DECISION ANALYSIS FOR THROMBOPROPHYLAXIS DURING PREGNANCY

DECISION ANALYSIS IN SHARED DECISION MAKING FOR THROMBOPROPHYLAXIS DURING PREGNANCY (DASH-TOP) STUDY

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ABSTRACT

Decision analysis is a quantitative approach to decision-making that could bridge the gap between decisions based solely on evidence and the unique values and preferences of individual patients, a feature especially important when existing clinical evidence cannot support clear recommendations and there is a close balance between harms and benefits for the treatment options under consideration. Low molecular weight heparin for the prevention of venous thromboembolism (VTE) during pregnancy represents one such situation. The objective of this thesis is to explore the use of a decision analysis intervention for shared decision-making for thromboprophylaxis during pregnancy.

This thesis begins with a scoping review that explores the ways in which decision analysis has been used to inform shared decision-making encounters, highlighting key challenges for implementing and evaluating this type of intervention. This is followed by a protocol that presents the methodology of an explanatory sequential mixed methods pilot study for the Decision Analysis in SHared decision making for Thromboprophylaxis during Pregnancy (DASH-TOP) tool. This tool was pilot tested through interviews of eligible women in Canada and Spain who were facing the treatment decision for the prevention of VTE in the antenatal period. While the tool was well received by patients, more effective ways of obtaining patient preferences and presenting the decision analysis results are required to enhance shared decision-making interactions. Finally, this thesis concludes with a reflection on the lessons learned from developing and evaluating a decision analysis intervention for shared decision-making.

The insights from this research have informed the development of an integrated online shared decision-making tool for VTE in the antenatal period, which the DASH-TOP team plans to evaluate in a randomized controlled trial. It is hoped that this information will also provide guidance to researchers interested in developing or evaluating decision analysis interventions for other clinical decisions.

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LIST OF ABBREVIATIONS

AHP	Analytic Hierarchy Process
ASH	American Society of Hematology
CanVECTOR	Canadian Venous Thromboembolism Clinical Trials and Outcomes Research
DASH-TOP	Decision Analysis in SHared decision making for Thromboprophylaxis during Pregnancy
DVT	Deep vein thrombosis
GRADE	Grading of Recommendations Assessment, Development and Evaluation
LMWH	Low molecular weight heparin
PE	Pulmonary embolism
PRISMA-ScR	Preferred reporting items for systematic reviews and meta-analysis: extension for scoping reviews
QALYs	Quality-adjusted life years
SD	Standard deviation
VAS	Visual analogue scale
VTE	Venous thromboembolism

PREFACE

This sandwich PhD thesis includes three manuscripts exploring the use of decision analysis in shared decision-making for thromboprophylaxis during pregnancy. One of the manuscripts has been published, while two have been submitted for publication. I am the first author of all three manuscripts. The contributions for each multi-authored manuscript are described below.

In the first manuscript, we present a scoping review that explores the ways in which decision analysis has been used to inform shared decision-making. My contributions include developing the research question and protocol for the review, performing the screening, data extraction, analysis, and write-up. Feng Xie, Pablo Alonso-Coello, Shannon Bates, Mark Eckman and Gordon Guyatt contributed to conceptualization of the review and methodology. Montserrat León-García, Ena Niño de Guzman Quispe, Carlos Canelo Aybar, Claudia Valli, Susan Mirabi, Arnav Agarwal, and Kevin Pacheco Barrios provided support with screening, data extraction and risk of bias assessment. All members of the review team provided feedback on the final manuscript, which was submitted to the Journal of Clinical Epidemiology on May 15, 2021.

In the second manuscript, we present the methodology of a pilot study that is part of the Decision Analysis in SHared decision making for Thromboprophylaxis during Pregnancy (DASH-TOP) study. The DASH-TOP study is led by co-PIs, Feng Xie and Pablo Alonso-Coello, with the support of Shannon Bates, Gordon Guyatt, Mark Eckman, Susan Jack, Rohan D'Souza, Nadine Shehata, Montserrat León-García, and myself. Feng Xie, Pablo Alonso-Coello, Shannon Bates, and Gordon Guyatt conceptualized the study.

The decision analysis intervention was developed by Mark Eckman. Montse León-García and I developed other components of the decision aid with support of the DASH-TOP team. I was responsible for developing the methodology of the pilot study and designing the data collection materials. All members of the DASH-TOP team provided feedback on the protocol. The manuscript was published in BMJ Open on March 21, 2021.

In the third manuscript, we present the results of the DASH-TOP pilot study. I was responsible for conducting data collection at the Canadian study site, while Montse León-García was responsible for data collection at the Spanish sites. With the support of Montse, I led data analysis and interpretation as well as writing the manuscript. Other members of the DASH-TOP team contributed to the interpretation of the results. All coauthors provided feedback on the manuscript, which was submitted to Medical Decision Making on July 8, 2021.

CHAPTER 1. INTRODUCTION

Venous thromboembolism (VTE) is a condition in which a blood clot forms in the deep veins of the leg, groin or arm (deep vein thrombosis [DVT]), most commonly those of the legs, and lungs (pulmonary embolism [PE]). Individuals with prior VTE are at an increased risk of thrombosis during subsequent pregnancies,[1,2] although the magnitude of this risk remains uncertain given that the existing evidence base is informed by studies with major limitations.[3] Globally, VTE is a leading cause of maternal morbidity and mortality.[4,5]

Guidelines typically recommend preventative low molecular weight heparin (LMWH) for pregnant individuals at high risk of VTE because it does not cross the placenta or increase the risk of serious adverse fetal outcomes, thrombocytopenia or osteoporosis.[6-8] It is, however, expensive, inconvenient and uncomfortable to administer[9]. LMWH is also associated with an increased risk of major bleeding and may impact access to epidural analgesia.[6,10] Given the competing risks and benefits of LMWH as well as the limitations of available evidence, the decision to take this medication is not straightforward and is likely to vary according to each patient's values and preferences[11].

The American Society of Hematology (ASH) guideline acknowledges that, within the context of prophylactic LMWH in the antenatal period, the best treatment option may differ among patients and healthcare providers.[12] Clinicians and patients with a lower risk threshold for recurrent VTE may choose a more aggressive treatment strategy involving LMWH, whereas withholding LMWH may be appropriate for those patients who are willing to accept a higher risk of recurrent VTE to forgo the drawbacks associated with

prophylaxis.[13] The guidance statement recommends that patients should be provided with the opportunity to participate in shared decision-making to arrive at an optimal decision.[14]

Shared decision-making is a process through which patients and healthcare providers work together to make a treatment decision.[15] Although there is no consensus regarding the definition of shared decision-making,[16] three elements are considered necessary: 1) recognizing a decision is required; 2) knowing and understanding the best available evidence; and 3) incorporating patient values and preferences into the decision.[17] Although a key element is the incorporation of patient values and preferences into the decision,[17] studies indicate they are often ignored or poorly understood by providers.[18,19]

Decision aids are commonly used to facilitate shared decision-making. Available in a variety of formats (e.g., online, print, video), they are designed to inform patients of available treatment options and their potential benefits, harms and costs.[20,21] Decision aids often entail an implicit method of values clarification, in which patients are encouraged to think about what's important to them.[22] A systematic review of 105 randomized controlled trials involving 31,043 patients found that, while decision aids helped patients make more informed decisions,[23] there is uncertainty as to how these tools support the process of integrating patient values and preferences into the decision-making process.

Decision analysis involves structuring a decision problem using an analytical framework (e.g., decision tree) that includes key clinical outcomes associated with each treatment option as well as the natural course of untreated illness along with their associated probabilities and utilities based on patients' values and preferences.

Probabilities, a measure of likelihood that an event will occur,[24] are obtained from published studies and can be personalized based on patients' clinical profile. Values and preferences for health outcomes, which are expressed as health utilities, can be obtained directly from patients.[25] Together, patient-specific probabilities and utility scores are entered into a decision analytic model to calculate the quality-adjusted life years (QALYs) for each treatment option under consideration. If multiple treatment options are being considered, the treatment with the highest QALYs represents the best option as it is expected to maximize the patient's length and quality of life.[25]

Despite the guideline recommendation for shared decision-making for prophylactic LMWH in the antenatal period, a paucity of decision support tools exist to help patients engage in treatment decisions for VTE.[26] The work presented in this thesis was conducted as part of the Decision Analysis in SHared decision making for Thromboprophylaxis during Pregnancy (DASH-TOP) study. The objective of the study is to evaluate the application of decision analytical methods to facilitate shared decision-making for thromboprophylaxis in the antenatal period. We designed chapters 2 to 4 as stand-alone manuscripts presenting analyses related to the study.

In Chapter 2, we present a scoping review of studies that have used decision analysis to facilitate shared decision-making for clinical decisions. There is some evidence suggesting the potential for personalized decision analysis to improve decision-making for clinicians.[27-29] However, a systematic evaluation of the extent to which healthcare providers have applied decision analysis to support shared decision encounters with patients is not available. The objective of this scoping review was to explore the

ways in which decision analysis has been used to inform shared decision-making by identifying what type of evidence is available with respect to the study design, patient population, decision-making context, type of decision analysis performed, and outcomes considered. As with other scoping reviews, the aim of this review was to provide an overview of a body of literature and not to produce a quantitative summary result to answer a specific research question. The results of this review were used to inform the development of the DASH-TOP tool and the methodology of the pilot study.

In Chapter 3, we present the protocol for the DASH-TOP pilot study. Given the complex nature of our decision support tool, a multitude of factors had to be considered during its evaluation, including a multi-component intervention, the sociodemographic and medical characteristics of the patient, their previous experiences with LMWH, and their decision-making style. We therefore selected a sequential explanatory mixed methods study design because the integration of qualitative and quantitative research methods allowed for a comprehensive evaluation of the tool.

In Chapter 4, we present the results of the DASH-TOP pilot study. The objective of this pilot study was to explore the application of decision analysis to a shared decision-making process for the decision of using prophylactic LMWH for pregnant individuals or those considering pregnancy who have experienced a VTE. The intent was to use the results from this study to inform the design of an online integrated version of the DASH-TOP tool as well as the methodology of a future randomised controlled trial that will enable a more robust evaluation of the decision analysis tool in a clinical encounter for the same decision.

In Chapter 5, we summarize the main findings of Chapters 2 to 4. The implications of the DASH-TOP pilot study and unanswered questions regarding the application of decision analysis for shared decision-making for thromboprophylaxis in the antenatal period are also discussed.

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CHAPTER 2. DECISION ANALYSIS FOR SHARED DECISION MAKING: A SCOPING REVIEW

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Decision analysis for shared decision making: A scoping review

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Abstract

Background: Evidence on clinical effectiveness alone is usually insufficient to guide a clinical decision. One also must account for each individual patient's presentation, circumstances, and their values and preferences. By offering a structured approach to decision-making that explicitly considers available clinical evidence and patient preferences, decision analysis could be a useful tool to help clinicians and patients engage in a shared decision-making process. In this scoping review, we present available evidence regarding the use of decision analysis for shared decision-making.

Methods: We searched five bibliographic databases (from inception until February 2021), reference lists of included studies, trial registries, a thesis database and websites of relevant interest groups to identify studies exploring the application of decision analysis in shared decision-making. Pairs of reviewers independently screened and selected studies for inclusion, extracted study information and assessed risk of bias.

Results: We identified 27 studies that varied greatly with regard to their patient population, design, content and delivery. A range of outcomes were evaluated to explore the effectiveness and acceptability of decision analytic interventions, with little information about the implementation process. Most studies found that these interventions were broadly beneficial. However, there is significant uncertainty surrounding their effectiveness and implementation in clinical practice.

Conclusion: Despite the compelling rationale on the potential for decision analysis to support shared decision-making, rigorous randomized controlled trials are needed to

confirm these interventions' effectiveness in different contexts, while qualitative studies should seek to understand their potential implementation.

Introduction

The clinical encounter requires regular and continuous decision-making.[1] Decision-making can be defined as a cognitive process that involves the selection of a course of action among several alternative possibilities.[2] In the clinical context, decisions can relate to a range of actions, including diagnostic tests, treatments or referrals.[3] Clinical decisions should ideally incorporate the best available evidence in light of the medical characteristics and the preferences of each patient.[4]

Healthcare providers are increasingly encouraged to recognize patients as experts in their own right with unique knowledge regarding their health and preferences, and involve them in clinical decisions through a shared decision-making process.[5] While the principles of shared decision-making are well described,[6] it has been difficult to accomplish in practice and is not widely implemented.[7,8]

Decision analysis is often used to facilitate decision-making in contexts outside the clinical encounter (e.g. economic evaluations of healthcare programmes)[9]. It has been proposed as a tool to support patient engagement in clinical decisions and foster discussion between provider and patient in a shared decision-making encounter.[1,10] Decision analysis involves structuring a decision using an analytical framework that includes all important outcomes associated with each treatment option along with their probabilities of occurring and the patient's preferences for these outcomes.[11] When probabilities and preferences are inputted into the analytical framework, each treatment's expected value is calculated (e.g. quality adjusted life years [QALYs]). The treatment

with the highest expected value represents the option with the best health outcomes according to available clinical evidence and the patient's preferences.[12]

By offering a structured approach to decision-making that explicitly incorporates patient preferences, decision analysis may help clinicians and patients engage in a shared decision-making process. For patients who want to actively engage in the process, decision analysis removes the cognitive challenge of simultaneously weighing the importance of the risks and benefits of each treatment option, alongside their associated probabilities. It also provides patients and healthcare providers with a tool that could facilitate further discussion of the treatment options under consideration. For patients who do not want to actively engage in the decision-making process,[13] decision analysis ensures that, at a minimum, their preferences are taken into consideration - a process that clinicians may not otherwise achieve.[14,15]

Despite the compelling rationale, decision analysis has infrequently been applied within a shared decision-making context. There is some evidence suggesting the potential for personalized decision analysis to improve decision-making for clinicians and patients.[16-20] However, a systematic evaluation to determining the extent to which healthcare providers have applied decision analysis to shared decision encounters with patients' involvement is not available. The objective of this scoping review is to explore and characterize available evidence of the ways in which decision analysis has been used to inform shared decision-making.

Methods

Study design

We conducted a scoping review according to standard methodology (PROSPERO registration number: CRD42018115731)[21,22] and followed the PRISMA Extension for Scoping Reviews (PRISMA-ScR) to report our study (see Appendix A for details).[23] As with other scoping reviews, the aim of this review was to provide an overview of a body of literature and not to produce a critically appraised and synthesised summary result to answer a specific research question.[24]

Eligibility criteria

We included studies if:

- The population consisted of patients facing a clinical decision; and
- The intervention involved the application of decision analysis in the context of a shared decision-making clinical encounter. The decision analysis process had to, at a minimum, include four steps: 1) the patient was presented with the important outcomes associated with the clinical decision as well information regarding the harms and benefits of the different treatment options; 2) the patient attached a value to each outcome under consideration; 3) the probability of each outcome occurring and the patient's value for that outcome were inputted into a decision analytical framework to produce a recommendation; and 4) the results of the decision analysis were shared with the patient and used to inform a clinical decision.

We applied no restrictions in terms of study design, comparators or types of outcomes considered. Eligible studies had to report results related to the decision analysis

intervention. We excluded reviews, editorials, books and conference abstracts and non-English language reports. There were no restrictions in terms of date of publication.

Information sources

We searched MEDLINE, Embase, PsychInfo, CINAHL and The Cochrane Library from inception to February 20, 2021. We also conducted a targeted search of grey literature sources including systematic review registries (PROSPERO), a thesis database (WorldCat) and the websites of relevant interest groups (Society of Medical Decision Making, The International Society for Pharmacoeconomics and Outcomes Research). To identify additional eligible studies, we manually screened the reference lists of all included studies.

