checks to ensure accuracy. These data will be marked as identifiers in REDCap and only aggregate, de-identified data will be extracted for analysis. Only aggregate, de-identified data will presented to conferences and published in a peer reviewed journal. Data will be entered directly into the REDCap database and no hardcopy data will be collected or stored. Electronic data will be destroyed by electronic shredding 7 years after publication.

**13a. Verbal Consent**

Participants will be required to verbally consent to the 30-35 day post-operative telephone call, designed to ensure that VTE has not occurred since discharge from the hospital. This ensures that the true incidence of VTE is being captured, rather than being lost to follow-up in a hospital other than the initial treating hospital.

Patients who cannot communicate speak English will not be expected to complete the survey. A Participant Information Sheet will be available to all patients regarding this aspect of the study. We believe that verbal consent is appropriate for the survey, however, we provided the added security that an information sheet is available to them, should they wish to review before answering the survey. If they would like to read the information sheet prior to undertaking the survey, it will be provided to them and an alternative date scheduled to undertake survey. Retrospective withdrawal from the survey will be possible up to the point of data analysis. This process will be either through verbal communication to the clinical contact at each site, or through a written withdrawal form, whichever is more convenient and least stressful for the participant. If this withdrawal request comes after data analysis has commenced, the withdrawal of the survey data will not be possible.

Consent will not be obtained for the use of patient information collected as part of standard care and stored in the patient medical records. A waiver of consent will be sought for access to this data.

**13b. Waiver of Consent**

A waiver of consent will be sought for all patients whose retrospective data is included in this study. All data collected will be obtained from patient medical records.

A waiver of consent is justified for the following reasons:

* There is no risk to participation - all the data collected is contained within the patient medical record and participation requires no additional effort/input from patients.
* The benefits from the research justify any risks of harm associated with not seeking consent – this study has potential to improve clinical outcomes, but this is dependent on the validity of the data and all-inclusive representation of the cohort being examined.
* There is no risk of harm to participants involved in this research. Data collection poses no risk to participants as the data collected does not exceed that which is collected at the hospital and recorded in the medical record
* There is no known or likely reason for thinking that participants would not have consented if they had been asked as there is no risk to participation.
* Researchers will ensure that the use and disclosure of information is compliant with privacy principles in all relevant privacy legislation
* All data is de-identified prior to analysis and any publication or reports will comprise aggregate data only.

**13c. Risk and Benefit**

There is no foreseeable risk of harm or discomfort to participants involved in this research. The data collected without consent poses no risk to participants as it does not exceed that which is collected at the hospital and recorded in the medical record. This data will be that relating to the normal course of treatment/intervention for patients undergoing laparoscopic cholecystectomies. The benefits form the research justify any risks of harm associated with not seeking consent. The study has potential to improve clinical outcomes.

**13d. Public Interest**

It is intended that this data will be used to assess and report the health outcomes for patients undergoing laparoscopic cholecystectomies. Reporting patient outcomes will help to identify gaps in best practice and inform policy and guideline development that aims to improve the safety, efficiency and outcome of laparoscopic cholecystectomies in regard to VTE incidence. Evaluation of the data will be relevant and of interest to the general public in addition to many other medical and allied health professionals.

1. **OUTCOMES AND SIGNIFICANCE**

As there is no gold standard with regards to chemical and mechanical thromboprophylaxis for patients undergoing surgery, either electively or as an emergency procedure, we cannot be sure that the incidence of VTE has been mitigated to the greatest extent possible. Whilst the background incidence of surgically provoked VTE is relatively small at 0.3% or 3 per 1000 individuals undergoing laparoscopic cholecystectomy, the morbidity and/or mortality associated with post-thrombotic syndrome is significant. Massive pulmonary embolus may result in immediate death for the individual concerned or it may lead to chronic thromboembolic pulmonary hypertension (CTEPH), which has an incidence of 3.4% post-acute pulmonary embolism. Left untreated, CTEPH has a 30% five-year survival rate1. Venous thromboembolism has a staggering effect upon the Australian economy and in 2008, it was estimated that VTE cost the Australian community $1.7 billion dollars. It is therefore imperative that we determine best practice guidelines for the prevention of surgically provoked VTE.

A recent retrospective analysis of elective laparoscopic cholecystectomies conducted over an 18 month period from 1 January 2018 – 30 June 2019, within 7 metropolitan hospitals in Melbourne determined a VTE incidence of 0.3%, when a variety of accepted chemical and mechanical means of thromboprophylaxis were used6. We wish to expand upon this existing knowledge and by limiting the timing of chemical thromboprophylaxis to be given at the completion of surgery and by the exclusive use of intra-operative SCCDs, we hope to diminish both the incidence of VTE and surgical bleeding.

The findings of this study may then be applied to other surgical procedures to determine the generalizability of mitigation of VTE risk across various surgical sub-specialities.

1. **BUDGET (Mandatory Field)**

This protocol has not received any research funding, nor have we applied for any grants. Data for this study is already being generated and captured by the various hospitals as part of National Safety Standards and good clinical practice guidelines governance. We are seeking in kind support from numerous surgical trainees for the inputing of this data into a centralised REDCap database. As an incentive, all research personnel who supply complete data for a minimum of 20 study participants will be offered authorship of the manuscript as part of the WestSURG collaborative that will be written for publication in a peer reviewed journal. We will also be seeking Department of Surgery in kind support from the various contributing hospitals, for assistance with the AI in terms of advertising to registrars and 6 monthly random data checks. A Melbourne Academic Centre for Health (MACH) grant is being sought to cover the cost of preparing and submitting to ethics.

Apart from in kind support, this study and the acquisition of data is cost neutral and does not dictate a change in behaviour in terms of the type of chemical thromboprophylaxis that may be used. As we are excluding the use of GCSs, both intra-operatively and post-operatively, there actually is a cost saving for the operating costs for all of the hospitals that will be contributing to this study.

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| **Source of Grant / Funding** | **Amount** | **Date** |
| MACH | $660 and costs associated with preparing HREC application | TBA |

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| IN-KIND SUPPORT (include estimation of staff time, administration costs etc.) | **COST $** | **Department Responsible** |
| High risk ethics application | $660 | If MACH grant unsuccessful: Northern Health Division of Surgery |
| Total in-kind support | $ 660 |  |

1. **REFERENCES**

[1] Tran HA, Gibbs H, Merriman E, et al. New guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand for the diagnosis and management of venous thromboembolism. *Med J Aust*. 2019; 210:227-35.

[2] Anderson DR, Morgano GP, Bennett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. *Blood advances*. 2019; 3:3898-944.

[3] Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012; 141:e227S-e77S.

[4] The CLOTS Trials Collaboration. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *The Lancet*. 2009; 373:1958-65.

[5] Morris RJ, Woodcock JP. Intermittent pneumatic compression or graduated compression stockings for deep vein thrombosis prophylaxis? A systematic review of direct clinical comparisons. *Ann Surg*. 2010; 251:393-6.

[6] Liu DS, Stevens S, Wong E, et al. Pre-operative and intra-operative chemical thromboprophylaxis increases bleeding risk following elective cholecystectomy: a multicentre (PROTECTinG) study. *ANZ J Surg*. 2020; 90:2449-55.

[7] Shalhoub J, Norrie J, Baker C, et al. Graduated Compression Stockings as an Adjunct to Low Dose Low Molecular Weight Heparin in Venous Thromboembolism Prevention in Surgery: A Multicentre Randomised Controlled Trial. *Eur J Vasc Endovasc Surg*. 2017; 53:880-5.

[8] Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *Journal of Clinical Epidemiology*. 1996; 49:1373-9.