Search strategy

The search strategy was developed through a collaborative process that involved an academic librarian, a clinician, and researchers with expertise in decision analytical frameworks and systematic literature review methodology. Three concepts informed the strategy: 1) decision analysis; 2) patient and/or physician; and 3) clinical decision-making. The initial search strategy was developed in Medline (Ovid) and then adapted to the other databases. An example of the Medline search strategy is available in Appendix B.

Data management

We imported the references from each database into EndNote (version 8.2, Clarivate Analytics, 2016) to remove duplicates. We conducted all screening using the Covidence platform and extracted data in a Microsoft Excel spreadsheet (version 16.10,

Microsoft, 2017). All reviewers were calibrated for study selection, data collection, and assessment of risk of bias.

Selection process

Two reviewers independently assessed study eligibility at the title and abstract level, followed by a full text review of potentially eligible articles. Reviewers resolved disagreements through discussion, with arbitration by a third reviewer when necessary.

Data collection

Two reviewers independently extracted data using a form developed by the research team. The data extraction form ensured documentation of study design, sample size, population characteristics, decision-making context, intervention(s) administered, type of decision analytic model, outcomes considered and results. The type of decision analytic model was classified according to the framework by Brennan et al,[25] a summary of each model's definitions is available in Appendix C. Reviewers resolved any discrepancies through discussion or, when necessary, arbitration by a third reviewer.

Risk of bias

Two reviewers independently assessed the risk of bias (RoB) for all studies with an experimental or quasi-experimental design. For randomized controlled trials, we assessed RoB using a version of the risk of bias tool developed by the Cochrane Collaboration and modified by the CLARITY Group at McMaster University.[26] For pre- post- test studies, we used the bias domains included in the ROBINS-I tool for (uncontrolled) before-after studies, as described by the Cochrane Handbook for

Systematic Reviews of Interventions.[27] We did not assess RoB for other study designs (e.g., qualitative study, case study, economic evaluation) that were not intended to make inferences about the effectiveness of the decision analysis interventions. We did not assess the quality of the decision analytic models that were used as interventions in each study.

Data synthesis

Characteristics of the decision analysis intervention(s), methods of data collection, and outcomes were narratively synthesized and presented in tabular formats.[21,28]

Ethics

Ethics approval was not required.

Results

Study characteristics

The results of our search and screening process are presented in Figure 1. We identified 27 publications, that were conducted as part of 21 unique studies and that met our inclusion criteria.[29-53] These studies were published between 1988 and 2018. The majority of studies were conducted in the United Kingdom (n = 12) or United States (n = 11).

The decision analytic interventions were implemented within a variety of clinical contexts, including vaccination for hepatitis B,[29] menopause,[30,53] prenatal diagnosis for Down syndrome,[33] treatment for localized prostate cancer,[41] anticoagulant therapy for atrial fibrillation,[37,38,40,43,48] and management of childhood anxiety.[54] A range of study designs were used to evaluate the interventions, including randomized controlled trials (n

= 9), pre- post- test designs (n = 2), mixed methods (n = 1), single arm studies (n = 5), qualitative studies (n = 5), economic evaluations (n = 1), video-based (n = 1) and case studies (n = 3). Sample sizes ranged from one to 1280 participants. Additional information on study characteristics is available in Table 1.

Characteristics of the decision analysis intervention

The majority (n = 16, 59%) of decision analytic interventions utilized a decision tree. Studies that used decision trees evaluated treatment decisions for urinary tract calculi, [44] hypertension,[31,46] prenatal diagnosis of Down syndrome,[33] amniocentisis,[49] mode of delivery after a previous cesarean,[34] menorrhagia,[35,36] localized skin cancer,[51] and childhood anxiety.[54] The second most frequent model type was the Markov model (n = 10, 37%). All of the studies that used a Markov model evaluated treatment decisions for long term conditions, such as breast cancer,[32,39,55] ovarian cancer,[32,42,45] and atrial fibrillation.[37,38,40,43,48] One study combined both decision analytic approaches; a decision tree to model immediate treatment options and complications and a Markov model to simulate long term outcomes and disease recurrence for patients with localized prostate cancer.[41]

Different exercises were used to elicit patient's values and preferences. The standard gamble was the most common method of preference elicitation (n = 13, 48%) followed by the visual analogue scale (n = 10, 37%) and time trade off (n = 6, 22%). Some studies reported that participants found the standard gamble task difficult due to its complexity and/or need to think in abstract[37,38,42,45] However, this finding was not unique to the standard gamble, with one study reporting that participants found assigning a

numerical value to their preferences on a rating scale challenging.[47] The authors of this qualitative study noted that problems experienced with the preference elicitation exercise seemed attributable to insufficient instruction rather than conceptual difficulty.[47] Given potential issues with the method of preference elicitation, one study allowed participants to 'opt-out' of the preference elicitation exercises and use population-based preferences if they wished. However, none of the participants in the study opted to do so.[45]

In addition to incorporating patient preferences into the decision analytic model, 19 (70%) studies reported incorporating individual clinical factors – which varied depending on the decision context. For example, one decision analytic model evaluating treatment options for prostate cancer was personalized according to the cancer pathologic characteristics, patient age and comorbidities as assessed by the Index of Coexistent Disease (ICED).[41] Another decision analytic model evaluating treatment options for newly diagnosed hypertensive patients was personalized according to participants' cardiovascular risk and calculated using clinical data and a Framingham risk equation.[46]

The decision analytic model output varied across studies and included expected utility, quality-adjusted life expectancy and quality-adjusted life years. Some studies provided additional detail on how this output was presented to participants. For example, a computerized clinical guidance programme for prophylactic oophorectomy presented the personalized decision analytic results in the form of a guidance statement that was accompanied by a comparison screen showing a figure summarizing the net benefits of undergoing oophorectomy versus no oophorectomy.[42] All the numbers underlying the model were available on separate screens. A sensitivity graph was also available if

patients or healthcare providers wished to see the effect of changing preferences on the results. The program produced a full report of the consultation, which could be printed out for the patient or healthcare provider.[42] Few studies provided this level of detail on how the decision analytic model output was presented. In addition, most studies (74%) did not report conducting sensitivity analyses to explore uncertainty surrounding model parameters – such as a change in patient preferences or the clinical data.

Data collection characteristics

Almost all studies (n = 25, 93%) collected data directly from patients, using interviews or questionnaires (Table 3). Two studies (7%) reported data obtained from the researcher through non-participant observation, such as notes and video recordings of the consultation.[47,48] One study (4%) obtained data directly from healthcare providers by asking the treating physician to describe the patient's preferences and concerns that were taken into account in their treatment recommendation and evaluate the appropriateness of decision analytic model recommendation for the patient.[41]

Most studies (n = 15, 56%) collected data at a single time point, often during the shared decision-making consultation (n = 23, 85%). The longest follow-up time was 12 months post intervention, whereby researchers from one study examined the medical records of participants to determine whether a treatment was initiated[29] and patients from another study completed a questionnaire to re-examine their preferences, subjective probabilities and likelihoods regarding the treatment options under consideration.[30]

Outcome characteristics

The studies evaluated a broad range of outcomes (Table 4), with the impact of the intervention on the patient's treatment decision being the most frequent outcome evaluated (n = 16, 59%). Among the 16 studies that evaluated the impact of decision analysis on treatment decisions,[29-35,40,41,43,44,46,51,52,54,55] one (6%) study reported an impact of the intervention on patient decisions, and seven (44%) studies reported no effect observed. Eight (50%) studies had no clear outcome, either due to their study design, method of analysis or reporting.

While decision analytic interventions were not often a catalyst for a change in treatment decisions, participants in multiple studies reported that the intervention helped clarify their decision [42,45,49] or made them more aware of the disparity between their own preferences and the clinical need for a treatment,[46] prompting further reflection[42,45] or discussion with their healthcare provider.[46,49] One study noted that risk estimates took on a new and intense meaning for patients after completing the standard gamble exercise.[49]

Results from experimental or quasi-experimental studies showed that interventions were broadly beneficial for a range of patient-reported outcomes related to the quality of the decision making process, such as decisional conflict,[31,33-36,40,52,53] satisfaction,[34,40,53] knowledge,[31,34-36,39,40] decision burden,[39] and anxiety. Studies that measured decisional conflict using shorter time horizons[35,53] or compared to a usual care group versus an active comparator[34] reported a statistically significant effect in favour of the decision analysis intervention. The results on anxiety were mixed, with only two out of five (40%) studies reporting an effect.[32,34] No study reported a statistically significant negative effect of the decision analysis intervention on any patient-reported outcome.

The process of implementation was infrequently evaluated beyond reporting the average length of consultation (n = 14, 52%), which ranged from 10 minutes[42] to 4.5 hours.[30,53] Generally studies that explored patients' experience using the decision analysis interventions found a high level of patient acceptability.[39,42,43,46,47,54] While there were no data regarding implementation from the healthcare provider perspective, in a video-based process study, the shared-decision making consultations provided some insight into the provider experience. The authors found that, even in consultations aimed at promoting shared decision-making, physicians were verbally dominant and worked primarily as information providers. There was almost no difference in shared decision-making behaviours across the study arms, however, only one physician delivered each intervention so the findings may be confounded by their consultation style rather than the shared decision-making intervention itself.[38]

Critical appraisal of included studies

There was a significant risk of bias among the 10 studies that had an experimental or quasi-experimental design, which enabled them to make inferences about the effect of the decision analysis interventions. All eight randomized controlled trials were determined to have a high risk of bias due to a lack of blinding.[30-35,37,53] Inadequate allocation concealment and missing outcome data were also identified as common sources of bias. The two pre- post- study designs had either a moderate[40] or serious[39] risk of bias, meaning that they cannot be considered comparable to a well-performed randomized trial. More detail on the RoB assessments is available in Appendix D.

Discussion

Main findings

This scoping review presents an overview of decision analysis interventions that have been developed and tested to inform shared decision-making. We identified 27 publications in which the decision analysis interventions varied greatly with regard to their patient population, design, content and delivery. A broad range of outcomes was used to evaluate the effectiveness and acceptability of decision analysis interventions, with little information available about the implementation process or feasibility for use in a clinical encounter. Results of included studies suggest that decision analysis interventions are acceptable and broadly beneficial according to a range of patient-reported outcomes, but the available evidence is subject to a high risk of bias.

Our results within the context of previous research

Previous reviews have considered the application of decision analysis to inform clinical decisions, but they were not systematic in nature.[1,10] While the authors of these reviews recognize the potential for decision analysis to facilitate evidence-based medicine and patient centered care, this scoping review identified some key considerations regarding the application of decision analysis interventions to inform shared decisions. These include challenges regarding the complexity of the preference elicitation exercises,[42,45,48] the lack of high quality clinical data[51] or overly optimistic model inputs,[41] how the order of presenting health states can affect patient preferences,[41] the use of prompts when inconsistent utilities assessment are noted,[41] the development of models that do not include outcomes or treatments that are important to patients,[41] and instructions or output that are not fully understood by patients.[47]

Our review also highlights several important points regarding the assessment of decision analysis interventions that are consistent with the broader literature on shared decision-making and decision aids. First, interventions were mostly evaluated for effectiveness, and the implementation process was seldom addressed.[56-59] While knowledge of the effectiveness of shared decision-making is important, a lack of understanding about the implementation process may limit the opportunities to increase effectiveness[7,56] as previous studies indicate significant challenges to implementing shared decision-making in clinical practice.[8,60-62] Second, there is a lack of outcome data collected from the perspective of healthcare providers,[63] a key actor in shared decision-making processes.[64] Potential benefits of decision analysis for providers include building rapport with patients, helping quantify patient preferences and understand risk-benefit trade-offs, providing support when there is a lack of high-quality evidence or when providers have limited experience treating a group of patients, as well as building the skills and knowledge base of trainees.[50,51] Third, the majority of data were collected around the time of the consultation (either immediately before, during or after) despite the fact that shared decisions may not be limited to the context of one consultation between a patient and healthcare provider.[63] Decision-making can be conceptualized as a process initiated, sustained and transformed over a range of encounters with individuals and technologies.[65] Fourth, included studies either did not have an experimental design or were subject to a high risk of bias, affecting confidence in observed effect estimates.[66] In addition, due to the design of included studies, it was difficult to determine what components of the decision analysis intervention (i.e., provision of information,

preference elicitation exercises, review of decision analysis model output) were useful or if any of the observed benefits were due to patients' desire for more support and/or information, regardless of the format.[46]

While we focused on formal decision analytic models (i.e., decision trees and Markov models) for this review, there exist other types of decision models that have been used to incorporate patient preferences and probability of outcomes in clinical decision-making.[67,68] One example is the Analytic Hierarchy Process (AHP), a form of multi-criteria decision analysis. Eckman and colleagues developed a AHP shared decision-making tool for cystic fibrosis patients.[69] This tool was able to examine trade-offs focused around endpoints and outcomes that would be difficult to measure in a decision tree, such as preventing lung infection, improving breathing function, improving functionality and feeling of well-being, minimizing the daily time required for each treatment, and minimizing the costs to patients.[69]

Strengths and limitations

This review has several strengths. Since this is the first review to summarize available evidence on the application of decision analysis within shared decision-making, we developed a broad search strategy that targets both electronic databases and grey literature sources to ensure that an exhaustive review of evidence was performed. We developed this approach through a collaborative process involving an academic librarian, a clinician, and researchers with expertise in decision analytical frameworks and the methodology of systematic literature reviews. To ensure that all studies of interest were included, we used broad inclusion criteria during the screening process.

A limitation of this review was that there is no consensus regarding the most appropriate outcome measures for assessing the effectiveness of shared decision-making interventions.[37] Among included studies, data were available for a broad range of outcomes, including attributes of the decision or decision-making process, patient behaviours and healthcare resource utilization. The heterogeneity in outcome measures and timing of outcome measurement made it difficult to evaluate the impact of decision analysis interventions across studies. This limitation largely reflects a shortcoming in the body of literature being examined.

Another difficulty related to this body of literature was the suboptimal reporting of the intervention and decision-making context. Among included studies, the decision analysis interventions were not always described in sufficient detail. This made it difficult to determine the validity of the decision analytic model or whether the intervention was truly being implemented within a shared decision-making context. The concept of shared decision-making itself is highly debated, with one review identifying 21 separate conceptual definitions.[70] Our inclusion criteria pre-specified four elements required to determine whether a shared decision-making encounter had occurred. Yet, our ability to identify these elements was limited by the study reporting.

Implications for practice and research

Despite the widespread consensus on the importance of patient engagement within the clinical context, there exist significant challenges to implementing shared decision-making in day-to-day practice. In this scoping review, we explored studies that have evaluated the role of decision analysis to facilitate shared decision-making for clinical

decisions. Our findings indicate that decision analysis interventions are acceptable and broadly beneficial for patients, but there is significant uncertainty surrounding their effectiveness as well as about their implementation in clinical practice. At this time, it may be too early for these interventions to be used in practice. Rigorous randomized controlled trials are needed to confirm the effectiveness of decision analysis interventions in different treatment contexts, while qualitative studies should seek to understand process and implementation issues to improve their chances of being implemented in the future.

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Tables and figures

Figure 1. Selection process

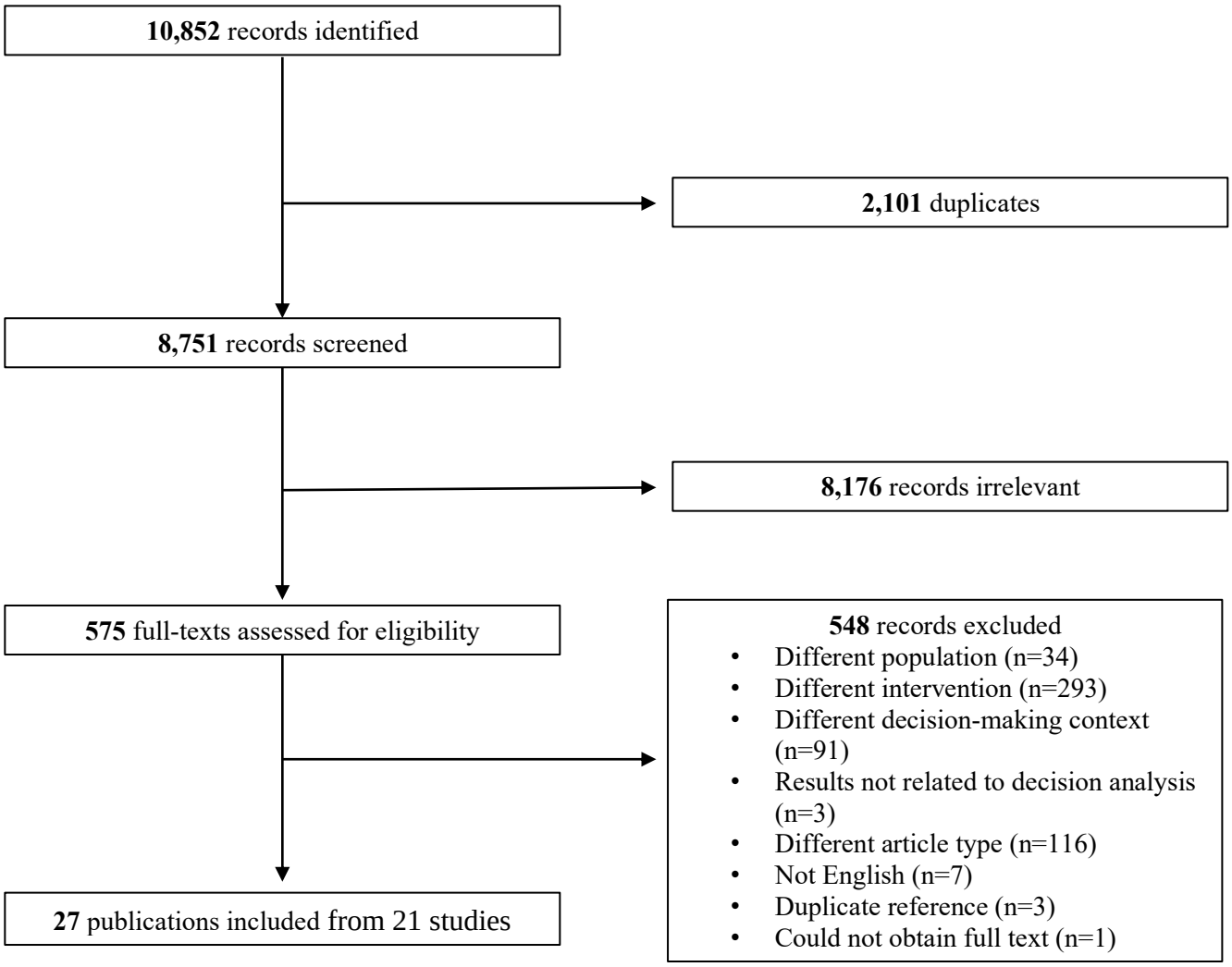

Table 1. Study characteristics

Author, year	Country	Study design	Decision context	Population (N)	Age	Intervention(s) and control
Clancy, 1988	USA	Randomised controlled trial	Hepatitis B vaccination	Hospital faculty and resident physicians eligible for Hepatitis B vaccination (1280)	Not reported	• Usual care • Information only • Information plus decision analysis
Rothert, 1977	USA	Randomised controlled trial	Estrogen replacement therapy or progesterone estrogen replacement therapy	Perimenopausal women (248)	Range 40 to 65 years	• Brochure • Lecture and discussion • Personalized decision support including decision analysis
Holmes-Rovner, 1999	USA	Randomised controlled trial	Estrogen replacement therapy or progesterone estrogen replacement therapy	Perimenopausal women (248)	Range 40 to 65 years	• Brochure • Lecture and discussion • Personalized decision support including decision analysis
Montgomery, 2003	UK	Factorial randomised controlled trial	Antihypertensive medication	Adults with newly diagnosed hypertension (212)	Mean 59 years	• Usual care • Decision analysis • Video/leaflet • Decision analysis and video/leaflet
van Roosmalen, 2004	Netherlands	Randomized controlled trial with two moments of randomization	Screening and prophylactic surgery for breasts and/or ovaries	Women who carry the BRCA1/2 mutation (88)	Mean 40 years	• Brochure and video • Shared decision-making tool including decision analysis
Bekker, 2004	UK	Randomised controlled trial	Prenatal diagnosis for Down syndrome	Women with a positive screening test for Down syndrome (117)	Mean 35 years	• Usual care • Usual care plus decision analysis
Montgomery, 2007	UK	Randomised controlled trial	Mode of delivery after a previous caesarean section	Pregnant women with a previous caesarean section (715)	Mean 33 years	• Usual care • Information program • Decision analysis program
Protheroe, 2007	UK	Randomised controlled trial with mixed methods	Treatment for menorrhagia	Women with menorrhagia (146)	Range 31 to 47 years	• Information leaflet • Information leaflet plus a Clinical Guidance Tree including decision analysis

Thomson, 2007	UK	Randomised controlled trial	Warfarin or aspirin treatment	Patients with atrial fibrillation aged over 60 (109)	Mean 73 years	• Paper-based guidelines • Decision aid with implicit values clarification • Decision aid with explicit values clarification plus decision analysis
Kaner, 2007	USA	Video-based study of randomised controlled trial	Warfarin or aspirin treatment	Older patients with atrial fibrillation (29)	Median age 72 years	• Paper-based guidelines • Concise decision aid • Extended decision aid including decision analysis
Stalmeier, 1999	Netherlands	Single arm pre- and post-test study	Breast cancer screening or prophylactic mastectomy	Women with a family history of breast cancer (51)	Mean 38 years	• Shared decision-making program including decision analysis
Eckman, 2018	USA	Single arm pre- and post-visit pilot study	Thromboprophylaxis	Patients with a diagnosis of non-valvular atrial fibrillation or atrial flutter (65)	Mean 66 years	• Shared decision-making tool including decision analysis
Unic, 2000	Netherlands	Single arm prospective descriptive pilot study	Breast cancer screening or prophylactic mastectomy	Women with a family history of breast cancer (51)	Mean 38 years	• Shared decision-making program including decision analysis
Knight, 2002	USA	Single arm pilot study	Treatment for localized prostate cancer	Men with newly diagnosed prostate cancer (13)	Mean 69 years	• Decision analysis
Pell, 2002	UK	Single arm pilot study	Prophylactic oophorectomy	Women with no ovarian pathology who agreed to have a hysterectomy (10)	Range 40 to 55 years	• Clinical guidance programme including decision analysis
Thomson, 2002	UK	Single arm feasibility study	Warfarin	Elderly atrial fibrillation patients	Mean 72 years	• Decision support tool including decision analysis
Lindhiem, 2017	USA	Single arm pilot study	Management of childhood anxiety	Children with depression and anxiety disorders and their parents (5*)	Range 7 to 17 years for children	• Decision support tool including decision analysis
Kuo, 1999	USA	Qualitative study	Management of urinary tract calculi	Patients with a history of stone diseases (180)	Mean 49 years	• Decision analysis
Bhavnani, 2002	UK	Qualitative pilot study	Prophylactic oophorectomy	Women about to undergo a hysterectomy (29)	Mean 46 years	• Decision chart • Clinical guidance programme including decision analysis

Weiss, 2004	UK	Qualitative study conducted alongside a randomised controlled trial	Antihypertensive medication	Adults with newly diagnosed hypertension (15)	Mean 60 years	• Usual care • Video/leaflet • Decision analysis • Decision analysis and video/leaflet
Emmett, 2007	UK	Qualitative pilot study	Mode of delivery after a previous caesarean section	Pregnant women with a previous caesarean section (26)	Mean 34 years	• Information program • Decision analysis program
Murtagh, 2007	USA	Qualitative study conducted alongside a randomised controlled trial	Warfarin or aspirin treatment	Older patients with atrial fibrillation (30)	Not reported	• Paper-based guidelines • Concise decision aid • Extended decision aid including decision analysis
Protheroe, 2007	UK	Mixed method study conducted alongside a randomised controlled trial	Treatment for menorrhagia	Women with menorrhagia (18)	Range 31 to 47 years	• Information leaflet plus a Clinical Guidance Tree including decision analysis
Pauker, 1987	USA	Case studies	Amniocentesis for prenatal diagnosis of maternal age-related chromosomal abnormalities	Pregnant couples referred for genetic counseling (10)	Mean 36 years	• Decision analysis
Gamble, 1995	USA	Case study	Surgical resection of a large abdominal aortic aneurysm	Male with an abdominal aortic aneurysm (1)	70 years	• Decision analysis
Chien, 2013	Taiwan	Case study	Palliative or surgical management of elderly patient with skin cancer	Elderly male diagnosed with skin cancer (1)	96 years	• Decision analysis
Hollinghurst, 2010	UK	Economic evaluation conducted alongside a randomised controlled trial	Mode of delivery after a previous caesarean section	Pregnant women with a previous caesarean section (524**)	33 years	• Usual care • Usual care plus information program • Usual care plus decision analysis program

* 5 parent-child dyads
** Data imputed for 115 women with known mode of delivery for a second dataset of 713

Table 2. Characteristics of the decision analysis intervention

Characteristic	N (%)
Type of decision analytic model	
Decision tree	16 (59%)
Markov	10 (37%)
Decision tree plus Markov	1 (4%)
Method of preference elicitation*	
Standard gamble	13 (48%)
Visual analogue scale	10 (37%)
Time trade-off	6 (22%)
Other	2 (7%)
Individual's clinical factors incorporated into the model	
Yes	19 (70%)
No/Not specified	8 (30%)
Output of the decision analytic model	
Expected utility	10 (37%)
Quality-adjusted life expectancy	6 (22%)
Quality-adjusted life years	3 (11%)
Other	1 (4%)
Not specified	7 (26%)
Sensitivity analyses conducted	
Yes	7 (26%)
No/Not specified	20 (74%)

Note: some studies had multiple methods of preference elicitation and types of output from the decision analytic model

Table 3. Data collection characteristics

Characteristic	N (%)
Who delivered the intervention	
Research team	15 (56%)
Healthcare provider	9 (33%)
Patient (self-administered)	3 (11%)
Who provided data	
Patient	25 (93%)
Healthcare provider	1 (4%)
Researcher	2 (7%)
Other	7 (26%)
Method of data collection	
Interview	14 (52%)
Survey/Questionnaire	16 (59%)
Medical records	4 (15%)
Observation (video/notes)	4 (15%)
Data collected at multiple time points	
Yes	12 (44%)
No	15 (56%)
Timing of data collection	
During consultation	23 (85%)
1 day – 2 weeks post-consultation	2 (7%)
3 weeks – 12 weeks post-consultation	7 (26%)
12 + weeks post-consultation	7 (26%)

Note: Some studies had multiple sources, methods and time points for data collection

Table 4. Type of outcomes measured

Outcome	N (%)
Treatment decision	16 (59%)
Decision analysis	
Decision analytic model recommendation	9 (33%)
Consistency between	
Treatment decision and decision analysis recommendation	14 (52%)
Physician recommendation and decision analysis recommendation	1 (4%)
Content-related outcomes*	6 (22%)
Decision-making process	
Impact on decision-making process*	12 (44%)
Decisional conflict	8 (30%)
Impact on treatment decisions*	5 (19%)
Participation	4 (15%)
Self-efficacy	1 (4%)
Decision Quality	
Knowledge	8 (30%)
Anxiety	6 (22%)
Satisfaction with decision	3 (11%)
Uncertainty	2 (7%)
Risk perception	2 (7%)
Decision burden	1 (4%)
Empowerment	1 (4%)
Informed decision-making	1 (4%)
Satisfaction with provider	1 (4%)
Healthcare resources	
Consultation length	14 (52%)
Treatment adherence	2 (7%)
Resource utilization	2 (7%)
Costs	1 (4%)

* Qualitative outcomes related to the use of the intervention

Appendix A. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	6
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	7
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	7 - 8
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix B
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	8 - 9

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	8 - 9
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	9
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	9
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	9 - 10
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	9 - 20
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	21, Appendix D
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	9 - 20
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	9 - 20
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	21
Limitations	20	Discuss the limitations of the scoping review process.	24
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	25
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	2

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to

systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

Appendix B. Medline (Ovid) search strategy

Line #	Search Terms
1	exp decision trees/
2	exp computer-assisted instruction/mt
3	decision tree.mp.
4	decision analytical framework*.mp.
5	decision analytic technique*.mp.
6	decision analytic model*.mp.
7	decision analysis.mp.
8	computerized decision support.mp.
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10	exp Patient Participation/
11	exp Patient-Centered Care/
12	exp Physician-Patient Relations/
13	exp Patient Education as Topic/
14	exp Patient Satisfaction/
15	exp Patient Preference/
16	patient*.ti.
17	physician*.ti.
18	doctor*.ti.
19	((health or healthcare) adj2 (provider or professional)).ti.
20	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21	exp Decision making/
22	exp Clinical decision making/
23	((support* or share* or sharing or informed or treatment or clinical or medical) adj2 (decid* or decision* or choice* or option*)).ti,ab.
24	((clinical or medical) adj2 (encounter or consult or consultation)).ti,ab.
25	exp Decision support techniques/
26	exp Decision support systems, clinical/
27	21 or 22 or 23 or 24 or 25 or 26

28	9 and 20 and 27
29	Limit 28 to (English language)

Appendix C. Decision analytic models

Models	Characteristics	Advantages	Limitations
Decision tree	Used mainly for representing acute diseases, based on hypothetical closed cohorts and reduced time horizon.	Simple and transparent.	Does not take into account the recurring events and time-span. Includes individuals with similar characteristics.
Markov model	Usually represents chronic diseases, based on hypothetical closed cohorts and long time horizon. Explains the time-span through cycles. Includes recurring events.	Are usually simple to develop, calculate and analyze.	Ignores the interaction between individuals or groups. The cycle duration in constant, throughout time. Usually considers few health states. In most of cases the individuals have similar characteristics.
Discrete event simulation	Represents chronic diseases based on microsimulation, through stochastic processes and long time horizon. Considers the time-span in a continuous form. The recurring events may be influenced by the characteristics of the patients, time-span, interactions between patients, and resource constraints.	Considers individuals with different characteristics, which tend to vary over time. Events may occur at any time. Resource constraint can be included in the model.	Needs the simulation of a great number of individuals so the model can be stable. Demands advanced knowledge in statistics and programming. Requires a great volume of parameters, not always available on literature. Needs to be calibrated.
Dynamic model	Focus on infectious diseases, with interactions between people and groups. Enables the inclusion of direct and indirect effects of an intervention, such as the reduction of susceptible individuals. Can be conducted through open or closed cohorts.	Externalities of the disease can be considered. The transition probabilities depend on the health situation of other individuals.	Demands advanced knowledge in statistics and programming. Time horizons tend to limit the attractiveness of this model.

Source: Silva, Everton Nunes da, Silva, Marcus Tolentino, & Pereira, Maurício Gomes. (2016). Analytical models in economic evaluation studies. *Epidemiologia e Serviços de Saúde*, *25*(4), 855-858. https://dx.doi.org/10.5123/s1679-49742016000400020

Appendix D. Risk of bias assessments

Table 1. Risk of bias for randomized controlled trials: Clancy, 1988

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Definitely no	- Originally randomized using random number tables but afterwards all incoming residents assigned to decision analysis group.
2. Was the allocation adequately concealed?	Probably no	- Not specified.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Definitely no	- Participants not blinded given the nature of the intervention.
b. Were healthcare providers/research team blinded?	Definitely no	- The research team contacted all physicians who received an individualized decision analysis and a random sample of physicians from other groups were asked if they knew their antibody status or if they had received the vaccine.
c. Were data collectors blinded?	Probably no	- Not specified.
d. Were outcome assessors blinded?	Probably yes	- Not specified. However, outcome measurement is not likely influenced by lack of blinding since the primary outcome (physicians' decisions about vaccination) was determined by examining medical records.
e. Were data analysts blinded?	Probably no	- Not specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Definitely no	- High rate of missing data, with only 95 out of the 753 (13%) physicians offered a decision analysis returning the mailed questionnaire. - Reasons for not completing the questionnaire unclear.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- No protocol provided but no evidence of selective reporting.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably no	- Possibility of selection bias due to non-randomized participants added to decision analysis group (there were significant differences in training status and vaccination intent among study groups) and low response rate (significantly more subjects who

		requested decision analysis intended to be vaccinated before the study began, and significantly more were residents, who were screened or vaccinated more often than faculty).

Table 2. Risk of bias for randomized controlled trials: Rothert, 1977 and Holmes-Rovner, 1999

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Probably yes	- Detail lacking but the authors note that participants were "randomly assigned to one of three interventions."
2. Was the allocation adequately concealed?	Probably no	- Not specified.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Definitely no	- Not specified but blinding would not be possible given the nature of the interventions.
b. Were healthcare providers/research team blinded?	Definitely no	- Not specified but blinding would not be possible given the nature of the interventions.
c. Were data collectors blinded?	Probably no	- Not specified.
d. Were outcome assessors blinded?	Probably no	- Not specified.
e. Were data analysts blinded?	Probably no	- Not specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Probably no	- 252 (84%) completed all sessions and 202 (81%) provided follow- up data. - Women who were postmenopausal were more likely to leave the study and there was a higher proportion of attrition among the small number of African American women. - Reasons for loss to follow-up not reported.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- No protocol provided but no evidence of selective reporting.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably no	- Possibility of selection since recruitment occurred through print and TV media, and from a specific university community. - Possibility of bias due to financial incentives (raffle for cash prizes) for participation.

Table 3. Risk of bias for randomized controlled trials: Bekker, 2004

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Probably yes	- Not specified.
2. Was the allocation adequately concealed?	Probably yes	- Participants were randomly allocated to one of two consultations using previously numbered, sealed, opaque envelopes.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Probably no	- While participants were not told which consultation was routine, they could not be completely blinded due to the nature of the intervention.
b. Were healthcare providers/research team blinded?	Definitely no	- The same professional delivered the routine and intervention consultations.
c. Were data collectors blinded?	Probably no	- Not specified.
d. Were outcome assessors blinded?	Probably no	- Not specified.
e. Were data analysts blinded?	Probably no	- Not specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Probably no	- Moderate loss to follow-up, with 68 out of 100 (68%) one-month questionnaires returned. - There were no differences in return rates of the one-month questionnaire by group allocation. - Those not returning the one-month questionnaire were more likely to have a family history of abnormality and to have GCSE qualifications or less.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- No protocol provided but no evidence of selective reporting.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably no	- Twice as many women in the routine care group had a family history abnormality compared to the usual care group. - Test uptake consistent with published literature and the study appears to be free of other sources of bias.

Table 4. Risk of bias for randomized controlled trials: Roosmalen, 2004

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Definitely yes	- The randomization schedule was generated by computer.
2. Was the allocation adequately concealed?	Probably no	- Method of allocation not specified but unlikely that it was adequately concealed since study participants and members of the study staff were not blinded to intervention assignment.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Definitely no	- Study participants were not blinded to intervention assignment.
b. Were healthcare providers/research team blinded?	Definitely no	- Study staff were not blinded to intervention assignment.
c. Were data collectors blinded?	Definitely no	- Data required involvement of the research team who would know which intervention the women received.
d. Were outcome assessors blinded?	Definitely no	- Outcomes assessed by patients, who were not blinded.
e. Were data analysts blinded?	Probably no	- Not specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Definitely yes	- Minimal loss to follow-up, with 88 out of 89 (99%) eligible women participating in the second part of the study reported in this publication. - Reasons for non-participation listed.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- No protocol provided but no evidence of selective reporting.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably no	- Visual inspection of Table 1 noted some baseline imbalances between groups with respected to age and family history of breast and/or ovarian cancer despite the authors reporting "no significant differences were found between the SDMI and control group." - The authors acknowledge that some of the significant differences observed in this study could be due to chance, given the number of statistical tests conducted. - The study appears to be free of other sources of bias.

Table 5. Risk of bias for randomized controlled trials: Montgomery, 2003

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Definitely yes	- Allocation schedule was computer-generated by an individual not involved in the study and executed by one of the authors.
2. Was the allocation adequately concealed?	Probably yes	- No clear detail provided as to how patients were allocated to interventions. However, allocation was executed by one of the authors, to whom the allocation was concealed in advance by the nature of the minimisation procedure.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Definitely no	- Given the nature of the interventions, there was no masking of participants.
b. Were healthcare providers/research team blinded?	Definitely no	- Given the nature of the interventions, there was no blinding for the researcher administering the interventions.
c. Were data collectors blinded?	Probably no	No blinding specified.
d. Were outcome assessors blinded?	Definitely no	- Blinding was not possible for outcome assessment, as this was conducted principally through self-completed questionnaires.
e. Were data analysts blinded?	Probably no	No blinding specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Definitely yes	- Loss to follow-up moderate, with 258 participants recruited and 212 (82%) analyzed. - Reasons for loss to follow-up noted. - No difference between consenting and non-consenting participants in terms of age and sex.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- No protocol provided but no evidence of selective reporting.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably yes	- All decision analysis consultations were given by one of the research team. - The study appears to be free of other sources of bias.

Table 6. Risk of bias for randomized controlled trials: Montgomery, 2007

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Definitely yes	- One member of the study team generated the randomisation sequence by computer.
2. Was the allocation adequately concealed?	Definitely yes	- A member of staff with no other involvement in the trial performed the allocation.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
f. Were patients blinded?	Definitely no	- Women in the intervention groups had an appointment with a member of the research team, who administered the intervention. Women in usual care did not have any appointment and proceeded with usual care.
g. Were healthcare providers/research team blinded?	Definitely no	- Stickers in the woman's medical records alerted health professionals to her participation in the study. Women in the decision analysis group received a printout of the decision analysis results, which they were encouraged to discuss this with their provider at antenatal visits. - Women allocated to receive an intervention had an appointment with a member of the research team, who administered the decision aid with a laptop computer.
h. Were data collectors blinded?	Probably no	- No blinding specified.
i. Were outcome assessors blinded?	Probably no	- No blinding specified.
j. Were data analysts blinded?	Probably no	- No blinding specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Probably yes	- Of 1148 women invited to participate in the trial, 742 were randomised, and primary outcome data were obtained for 600 (81%) for the decisional conflict scale and 713 (96%) for mode of delivery. - Women who consented to participate were slightly older (P=0.05) and less deprived (P=0.02) than those who did not take part.
5. Are reports of the study free of selective outcome reporting?	Definitely yes	- The study protocol is available (Montgomery AA, DiAMOND Study Group. The DiAMOND trial protocol: a randomised

		controlled trial of two decision aids formode of delivery among women with a previous caesarean section [ISRCTN84367722]. BMC Pregnancy Childbirth 2004;4;25.) - Pre-specified outcomes have been reported in the pre-specified way. - Erratum to published protocol available online.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably yes	- The study appears to be free of other sources of bias.

Table 7. Risk of bias for randomized controlled trials: Protheroe, 2007

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Definitely yes	- Allocation was achieved using computer generated randomization.
2. Was the allocation adequately concealed?	Definitely yes	- Allocation was concealed from the individual who was making judgments of eligibility.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Definitely no	- Women randomized to the control group received a freely available patient information leaflet. Women randomized to the intervention group received the information leaflet and a decision aid in the form of a self-directed, computerized Clinical Guidance Tree.
b. Were healthcare providers/research team blinded?	Definitely no	- While intervention was designed to be self-directed, the use of the decision aid was facilitated by a researcher whose presence will affect outcomes. Efforts were made to minimize this by explaining to participants that the presence of the researcher was merely to facilitate the use of the computer program.
c. Were data collectors blinded?	Probably no	- No blinding specified.
d. Were outcome assessors blinded?	Probably no	- No blinding specified.
e. Were data analysts blinded?	Probably no	- No blinding specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Probably yes	- It is possible that there are systematic differences between participating and nonparticipating practices. Within each practice, similar proportions of women invited to participate agreed to do so, and there were no marked differences between participants and nonparticipants in terms of age. - 116 out of 144 (81%) participants provided 6-month follow-up data.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- A study protocol is not cited but it appears that the published reports includes all expected outcomes.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably yes	- The study appears to be free of other sources of bias.

Table 8. Risk of bias for randomized controlled trials: Thomson, 2007

Item	Judgement	Rationale
1. Was the allocation sequence adequately generated?	Definitely yes	- Electronically-generated random permuted blocks via a web-based randomisation service.
2. Was the allocation adequately concealed?	Definitely yes	- Central allocation using a web-based randomisation service provided by the Centre for Health Services Research.
3. Blinding: was knowledge of the allocated interventions adequately prevented?		
a. Were patients blinded?	Definitely no	- Blinding not possible given the nature of the intervention.
b. Were healthcare providers/research team blinded?	Definitely no	- All participants were seen in one of two research clinics each conducted by a single doctor, trained in delivering either the decision aid or guidelines but blinded to the alternative method.
c. Were data collectors blinded?	Probably no	- No blinding specified.
d. Were outcome assessors blinded?	Probably no	- No blinding specified.
e. Were data analysts blinded?	Probably no	- No blinding specified.
4. Was loss to follow-up (missing outcome data) infrequent?	Probably yes	- 145 participants randomized and 105 (72%) had 3 month follow-up data. - Reasons for non-participation listed but no analysis on the difference between participants versus non-participants.
5. Are reports of the study free of selective outcome reporting?	Probably yes	- A study protocol is not cited but it appears that the published reports includes all expected outcomes.
6. Was the study apparently free of other problems that could put it at risk of bias?	Probably yes	- Early in the trial, the observational study showed that participants in the explicit arm found the elicitation of utilities using the standard gamble to be difficult, so this arm was discontinued. The authors state that this does not affect the validity of the comparison between the remaining arms, the design of which remained unchanged. - The study appears to be free of other sources of bias.

Table 9. Risk of bias for pre- post study: Staleimer 1999

Domain	Judgement	Support for judgement
Bias due to confounding	Serious	- Inclusion criteria are mentioned and important baseline characteristics of the participants, such as age, education and genetic status, are reported. - Potential for 62 extraneous events or changes in context around the time of the intervention (woman learning her genetic status as a mutation carrier) to influence certain outcomes (emotional reactions). Additional analyses (binary variables created for known genetic status known) were conducted to explore impact on outcomes. - Measurements of outcomes were made over four sessions. Pre-intervention time point may not be sufficient to permit characterization of pre-intervention trends and patterns since data were collected after a utility assessment, which may influence certain outcome measures (decision burden, uncertainty).
Bias in selection of participants into the study	Low	- All participants who would have been eligible for the target trial were included in the trial and women were followed from pre to post intervention. - No evidence for changes in selection of participants after the start of the intervention. Due to structure of the intervention, the start of intervention, intervention delivery and follow-up coincide for participants.
Bias in classification of interventions	Moderate	- Intervention and eligibility status were clearly defined. - While all women received the same intervention, the delivery of decision analysis results depended on genetic status. For women whose genetic statuses were unknown, decision-analytic results were presented under the alternative assumptions of being a carrier and of being a non-carrier of a mutation. If a woman's genetic status became known after the last session, she was invited to repeat it.
Bias due to deviations from intended interventions	Low	- There is no evidence for deviations from the intended intervention beyond what is expected in usual practice.
Bias due to missing data	Low	- Proportions of women refusing to participate (18/72) somewhat high but the drop-out (3/54) is small. - Reasons for non-participation are listed. - While the proportions slightly differ between participants and non-participants, there were no statistically significant differences in terms of age, marital status, employment or education.
Bias in measurement of the outcome	Serious	- The outcome measure could have been influenced by the implementation of the intervention since participants were encouraged to ask questions and to discuss relevant topics with the research team as they completed the questionnaire. - It was noted that family members were allowed to be present during the sessions.

		However, their involvement, the number of sessions attended and influence on the outcome measures is not analysed or reported.
Bias in selection of the reported result	Low	- All initially specified outcomes were reported adequately, and reliability analyses were conducted for all measures containing multiple items. - There was no multiple analysis. - Subgroup analyses conducted according to whether the woman's genetic status was known.
Overall	Serious	- The study is judged to be at serious risk of bias in at least one domain, but not at critical risk of bias in any domain. - The study has some important problems.

Table 10. Risk of bias for pre- post study: Eckman 2018

Domain	Judgement	Support for judgement
Bias due to confounding	Low	- Inclusion criteria are mentioned and important baseline characteristics of the participants, such as age, education and gender are reported. - No indication that potential extraneous events or changes in context around the time of the intervention could influence outcomes. - Pre-intervention time point sufficient to permit characterization of pre-intervention trends and patterns.
Bias in selection of participants into the study	Low	- All participants who would have been eligible for the target trial were included in the trial and followed from pre to post intervention. - No evidence for changes in selection of participants after the start of the intervention. - Due to structure of the study, start of intervention, intervention delivery and follow-up times coincide for participants.
Bias in classification of interventions	Low	- Intervention and eligibility status were clearly defined. - All participants received the same intervention. - No distinction between pre-intervention or post-intervention time points that could have been influenced by the outcome data.
Bias due to deviations from intended interventions	Moderate	- It is unclear how the involvement of cardiologists affected intervention delivery (eg, number of cardiologists using the tool, training received for the tool, level of comfort regarding technical components of the tool, and style of consultation). Following the utility assessment (and before follow-up data collection) each patient met with their cardiologist in the Arrhythmia Center for a shared decision-making discussion, using results of the tool along with their expertise and judgement to review whether the patient's current treatment decision still made sense in light of best evidence, reflected in the tool, and the patient's preferences. - There is no other evidence for deviations from the intended intervention beyond what is expected in usual practice. - No indication that outcome measurement methods changed between pre- and post-intervention periods.
Bias due to missing data	Moderate	- Proportion of consenting patients who did not complete the study (11/76) moderate. - Reasons for non-participation are listed. - No analyses conducted to compare participants versus non-participants.
Bias in measurement of the outcome	Low	- The methods of outcome assessment were comparable before and after the intervention. - No evidence of error in measuring the outcome related to intervention status.
Bias in selection of the reported result	Low	- Hypotheses are pre-specified and reported results correspond to a statistical analysis plan detailing intended outcomes and analyses.

		- There was no multiple analysis. - Subgroup analyses were not conducted.
Overall	Moderate	- The study is judged to be at low or moderate risk of bias for all domains. - The study appears to provide sound evidence for a non-randomized study but cannot be considered comparable to a well-performed randomized trial

CHAPTER 3. DECISION ANALYSIS IN SHARED DECISION MAKING FOR THROMBOPROPHYLAXIS DURING PREGNANCY (DASH-TOP): A SEQUENTIAL EXPLANATORY MIXED METHODS PILOT STUDY PROTOCOL

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Decision Analysis in SHared decision making for Thromboprophylaxis during Pregnancy (DASH-TOP): A sequential explanatory mixed methods pilot study protocol

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Abstract

Introduction: Decision analysis is a quantitative approach to decision-making that could bridge the gap between decisions based solely on evidence and the unique values and preferences of individual patients, a feature especially important when existing evidence cannot support clear recommendations and there is a close balance between harms and benefits for the treatment options under consideration. Low molecular weight heparin (LMWH) for the prevention of venous thromboembolism (VTE) during pregnancy represents one such situation. The objective of this paper is to describe the rationale and methodology of a pilot study that will explore the application of decision analysis to a shared decision-making process involving prophylactic LMWH for pregnant women or those considering pregnancy who have experienced a VTE.

Methods and analysis: We will conduct an international, mixed methods, explanatory, sequential study, including quantitative data collection and analysis followed by qualitative data collection and analysis. In Step I, we will ask women who are pregnant or considering pregnancy and have experienced VTE to participate in a shared decision-making intervention for prophylactic LMWH. The intervention consists of three components: a direct choice exercise, a values elicitation exercise, and a personalized decision analysis. After administration of the intervention, we will ask women to make a treatment decision and measure decisional conflict, self-efficacy, and satisfaction. In Step II, which follows the analysis of quantitative data, we will use the results to inform the qualitative interview. Step III will be a qualitative descriptive study that explores

participants' experiences and perceptions of the intervention. In Step IV, we will integrate findings from the qualitative and quantitative analyses to obtain meta-inferences.

Ethics and dissemination: Site-specific ethics boards have approved the study. All participants will provide informed consent. The research team will take an integrated approach to knowledge translation.

Introduction

Thromboprophylaxis during pregnancy

Venous thromboembolism (VTE) is a condition in which a blood clot forms in the deep veins of the leg, groin or arm (deep vein thrombosis [DVT]) and travels to the lungs (pulmonary embolism [PE]). Globally, VTE is a leading cause of maternal morbidity and mortality.[1,2] In high-income countries, the incidence of VTE is 1.2 in 1,000 pregnancies and deaths in 1.1 per 100,000 deliveries.[3] Women with prior VTE are at an increased risk of thrombosis during subsequent pregnancies,[4,5] although the magnitude of this risk remains uncertain given that the existing evidence base is informed by studies with major limitations.[6]

Because it does not traverse the placenta and is associated with a low risk of heparin induced thrombocytopenia and osteopenia, low molecular weight heparin (LMWH) represents the preferred treatment option for the prevention of VTE during pregnancy over other antithrombotic therapies, such as unfractionated heparin.[7-9] It is, however, expensive and requires daily subcutaneous injections.[10] Prophylactic LMWH may be associated with an increased risk of major bleeding, especially around the time of delivery, and may limit access to regional analgesia.[7,11] There continue to be challenges in determining the appropriate pregnancy-specific dose and role of laboratory monitoring. Due to uncertainty regarding available evidence as well as the costs associated with administration and monitoring, the American Society of Hematology recommends that the decision between prophylactic LMWH during pregnancy versus expectant management involving no LMWH be made using a shared decision-making process.[9] The

use of decision aids is suggested for this type of conditional recommendation (i.e., recommendation based on weak evidence) as they may help individuals make decisions consistent with their risks, values, and preferences. Despite this call for shared decision-making, a paucity of decision support tools exist to help patients engage in treatment decisions for VTE.[12]

Shared decision-making and the clinical encounter

Shared decision-making is a continuum process through which patients and clinicians work together to make a treatment decision.[13] Although there is no consensus regarding the definition of shared decision-making,[14] three elements are considered necessary: 1) recognizing a decision is required; 2) knowing and understanding the best available evidence; and 3) incorporating patient values and preferences into the decision.[15] Although a key element is the incorporation of patient values and preferences into the decision,[15] studies indicate they are often ignored or poorly understood by providers.[16,17]

A number of decision support technologies to facilitate shared decision-making exist. Decision aids are the most commonly used tool. Available in a variety of formats (e.g., online, print, video), decision aids are meant to inform patients regarding treatment options and their associated potential benefits, harms and costs.[18,19] These tools often entail an implicit method of values clarification, in which patients are encouraged to think about what's important to them.[20] A systematic review of 105 randomized controlled trials involving 31,043 patients found that, while decision aids helped patients make more

informed decisions,[21] there is uncertainty as to how these tools support the process of integrating patient values and preferences into the decision-making process.

The International Patient Decision Aid Standards Collaboration recommends that decision aids include a value elicitation exercise alongside the presentation of evidence.[22] A variety of methods can help patients appraise their values regarding treatment options under consideration. For example, patients can complete a ranking exercise to express the relative importance of each outcome. Although eliciting patients' values is important, it does not ensure that they are incorporated into the decision-making process. Furthermore, patients and providers then face the cognitive challenge of weighing the harms and benefits of each treatment option alongside their probabilities of occurring and the patient's values and preferences.[23-25]

Decision analysis

Decision analysis is a decision support technology that could bridge the gap between decisions based solely on evidence and the values and preferences of individual patients. It involves structuring a decision problem using an analytical framework (e.g., decision tree) that includes key clinical outcomes associated with each treatment option as well as the natural course of untreated illness along with their associated probabilities and utilities or other weighting factors based on patients' values and preferences. Probabilities, a measure of likelihood that an event will occur,[26] are obtained from published studies, and may themselves be personalized based on individual patient's clinical risk profile. Values and preferences for health outcomes, which are expressed as health utilities, can be obtained directly from patients.[27] Utility assessment involves

comparisons to anchor health states (i.e., perfect health and death), and may involve gambles that entail a risk of undesirable outcomes, or tradeoffs between quality and quantity of life. Utility scores can be elicited directly from patients using exercises such as the standard gamble, time trade off and visual analogue scale.[28] Utility scores typically are anchored 1 representing "Perfect health" and 0 representing the "Dead" state. Utility scores can be used in a personalized decision analysis to calculate the quality-adjusted life years (QALYs) for each treatment option under consideration. For example, if a treatment results in a life expectancy of 10 years, but the quality of life for the resulting health state has a utility of 0.9, the treatment would yield 9.0 QALYs. If multiple treatment options are being considered, the treatment with the highest quality-adjusted life expectancy represents the best option.[27] Thus, patient-specific probabilities and utility scores can be used in a decision analysis to calculate personalized results and obtain an explicit guidance statement to facilitate decision-making.[29,30]

Decision analysis for shared decision-making

Several studies found a disagreement between the results of the decision analysis and treatment guidelines.[31-33] This suggests that guidelines, despite including a range of inputs (clinical evidence, patient preferences) and potential outcomes, might not adequately respond to individual patient treatment decisions.

Current evidence, although limited, shows the potential for personalized decision analysis to improve shared decision-making in clinical contexts.[31-41] While decision analysis is increasingly being used to inform the management of pregnancy-related conditions,[42] its use is fraught with challenges. These include competing interests of

mother and fetus, the use of appropriate time horizons and challenges with using QALYs as an outcome measure for combined maternal-fetal health states.[43] As a result, it is unclear how or if decision analysis should be incorporated within shared decision-making surrounding VTE and pregnancy, which necessitates a robust approach to shared decision-making given the close balance between benefits and harms of LMWH and limitations of available evidence.

Objective

The objective of this study is to explore the application of decision analysis to a shared decision-making process for the decision of using prophylactic LMWH for pregnant women or those considering pregnancy who have experienced a VTE. The study will also inform the design and execution of a future randomized controlled trial that will evaluate the additional value of decision analysis in the clinical encounter for the same decision.

Methods and analysis

In this study, we will use an explanatory sequential mixed methods design, which consists of quantitative data collection and analysis followed by qualitative data collection and analysis. This type of study design will allow for a comprehensive evaluation of decision analysis within a shared decision-making encounter for VTE and pregnancy.

In a mixed methods study, separate research questions are specified for the quantitative and qualitative components of the study, as well as an overarching mixed

methods question.[44] The following research questions will guide the conduct of this study:

- Quantitative research question
    - Using a shared decision-making process that incorporates decision analysis, what is the level of decision quality among women that are pregnant or considering pregnancy who have experienced VTE and must decide whether to take LMWH?
- Qualitative research question
    - What are the experiences and perceptions related to a shared decision-making process that incorporates decision analysis among women that are pregnant or considering pregnancy who have experienced VTE and must decide whether to take LMWH?
- Mixed methods research question
    - How do the qualitative findings provide an enhanced understanding of quantitative results on decision quality, to evaluate the application of decision analysis to a shared decision-making process among women who are pregnant or considering pregnancy and have experienced a VTE and must decide whether to take LMWH?

Figure 1 presents the study flow of this multicentre, single arm, intervention pilot study. In Step I, we will administer the intervention and measure decision quality among women who are pregnant or considering pregnancy and have experienced a VTE and must decide whether to take prophylactic LMWH. Step II follows the analysis of

quantitative data, whereby we will use the quantitative results to inform qualitative data collection. In Step III, we will conduct a qualitative descriptive study with all participants to explore their experiences and perceptions related to the intervention. In Step IV, we will integrate findings from the quantitative and quantitative analyses to obtain inferences that add insight beyond what could be understood from either dataset on their own (meta-inferences).[44]

STEP I: Administration of intervention and quantitative data collection

Study design

In Step I, we will ask women who are pregnant or considering pregnancy and have experienced VTE to participate in a shared decision-making intervention for prophylactic LMWH. The intervention will use a personalized decision analysis as a complementary approach to a decision aid. Since this study aims to pilot test the use of the decision analysis tool and explore preliminary findings, a control group was not included because the study was not designed to compare effects between intervention and control groups.

Study setting

The study will recruit women from hospitals in Canada (n=2 sites) and Spain (n=4 sites). The decision to conduct an international study was made in consideration of the small size of the target population. Since it is estimated that complications due to VTE occur in approximately 1 in 1,000 pregnancies,[45] an international study will increase feasibility of recruitment and generalizability of results.

In a previous study conducted by the research team, we compared the use of direct-choice and decision analysis among 123 women with a history of VTE who were pregnant or planning pregnancy. During this study, we observed some differences between countries, including Canada and Spain.[46] Given that the research teams in these two countries have conducted similar studies together and staff at the selected study sites are already trained, these two countries were selected for the pilot sites.

Participants

The target population consists of women with a prior VTE who are pregnant or planning pregnancy and who have been referred for counseling regarding prophylactic LMWH. Women will be eligible for inclusion if they have a history of lower extremity DVT or PE, are currently pregnant or planning pregnancy, and considering LMWH. Women will be excluded from the study if they are currently receiving thromboprophylaxis or therapeutic anticoagulation, are less than 18 years of age, have contraindications or intolerances to LMWH, or are unwilling and/or unable to provide informed consent. At each site, the clinician will review medical charts to identify eligible women based on their pregnancy status and presence of a previous blood clot. The clinician will contact potential participants and ask if they are willing to be approached by a member of the research. With the woman's permission, the research team will contact the woman by telephone to explain the study, confirm eligibility and schedule the interview.

Since greater priority will be given to the qualitative component of this mixed methods study, the sample size will be determined in consideration of the amount of

information required to address the qualitative research question.[47] There are no formal rules for calculating a priori a sample size for qualitative studies, instead an estimate of the number of participants required is provided. We have estimated that we will need an initial purposeful sample of 30 women (n=5 per site) given that this is a fairly homogenous population of women with respect to their medical diagnoses and who are making these decisions within pregnancy. However, as data collection and analysis is concurrent in qualitative studies, if we determine towards the end of our recruitment that certain concepts are not fully saturated, then the decision will be made to continue recruitment until we reach saturation or "the point at which the data collection process no longer offers any new or relevant data."[48]

Intervention

The intervention will explore the decision-making process comparing strategies of administering prophylactic LMWH once daily when pregnancy is confirmed and continuing until delivery[7] versus expectant management without LMWH. The intervention has been designed with three components: a direct choice exercise, values elicitation exercise, and personalized decision analysis. All participants in the study will receive the intervention. A member of the research team will deliver the intervention and collect data in person or online using a web-based platform. The process is expected to take between 1 and 1.5 hours. Through this interview, some women may find the additional counselling and information received helpful in making their decision about the use of LMWH. All women will participate in the study prior to meeting with their healthcare provider so that they can apply this new information to their decision and

follow-up with a healthcare professional if they have any questions. We don't anticipate there is any risk associated with this interview in general nor with the length of time required to complete the interview; however, we do inform participants that they can stop participation at any point during the intervention and are free to not respond to questions they are uncomfortable with.

To start, women will be asked to consider four health states relevant to this decision: 1) use of LMWH; 2) major obstetrical bleed; 3) DVT; and 4) PE. Health state descriptions are available in Appendix A. Women will then complete a direct choice exercise that includes the review of an interactive electronic decision aid developed using the MagicApp platform.[49] The decision aid describes the harms and benefits of LMWH for prevention of pregnancy-related VTE. In line with IPDAS recommendations, information is presented in numeric and graphic format.[22] Figure 2 presents a screenshot of the decision aid.

The direct choice exercise will be followed by three value elicitation exercises (rank ordering, visual analogue scale and standard gamble)[50] that will be completed using Gambler II software.[51] Women will consider the four health states listed above. For the ranking exercise, women will rank the health states from most to least preferred. For the visual analogue scale, women will place each health state along a "feeling thermometer" that represents their preference on a scale of 0 (dead) to 100 (perfect health). Figure 3 presents a screenshot of the visual analogue scale exercise. The standard gamble uses a poison pill analogy to describe a gamble in which the patient can accept an intermediate health state, such as a PE, or take a medication that can prevent that from occurring. The

patient need only take a single pill from the bottle, but unfortunately some varying number of pills in the bottle are "poison" and may result in death. If a patient is indifferent between, for instance, a 0.1 risk of getting a poison pill to avoid a PE and prophylactic LMWH, then the utility of that health state would be calculated as (1 – 0.1) or 0.9.[35] Death will be used as the anchor for standard gambles relating to major obstetrical bleed, DVT and PE health states. In the standard gamble for the use of LMWH, DVT will be the anchor.

The visual analogue scale and ranking tasks will serve as warm-up exercises, with the standard gamble determining the value rating inputted into the decision analytic model. The standard gamble is considered to be a gold standard in preference elicitation methods as it has demonstrated acceptability and reliability,[52,53] as well as established theoretical underpinnings of expected utility theory.[54,55] Unlike ranking and the visual analogue scale, it evaluates preferences under conditions of uncertainty.

Once the utilities for a given patient have been obtained, they will be inputted into the decision analytic model along with patient-specific probabilities for VTE risk sourced from clinical guidelines.[9] The decision analytical model is a Markov state transition model that examines two treatment options under consideration: prophylactic LMWH versus expectant management without LMWH.[10] The model has a lifetime time horizon and a 6-week cycle length to simulate both antepartum and lifetime events. The model will be personalized according to women's age and risk of VTE, and utilities for each health state.[56,57] Based on this information, the decision analytical model will estimate the QALYs for each treatment option. The treatment with the greatest expected QALYs will

represent the recommended strategy. Figure 4 presents a screenshot of the decision analysis recommendation.

Data collection

At the start of the study, the research team will document women's age, level of education, pregnancy status, pregnancy number, details regarding prior VTE (e.g., type of event, presence of precipitating clinical risk factors), type and duration of treatment for prior VTE, and experience with LMWH (e.g., bruising, heparin-induced thrombocytopenia).

After completing the direct choice, values elicitation exercises and receiving the results of their personalized decision analysis, women will be asked to make a preliminary treatment decision. Women will make a final decision during the consultation with their provider. Women will complete a self-administered questionnaire to evaluate decision quality using the Modified Decisional Conflict Scale,[58] Decision Self-Efficacy Scale,[59-61] and Satisfaction with Decision Scale.[62] The Decisional Conflict Scale is a 16-item instrument that includes five subscales: Informed, Values, Support, Uncertainty, and Effective Decision. Response options, which range from 1 for 'strongly disagree' to 5 for 'strongly agree', are combined into a summary score that ranges from 0 to 100, with 100 indicating an extremely high level of decisional conflict. The Decision Self-Efficacy Scale is an 11-item instrument that measures confidence or belief in one's ability in decision-making. Items are given a value between 0 and 4, with 0 indicating 'not at all confident' and 4 'very confident'. These values are combined into a summary score that ranges from 0 for 'not confident' to 100 for 'extremely confident'. The Satisfaction with

Decision Scale measures satisfaction with healthcare decisions. It is a 6-item instrument that generates a summary score, ranging from 6 for 'low level of decision satisfaction' to 30 for 'high level of decision satisfaction'. While it is acknowledged that these measures of decision quality have limitations,[63] they are widely used and have been validated in different patient populations.[58,64-68] Selecting three measures will provide a starting point for understanding different facets of the shared decision-making process. The self-administered questionnaire is available in Appendix B.

Data analysis

We will use descriptive statistics to summarize women's age, level of education, pregnancy status, number and characteristics of previous VTE, and experience with LMWH. We will assess decision quality using the scores obtained from the Decisional Conflict Scale, Self-Efficacy Scale, and Satisfaction with Decision Scale. We will examine concordance between the woman's decision regarding LMWH and recommendation from the personalized decision analysis.

STEP II: Integration of quantitative results and planning of qualitative data collection

Based on the results of Step I, women will be stratified into four categories according to their treatment decision (LMWH, No LMWH), decision analysis recommendation (LMWH, No LMWH) and the concordance/discordance between the two. Figure 5 presents the categorization matrix. This is a form of integration in mixed methods research where one dataset (i.e., quantitative) is analyzed and used to inform subsequent data collection (i.e., qualitative).[69] The purpose is to identify what quantitative results need further explanation.

STEP III: Qualitative descriptive study

Study design

Step III is a qualitative descriptive study that will occur after the quantitative component is complete. Qualitative description is a method of inquiry that explores individuals' perceptions and experiences of a phenomenon.[70] The aim is to generate rich and straightforward descriptions of an experience that is rooted in the language used by participants.[71]

Participants

After completion of the multicentre, single arm, intervention study, all women will be invited to participate in the qualitative descriptive study.[72] Women will be stratified into four categories according to their treatment decision, decision analysis recommendation and the concordance/discordance between the two.

Data collection

In-depth, semi-structured interviews will be conducted to explore women's experiences and perceptions as they relate to: 1) the decision-making process; 2) the direct choice exercise; 3) the personalized decision analysis; and 4) their knowledge of LMWH. Explicitly linking to the quantitative results, four versions of the interview guide have been designed to address women's treatment decision, decision analysis recommendation, and the concordance/discordance between the two. The interview guide was developed and tested by the research team, which comprised clinicians, patients, and researchers with expertise in pregnancy-related VTE, shared decision-making and

qualitative methods. It is available in Appendix C. A member of the research team will conduct the interviews, which will be audio-recorded and transcribed verbatim.

Data analysis

Data from the interviews will be analyzed using a method of thematic analysis. Thematic analysis refers to the systematic search for and identification of themes that are present in data.[73] The aim is to obtain an understanding of a phenomenon by identifying themes or patterns through a process of coding.[74] Given the exploratory nature of this qualitative descriptive study, there will be no predetermined coding scheme.

Two members of the research team with training in qualitative analyses will conduct the thematic analysis following the 6-step approach outlined by Braun and Clarke (i.e., familiarizing with the data, generating initial codes, searching for themes, reviewing the themes, defining and naming themes, and producing the final report).[75] This process entails an iterative analysis within and across the transcripts of women from each of the four groups outlined in Figure 5, to gain insight into why there is concordance/discordance between treatment decisions and decision analysis recommendations among pregnant women with a previous VTE.[46]

Looking for overarching themes and relations between them, the investigators will independently code a sample of the transcripts independently to generate an initial codebook and definitions. They will meet with a third study investigator to discuss emerging themes and definitions of codes until consensus on a codebook is reached. To ensure reliability, two team members will code the transcripts using this codebook. They will document and discuss any inconsistencies. NVivo software[76] will facilitate this

analysis. Qualitative data collection and coding will be conducted in the language of origin. Canadian and Spanish team members will work collaboratively on developing a single codebook for the Spanish and English analyses, discussing emerging themes and discrepancies as part of this process. An investigator with proficiency in English and Spanish will compare the summaries of findings and write a synthesis of themes that highlights important differences if they exist.

STEP IV: Integration of quantitative and qualitative findings

Once the quantitative and qualitative analyses have been analyzed separately, the findings will be integrated using a joint display. A joint display is a table in which the quantitative and qualitative data are displayed alongside each other to enable an explicit comparison between datasets.[44] This is a form of integration at the interpretive level, whereby each data set remains analytically separate from the other.[77] The intent is to give a voice to study participants and ensure that quantitative findings are grounded in participants' experiences.

The joint display will present each theme from the qualitative analyses according to the mean scores obtained from the Decisional Conflict Scale, Self-Efficacy Scale, and Satisfaction with Decision Scale as well as the women's risk of VTE, utility values, treatment decision and decision analysis recommendation. If there are any outliers or differences across groups, the integrated analyses will aim to explain these through qualitative data. For example, qualitative data can be used to explore any inconsistencies in utility values that are produced by the standard gamble and inputted into the decision analytic framework.

There are many reasons an inconsistency could occur. Pregnancy can be accompanied by extreme risk aversion,[78] which could skew the standard gamble utility value and subsequent treatment recommendation. A qualitative evaluation of a shared decision-making intervention in atrial fibrillation reported that patients struggled to grasp the standard gamble concept,[79] which could result in utility values that are not representative of patients' preferences. By leveraging qualitative data on women's experiences and perceptions of the intervention and decision-making process, integration will enable the research team to obtain meta-inferences and a deeper understanding of the application of decision analysis to shared decision-making surrounding LMWH for pregnant women or those considering pregnancy who have experienced a VTE.

A joint display is an important tool for establishing the relationship between intervention effects and the patient experience. If the analysis identifies contradictions between quantitative and qualitative findings,[80] we will verify the methodological rigor of each component of the study, the comparability of datasets, and the delivery of the intervention.[81] We will also consider how these contradictions can generate new research questions.[82]

Methodological rigor

Although an international study ensures feasibility of recruitment, it poses a challenge of maintaining consistency in data collection across sites. We have taken several steps in the planning of this study to mitigate this issue. At each site, we will have highly qualified personnel who have experience working on a shared decision-making project for VTE prophylaxis. Professional translation agencies have translated the scripts

and interview guides developed in English into Spanish. Data collection materials have been tested with 3-5 patients at each site to ensure adequate understanding. To facilitate a standardized approach for administering the intervention, we have developed scripts based on feedback from patients, nurses and clinicians. All members of the research team will receive training on how to use required software programs.

Once recruitment starts, a range of strategies will be used to verify credibility (internal validity), dependability (reliability or consistency of findings) and confirmability (neutrality) of data. A list of these strategies is presented in Table 1. Given the complexity of mixed methods research,[83] the rigour of the quantitative, qualitative, and mixed methods components of the study will be assessed separately.[84]

Patient and public involvement

Three patients (n = 1 from Spain and n = 2 from Canada) joined the study team as patient advisors. The Canadian Venous Thromboembolism Clinical Trials and Outcomes Research (CanVECTOR) Network allowed our team to use their Partners Platform to recruit two Canadian patient-advisors. As part of this program, patients receive training on how to participate in the research process. For the Spanish site, a patient who is also nurse at one of the participating hospitals was asked to participate as an advisor.

The three patient advisors matched inclusion criteria for the study. They reviewed all study materials and met with the research team to provide feedback on the study design, intervention, scripts and data collection materials. The development of the qualitative research questions and selection of quantitative outcome measures were directly informed by these patients' priorities, experience, and preferences. An additional

five patients participated in preliminary testing of the intervention to provide feedback on the overall research process and ensure adequate understanding.

Patients will not be directly involved in the recruitment and conduct of the study. The results of the decision analysis will be communicated with patients participating in the study. Additional study materials (i.e., print outs of decision aid and health state descriptions) and published results will be made available to participants upon request.

Ethics and dissemination

Site-specific ethics boards have approved the study.

This study takes an integrated approach to knowledge translation that applies the principles of knowledge translation to the entire research process.[85] Eight patients have contributed to the design and pre-piloting of data collection materials. We will publish findings in peer-reviewed journals and present at key conferences, including meetings of the American Society of Hematology, International Society on Thrombosis and Haemostasias, Society of Medical Decision Making, and Guidelines International Network. We will also disseminate results within the GRADE community.

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Tables and figures

Table 1. Checklist of Strategies to Ensure Rigour in the Conduct and Reporting of the Study

Research step	Criteria	Action taken
Quantitative Component	Dependability	Data collection will be conducted using standardized scripts.
	Credibility, Confirmability	Reflexive notes will be taken during data collection to record situational information.
	Confirmability	Reasons for non-participation will be noted.
	Confirmability	All statistical analyses will be performed according to a pre-specified protocol.
Qualitative Component	Dependability	Data collection will be conducted used standardized scripts.
	Confirmability	Reasons for loss to follow-up will be noted.
	Credibility, Confirmability	Reflexive notes will be taken during data collection to record situational information.
	Dependability	A sample of the transcripts (*e.g.* 10%) from each site will be checked against the audio recordings.
	Credibility	More than one person will be involved in the analysis of interview data.
	Credibility	Persons involved in the analysis of interview transcripts will look for disconfirming data while developing themes to ensure that all aspects of the interviews were considered.
	Dependability	An investigator with proficiency in English and Spanish will compare the English and Spanish findings.
Mixed Methods Component	Credibility	The justification for using a mixed methods approach to answer the research question(s) will be described.
	Credibility	The study design will be described in terms of the purpose, priority and sequence of methods.

	Credibility	The process of integration will be described in terms of where it occurred, how it occurred and who participated in it.
	Credibility	The limitation of one method associated with the presence of the other method will be described.
	Credibility	Insights gained from mixing or integrating methods will be described.
	Credibility	The integration of quantitative and qualitative research methods will occur at multiple points of the mixed methods study (*e.g.* research question, sampling strategy and analysis).
	Confirmability, Dependability	Each data source will be triangulated to confirm convergence or divergence across datasets and study sites.
	Credibility	Inconsistencies between quantitative and qualitative findings will be explored.
	Credibility	The inferences derived from the quantitative and qualitative findings will be incorporated into meta-inferences.
Entire study	Confirmability	An audit trail will be maintained by the research coordinator to document all study decisions (and their rationale) and all sampling, data collection and analysis procedures implemented.
	Confirmability	Any deviations from the published protocol will be noted and justified to promote transparency of the research methods.

Figure 1. Study Flow Diagram for the DASH-TOP Study

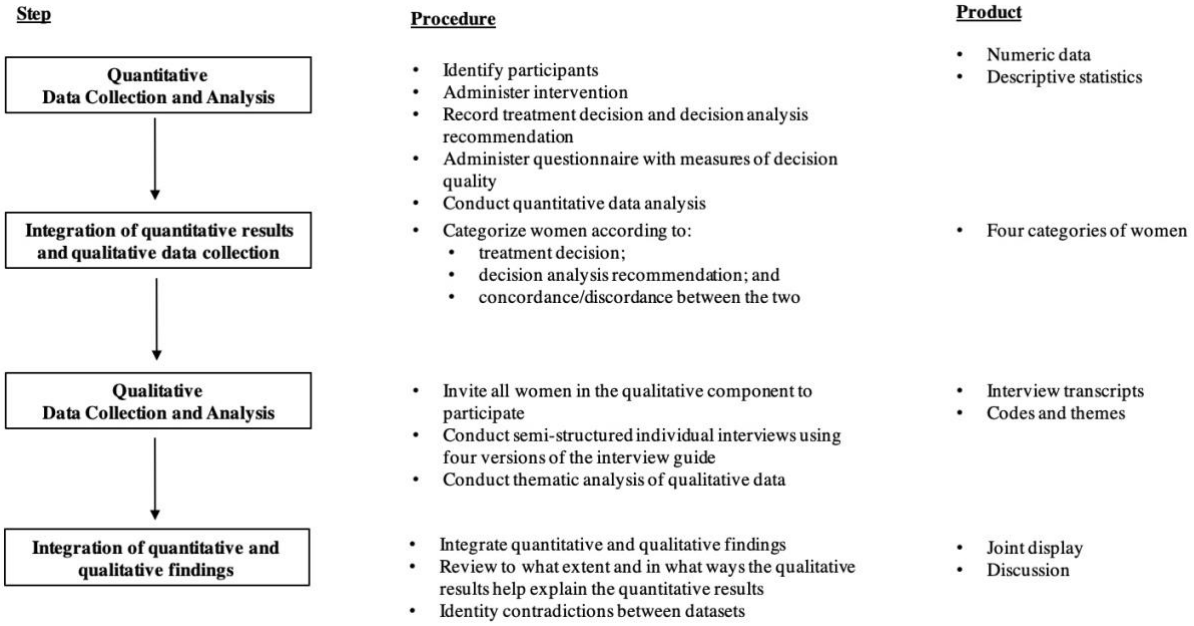
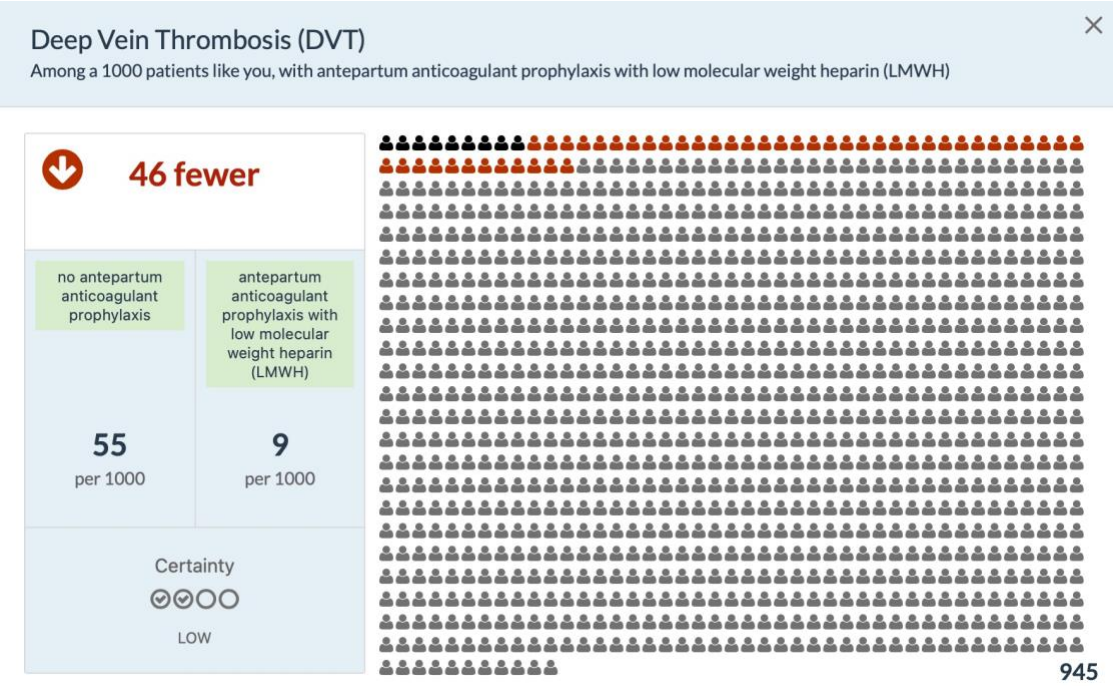


Figure 2. Screenshot of decision aid



Caption: This screenshot presents women with their estimated risk of experiencing a deep vein thrombosis (DVT). Risks are presented in both numerical and graphical format.

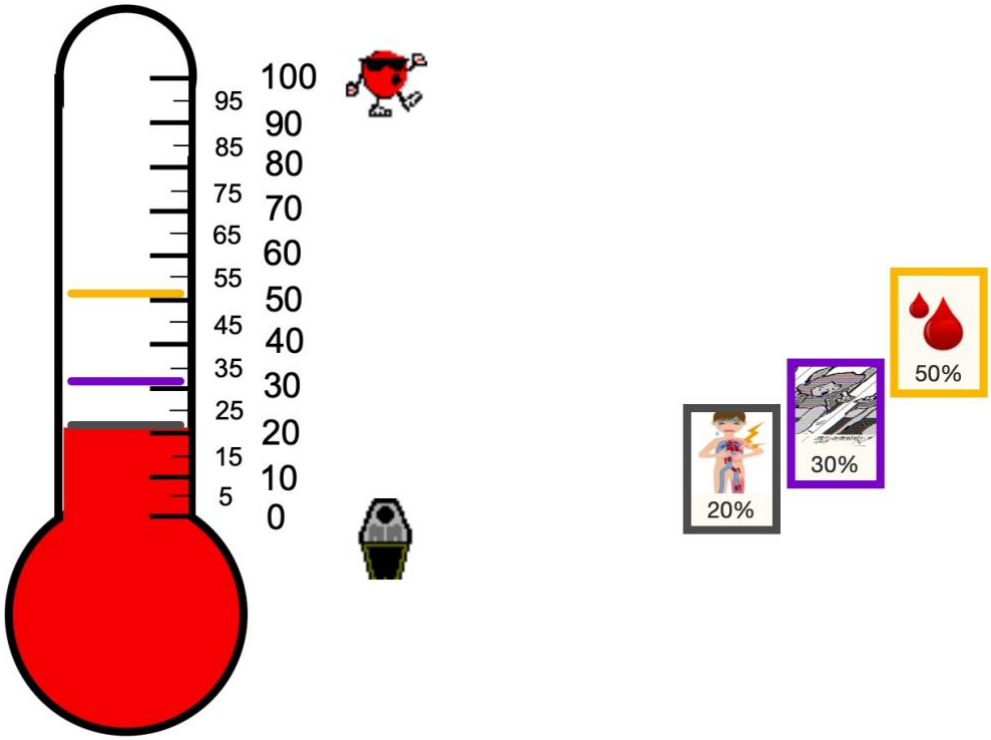
Numerically, the risk of DVT during pregnancy is 5.5%. This means that, out of 1,000 women, approximately 55 will experience a DVT if they do not take low molecular weight heparin (LMWH) and 9 will experience a DVT if they do take LMWH. Overall, 46 fewer women will experience a blood clot when taking LMWH compared to not taking LMWH.

The graphic represents a room of 1,000 women. The 945 figures who are coloured in gray represent those women who were not destined to experience a DVT and would take daily injections of medication for the rest of their pregnancy with no benefit. The 9 black

figures represent women who will take the medication regularly and still experience a DVT during pregnancy because LMWH is not 100% effective. The orange figures represent the 46 women who would have experienced a DVT in their pregnancy and will avoid the blood clot because they took LMWH.

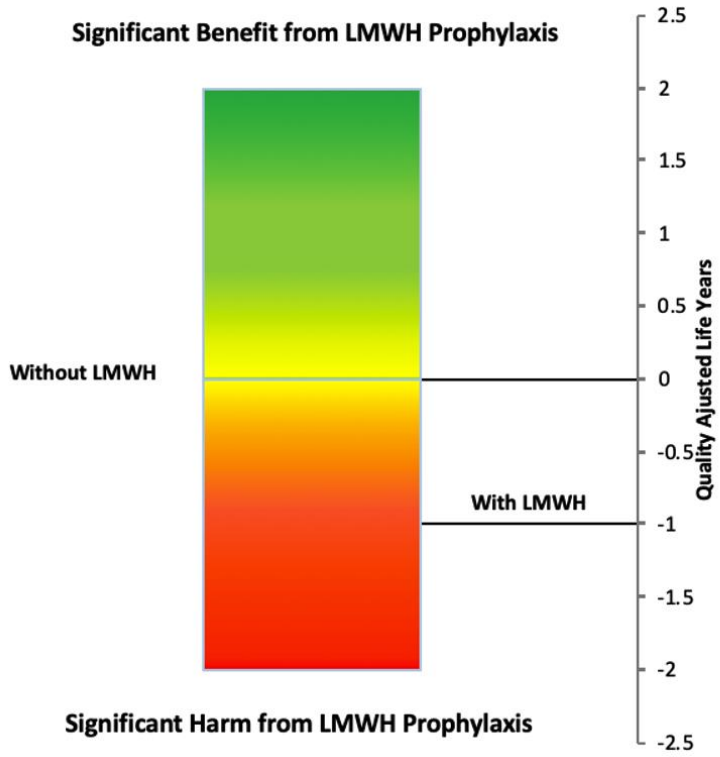
The overall certainty of the evidence informing these estimates is low due to the types of studies that were conducted and the small sample sizes.

Figure 3. Screenshot of visual analogue scale



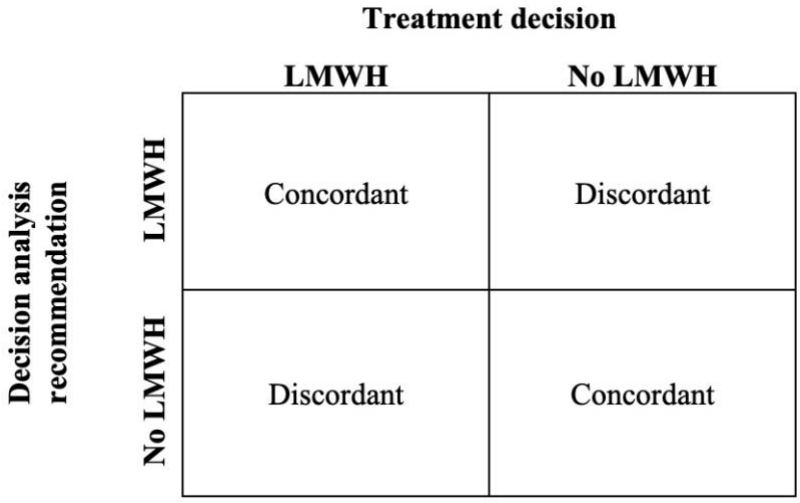
Caption: This screenshot demonstrates a visual analogue scale where participants are asked to place each health state along a "feeling thermometer" that represents their preference on a scale of 0 (dead) to 100 (perfect health). In this hypothetical example, pulmonary embolism, deep vein thrombosis and major bleed are rated as 20, 30 and 50 out of 100, respectively.

Figure 4. Screenshot of decision analysis recommendation



Caption: This screenshot shows how the personalized decision analysis results are presented to participants. In this example, the decision analytic framework calculated that the average quality adjusted life year (QALY) expected for treatment with low molecular weight heparin (LMWH) was -1 compared to expectant management without LMWH. In this case, no LMWH would be the recommended strategy because it has the greatest expected QALYs and represents the treatment option that maximizes the woman's quality of life based on available clinical evidence and the patient's preferences.

Figure 5. Categorization matrix based on quantitative results



Abbreviations: LMWH = low molecular weight heparin

Appendix A. Health state descriptions

Health state description for taking low molecular weight heparin

PRACTICAL ISSUES ABOUT TAKING LOW MOLECULAR WEIGHT HEPARIN (LMWH) TO PREVENT BLOOD CLOTS DURING PREGNANCY	
 Pregnancy and nursing	• You will take low molecular weight heparin for the rest of your pregnancy. • Because you are taking heparin, your doctor may need to make special plans for your delivery. If you go into labour when your blood is thinned, you may not be able to use the best way to reduce the pain of labour (a freezing needle in your back or epidural) and you may have a higher risk of bleeding. To prevent this, your doctor may decide that your delivery will be planned (also called an induction). If you go into labour early, your epidural may be delayed or you may not be able to receive one at all. • There are no long-term risks for you or for your baby from taking low molecular weight heparin during your pregnancy.
 Medication routine	• You or a family member needs to learn to administer low molecular weight heparin using needles beneath the skin for the rest of your pregnancy. • Your daily low molecular weight heparin needles may sting. • You will continue low molecular weight heparin for at least 6 weeks after your baby is born, either with needles or with a tablet. If you choose the tablet, you will need to have blood tests on a regular basis to make sure you are using the right dose.
 Adverse effects, interactions and antidote	• You may get a bruise at the place where you used the needle. • If you get a rash with the injections, you may need to use a different type of heparin. Less than 1% of pregnant women taking low molecular weight heparin will develop a more serious allergic reaction that can

	actually increase your risk of blood clots and will make it necessary to change to a different blood thinner. • You may experience thinning of the bones. We think it is unlikely that this thinning of the bones will lead to an increased risk of fracture; however, we don't know this for sure. • There are no long-term risks for you or for your baby from taking low molecular weight heparin during your pregnancy. Taking low molecular weight heparin does not increase your risk of miscarriage.

Health state description for deep vein thrombosis

PREGNANCY-ASSOCIATED BLOOD CLOT IN LEG – DEEP VEIN THROMBOSIS (DVT)	
Symptoms & Signs	• Your leg hurts and it swells. It hurts more if you go for more than a short walk.
Diagnosis & Treatment	• Your doctor does an ultrasound test that shows that you have a blood clot leg. You stay in the Emergency Department overnight. • You worry about the bad things that may happen to your baby because of this blood clot. • Your doctor treats you with blood thinning needles of low molecular weight heparin beneath your skin each day. You or a family member learns to give these needles. • Treatment of your blood clot goes on for your whole pregnancy and for at least 6 weeks after you have your baby. • After you have your baby, your doctor might give you the same needle or switch you to a tablet. If you use the tablet you will have to travel for regular blood tests.
Risks & Inconvenience	• The needles sting. You bruise at the place where you put in the needle. • You may get skin problems like itching or an itchy rash. If you get these problems, you may have to use a different type of heparin. • Even though your doctor tells you that your baby is safe, you are worried that these blood thinning needles may not be safe for your baby. • You doctor tells you that there may be a small increase in the risk of serious bleeding, thinning of the bones (osteoporosis) and having an allergic reaction to heparin called heparin-induced thrombocytopenia. If there is a risk, it is very small. • Because you are using low molecular weight heparin, your doctor will need to make special plans for your delivery. If you go into labour when your blood is thinned, you may not be able to use the best way to reduce the pain of labour (a freezing needle in your back or epidural) and you may have a higher risk of bleeding. To prevent this, your delivery will be planned (also called an induction). If you go into

	labour early, your epidural may be delayed or you may not be able to receive one at all.
Long-term Consequences	• There are no problems for your baby from the blood clot or from the low molecular weight heparin. • Your leg goes back to normal. After needles or tables are stopped, you feel worried sometimes if you have pains in your leg. • You have a higher risk of blood clots in the future (your risk may be 3 to 5% in the first year after you stop treatment; lower after that). • Your doctor asks you if you would like to be tested for a clotting disorder. • Your doctor tells you that you may have to take low molecular weight heparin needles if you get pregnant again.

Health state description for pulmonary embolism

PREGNANCY-ASSOCIATED BLOOD CLOT IN THE LUNGS – PULMONARY EMBOLISM (PE)	
Symptoms & Signs	• For the past 3 days you find it hard to breathe while sitting. You have to rest if you climb stairs or walk outside of your home. • You have pain in your chest when you take a breath. • You feel very worried about your health and your baby.
Diagnosis & Treatment	• You have a test. When you have the test, you get a small dose of radiation. The radiation probably does not have any risk for you or your baby. If there is any risk, it is very small. The test tells your doctor that you have a blood clot in your lungs. You have to stay in hospital for several days. • You worry about the effects this test and your blood clot might have on your baby. • At first, your doctor treats you with blood thinners in your veins. After that you use needles of low molecular weight heparin. You take these needles beneath your skin every day for the rest of your pregnancy. You or a family member learns to give these needles. • Treatment of your blood clot goes on for your whole pregnancy and for at least 6 weeks after you have your baby. • After you have your baby, your doctor might give you the same needles or switch you to a tablet. If you take the tablet, you will have to travel for regular blood tests.
Risks & Inconvenience	• The needles sting. You bruise at the place where you put in the needle. • You may get skin problems like itching or an itch rash. If you get these problems, you may have to use a different type of heparin. • Even though your doctor tells you that your baby is safe, you are worried that these blood thinning needles may not be safe for your baby. • Your doctor tells you that there may be a small increase in the risk of serious bleeding, thinning of the bones (osteoporosis), and having an allergic reaction to heparin called heparin-induced thrombocytopenia. If there is a risk, it is very small.

	• Because you are using low molecular weight heparin, your doctor will need to make special plans for your delivery. If you go into labour when your blood is thinned, you may not be able to use the best way to reduce the pain of labour (a freezing needle in your back or epidural) and you may have a higher risk of bleeding. To prevent this, your delivery will be planned (also called an induction). If you go into labour early, your epidural may be delayed or you may not be able to receive one at all.
Long-term Consequences	• There are no problems for your baby is not affected from the blood clot or from the low molecular weight heparin needles. • Your breathing goes back to normal. After the needles or tablets are stopped, you feel worried sometimes if you have a pain in your chest or if you find it hard to breathe. • You have a higher risk of blood clots in the future (your risk may be 3 to 5% in the first year after stopping treatment; lower after that). • Your doctor asks you if you would like to be tested for a clotting disorder. • Your doctor tells you that you may have to take low molecular weight heparin needles if you get pregnant again.

Health state description for major obstetrical bleed

MAJOR BLEED	
Symptoms & Signs	• You start to have pain in your abdomen, contractions and bleeding from your vagina in the later part of your pregnancy.
Treatment	• You have to stay in the hospital. • Your doctor places a needle in your vein. You get fluids through this needle. • Your stop taking your low molecular weight heparin. • You have more blood tests. • The doctor does an ultrasound to see how your baby is doing. • Your doctor does a test to see if you baby's heart is beating the way it should. • You stay in hospital for two or three days until your doctors are sure that your bleeding has slowed down or stopped. • Your doctor will see you frequently after you go home from the hospital.
Recovery	• You are worried about your baby's health. • You may deliver early and may be more likely to need a caesarean section.
Long-term Consequences	• Your baby is okay. • You feel worried with future pregnancies. • When you get pregnant again, your risk of similar bleeding problems is greater than if you had never had the bleeding problem. • In any future pregnancies, you will need to visit your doctor more often than if you had never had the bleeding problem.

Appendix B. Decision quality scales

Decisional Conflict Scale

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I know which options are available to me	1	2	3	4	5
I know the benefits of each option	1	2	3	4	5
I know the risks and side effects of each option	1	2	3	4	5
I am clear about which benefits matter most to me	1	2	3	4	5
I am clear about which risks and side effects matter most	1	2	3	4	5
I am clear about which is more important to me (the benefits or the risks and side effects)	1	2	3	4	5
I have enough support from others to make a choice	1	2	3	4	5
I am choosing without pressure from others	1	2	3	4	5
I have enough advice to make a choice	1	2	3	4	5
. I am clear about the best choice for me	1	2	3	4	5
. I feel sure about what to choose	1	2	3	4	5
. This decision is easy for me to make	1	2	3	4	5
. I feel I have made an informed choice	1	2	3	4	5

. My decision shows what is important to me	1	2	3	4	5
. I expect to stick with my decision	1	2	3	4	5
. I am satisfied with my decision	1	2	3	4	5

Decision Satisfaction Scale

	Strongly disagree	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
I was adequately informed about the different treatments available for my blood clot	1	2	3	4	5
The decision I made was the best decision possible for me personally	1	2	3	4	5
My decision was consistent with my personal values	1	2	3	4	5
I expect to successfully carry out (or continue to carry out) the decision I made	1	2	3	4	5
I had as much input as I wanted in the choice of treatment for my blood clot	1	2	3	4	5
I am satisfied with the decision that was made about treatment for my blood clot	1	2	3	4	5

My confidence in making an informed choice

Below are listed some things involved in making an informed choice. Please show how confident you feel in doing these things by circling the number from 0 (not at all confident) to 4 (very confident) for each item listed below.

I feel **confident** that I can:

Get the facts about the medication choices available to me	**Not at all confident**	0	1	2	3	4	**Very confident**
Get the facts about the benefits of each choice	**Not at all confident**	0	1	2	3	4	**Very confident**
Get the facts about the risks and side effects of each choice	**Not at all confident**	0	1	2	3	4	**Very confident**
Understand the information enough to be able to make a choice	**Not at all confident**	0	1	2	3	4	**Very confident**
Ask questions without feeling dumb	**Not at all confident**	0	1	2	3	4	**Very confident**
Express my concerns about each choice	**Not at all confident**	0	1	2	3	4	**Very confident**
Ask for advice	**Not at all confident**	0	1	2	3	4	**Very confident**
Figure out the choice that best suits me	**Not at all confident**	0	1	2	3	4	**Very confident**
Handle unwanted pressure from others in making my choice	**Not at all confident**	0	1	2	3	4	**Very confident**
Let the clinic team know what's best for me	**Not at all confident**	0	1	2	3	4	**Very confident**
Delay my decision if I feel I need more time	**Not at all confident**	0	1	2	3	4	**Very confident**

Appendix C. Interview guide

Interview data

Study ID	
Interview Date (day/month/year)	
Interview Location	
Interviewer	
Length of Interview (minutes)	
Direct choice decision	
Decision analysis result	
Decision analysis decision	
Concordant or discordant decision	

Introduction

The purpose of this interview is to learn about how you made the decision regarding whether or not to take low molecular weight heparin during your pregnancy.

We are most interested in learning about your personal experience with low molecular weight heparin and how you came to your treatment decision. There are no right or wrong answers.

Interview Questions

The questions in this interview are divided into four categories and will explore your experiences and perceptions as they relate to: 1) your decision-making process; 2) the direct choice exercise; 3) the personalized decision analysis; and 4) your knowledge about preventive treatment with low molecular weight heparin.

1.0 Decision-Making Process	**As part of this study, you were asked to make a decision about taking heparin during your current/future pregnancy to prevent blood clots.** What is your preferred level of engagement when it comes to making a clinical decision? [If no reaction from the woman, we could provide an example (e.g. "for example, do you prefer to have your health care provider make the treatment decision or do you do your own homework and ask questions?")] 2 Please describe to me the process you used to make your decision about low molecular weight heparin, which in your case was to take/not take low molecular weight heparin? 3 What types of information did you use to make your decision? [Try to discover previous knowledge/experience or personal research conducted on own] Which information was most helpful in informing the decision you made? Which information was the least helpful in informing the decision you made? [If no reaction from the woman, we could provide an example (e.g. "for example, the decision aid had descriptions of relevant health outcomes" or "do you ask the doctor questions, review pamphlets, look up information online")] 4 What factors do you think that influenced your final decision? Are there any personal factors that influenced your decision? These can include your values, preferences, concerns, or previous experiences with treatment. Are there factors related to your health care provider that influenced your decision? Are there other factors prior to completing the direct choice/ personalized decision analysis exercise today that influenced your decision? 5 What was the experience of being asked to make this decision like for you? [For all responses, follow up with a "why?" question]

	At any point in time, did you experience feelings of confusion during the decision-making process? [if yes, have them describe when they experienced confusion] What strategies did you use to address these feelings of confusion?
	Once you made your final decision, how confident did you feel about the decision you made? What factors increased your level of confidence and why?
	1.6 Please explain to me how comfortable you are with the decision you made? Why?
2.0 Direct Choice	As part of this study, you participated in a direct choice exercise in which you were presented with information about the risks and benefits of treatment along with different health outcomes.
	2.1. Was the amount of information provided in the direct choice exercise appropriate? Why?
	2.2. Did you have a clear understanding about the risks and benefits of heparin after completing the direct choice exercise? a) Could you review the information and explain aloud the risks and benefits of treatment using actual numbers?
	2.3. How did you weight the different aspects of information that were presented (e.g. the risks of experiencing another blood clot versus your personal preferences)? a) Could you explain your rationale?
	2.4. What ultimately drove your decision to take/not take low molecular weight heparin during your pregnancy?
	2.5. What was the overall experience like for you in making a decision after the direct choice exercise?
3.0 Decision Analysis Process	Following the direct choice exercise, you received the results from your personalized decision analysis. Decision analysis involves asking you about your preferences for health outcomes related to the treatment decision. Using a mathematical formula, we then combine this information with the risk probability of each health outcome to formulate a treatment recommendation. This recommendation is based on a score that takes into account the likelihood of each health outcome occurring and the importance

you assigned to them. It indicates whether a treatment is likely to lead to an increase or decrease in your quality of life.

3.1a Please describe your experience with the rating scale, feeling thermometer and gamble exercises that we completed.

3.1b Did these exercises help clarify your personal preferences for the different health outcomes (e.g. experiencing a blood clot)?

3.1c Do you think these exercises reflected your personal preferences?

3.2 What were your thoughts and reactions when you were told the results from the personalized decision analysis process?

CONCORDANT DECISIONS [The research assistant would get the information on concordant and discordant decisions from the table at the beginning of the interview guide]

3.3a For you, there was consistency between the decision you made after the direct choice exercise and the results from the decision analysis process.

After reviewing treatment information, YOU made the decision to **take/not take** low molecular weight heparin. The result of the decision analysis also supported this decision to **take/not take** low molecular weight heparin.

How did this consistency make you feel? Why?

DISCORDANT DECISIONS: [as above, the research assistant will explain the discordance to set the context]

3.3b For you, there was a difference between the decision you made after the direct choice exercise and the results from the decision analysis process.

After reviewing treatment information, YOU made the decision to **take/not take** low molecular weight heparin while the result of the personalized decision analysis recommended that you **take/not take** low molecular weight heparin. We would like to insist on the fact that there is no right or wrong decision in this context.

Having said this, the discordant decision could reflect a difference between the methods we used to formulate a treatment recommendation with the mathematical formula and the factors you considered as a patient.

Our objective is to identify the cause of this difference. We would like to start by ask how did this inconsistency make you feel? Why?

If the participant modified her initial decision:

3.4a Please explain why you changed your decision after receiving the results from the decision analysis?

3.4b How do you think the results from the decision analysis influenced your levels of confidence or comfort with your final decision?

3.4c Did you find having the results of the decision analysis useful for making your decision?

3.4d Would you find having the results of a decision analysis useful for making other difficult health care decisions?

3.4e Would you have preferred to have only gone through the personalized decision analysis exercise instead of making the decision yourself first with the decision aid? In other words, would you rely on the personalized decision analysis exercise rather than making the decision by yourself?

If the participant did not modify her initial decision:

3.4f Please explain why you maintained your decision after receiving the results from the personalized decision analysis?

3.4g How do you think the results from the personalized decision analysis influenced your levels of confidence or comfort with your final decision?

3.4dh Did you find having the results of the decision analysis useful for making your decision?

	3.4i Would you find having the results of a personalized decision analysis useful for making other difficult health care decisions?
	3.4j Would you have preferred to have only gone through the decision analysis exercise instead of making the personalized decision yourself first with the decision aid? In other words, would you rely on the personalized decision analysis exercise rather than making the decision by yourself?
4.0 Treatment Knowledge	To finish, we have some quick questions regarding your knowledge of low molecular weight heparin. Throughout this study, you have been provided with information about the use of low molecular weight heparin to potentially reduce the risk of blood clots during pregnancy.
	4.1 From your perspective, what are the benefits of treatment, which involves daily injections of low molecular weight heparin throughout pregnancy, to prevent blood clots?
	4.2 From your perspective, what are the potential drawbacks related to daily injections of low molecular weight heparin throughout pregnancy?
	4.3 Is there any additional information that you would like to share about the process of making a decision about treatment for blood clots?

CHAPTER 4. DECISION ANALYSIS IN SHARED DECISION MAKING FOR THROMBOPROPHYLAXIS DURING PREGNANCY (DASH-TOP): A SEQUENTIAL EXPLANATORY MIXED METHODS PILOT STUDY

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Abstract

Introduction: Individualized decision-analysis has long been suggested as having the potential to enhance shared decision-making between patients and clinicians. To gain insight into the potential of formal methods of integrating patient preferences and clinical evidence to inform treatment decisions, we explored patients' experience with a personalized decision analysis intervention for prophylactic low molecular weight heparin (LMWH) in the antenatal period.

Methods: Sites in Canada (n=1) and Spain (n=4) provided the setting for a sequential explanatory mixed methods study. Individuals with a prior venous thromboembolism (VTE) who were pregnant or planning pregnancy and had been referred for counseling regarding antepartum prophylactic LMWH completed a shared decision-making intervention designed to compare treatment strategies of administering prophylactic LMWH once daily until delivery versus expectant management without LMWH. The intervention included three components: 1) direct choice exercise; 2) preference elicitation exercise, and 3) personalized decision analysis. Participants completed a self-administered questionnaire to evaluate decision quality. Then, in-depth semi-structured interviews were conducted to explore their experience and perceptions of the decision-making process.

Results: Fifteen patients participated in the study. Although participants identified aspects of the intervention that provide potential enhancements to current shared decision-making, they ascertained potentially problematic issues too. Some participants could not understand how to complete the standard gamble exercises and others

highlighted the need for more informative ways of presenting the decision analysis results.

Conclusion: Our results highlight the challenges and opportunities for those who wish to incorporate decision analysis to support shared decision-making for clinical decisions.

Introduction

Venous thromboembolism (VTE) is a rare but serious condition that commonly manifests as a thrombus in the deep veins of the leg, inguinal region, or arm (deep vein thrombosis [DVT]) or arteries of the lungs (pulmonary embolism [PE]). Despite a low incidence rate (1.2 in 1,000 pregnancies)[1], VTE is a leading cause of maternal mortality (1.1 per 100,000 deliveries) in high-income countries.[1] Individuals with a prior VTE are 4-5 time more likely to experience thrombosis during subsequent pregnancies compared to non-pregnant individuals of the same age.[2-4]

A review of clinical practice guidelines identified low molecular weight heparin (LMWH) as the preferred treatment option for the prevention of VTE during pregnancy.[5-7] However, universal thromboprophylaxis may not be cost-effective or safe due to the risk of bleeding. Due to the low certainty of effectiveness,[8] the American Society of Hematology (ASH) issued a conditional recommendation for prophylactic LMWH during pregnancy versus expectant management involving no LMWH among women with prior unprovoked VTE or hormone associated VTE.[7] Specifically, the guideline panel recommended that patients and clinicians engage in a shared decision-making process to ensure that the LMWH treatment decision is consistent with each patient's risks, values, and preferences.[7]

Despite recommendations for shared decision-making, a systematic review identified only one study exploring the use of a decision aid in the care of non-pregnant patients with or at risk of VTE.[9] In this study, patients with a prior VTE reviewed the risks and benefits of vitamin K antagonist therapy and valued the different outcomes

related to a decision regarding duration of anticoagulation treatment.[10] Investigators reported substantial variability in patients' values and treatment preferences, suggesting that individual patient decisions should be consistent with their specific goals as well as consider their values and concerns. The authors noted that the explicit quantitative assessment of patients' preferences could be incorporated into a personalized decision analysis to evaluate whether the effectiveness of treatment with vitamin K antagonists outweighs the risks and burden of treatment.[10]

Decision analysis offers a structured approach to decision-making that explicitly considers available clinical evidence alongside patient preferences by using an analytic framework to generate a treatment recommendation. Personalized decision analysis has been used to support patients and clinicians engage in shared decision-making in a variety of clinical contexts, including pregnancy.[11] Most studies reported that the decision analysis interventions were broadly beneficial. However, there is still important uncertainty surrounding their effectiveness.

The objective of this pilot study was to use mixed methods to obtain insight into patients' experiences with personalized decision analysis that combines individual preferences with clinical evidence to support a shared decision-making process for prophylactic LMWH in the antenatal period.

Methods

We conducted a sequential explanatory mixed methods pilot study that was guided by three research questions:

- Quantitative research question:

    - Using a shared decision-making process that incorporates decision analysis, what is the level of decision quality among patients that are pregnant or considering pregnancy who have experienced VTE and must decide whether to take LMWH?

- Qualitative research question:
    - What are the experiences and perceptions related to a shared decision-making process that incorporates decision analysis among patients that are pregnant or considering pregnancy who have experienced VTE and must decide whether to take LMWH?
- Mixed methods research question:
    - How do the qualitative findings provide an enhanced understanding of quantitative results on decision quality, to evaluate the application of decision analysis to a shared decision-making process among patients who are pregnant or considering pregnancy and have experienced a VTE and must decide whether to take LMWH?

The DASH-TOP (Decision Analysis in Shared decision making for Thromboprophylaxis during Pregnancy) study protocol has been published previously.[12]

Participants

The sample comprised women with a prior VTE who were pregnant or planning pregnancy and who had been referred for counseling regarding prophylactic LMWH in the antenatal period. Participants were categorized as high risk for a subsequent thrombosis if they had thrombophilia and/or no major transient risk factor (leg casting,

major surgery, hospital admission, immobilization, active cancer) associeted with their previous VTE event. Given the exploratory nature of this pilot study, the research team used a convenience sampling strategy. Eligible participants were recruited from hospitals in Canada (1 site) and Spain (4 sites) between November 2019 and March 2021. All participants provided informed consent.

Intervention

The intervention was designed to compare treatment strategies of administering prophylactic LMWH once daily when pregnancy is confirmed and continuing until delivery[5] versus expectant management without LMWH. It included three components: 1) direct choice exercise; 2) preference elicitation exercises, and; 3) personalized decision analysis. All participants in the study received the intervention, which was administered by a member of the research team.

To start, participants were presented with a description of four health states relevant to this decision: 1) use of LMWH; 2) major obstetrical bleed; 3) DVT; and 4) PE.[13] Participants then completed a direct choice exercise that included the review of an interactive electronic decision aid that describes the harms and benefits of LMWH for prevention of pregnancy-related VTE.

To obtain participants' preferences for the four health states under consideration, three value elicitation exercises (rank ordering, visual analogue scale and standard gamble) followed the direct choice exercise. The visual analogue scale and ranking tasks served as warm-up exercises, with the standard gamble determining the value rating entered into the decision analytic model because it is best suited to evaluate preferences

under conditions of uncertainty and has established theoretical underpinnings for expected utility theory.[14,15]

Patients' preferences were entered into a decision analytic model along with information regarding their age and risk of VTE.[7] The decision analytical model is a Markov state transition model with a lifetime time horizon that estimates quality-adjusted life years (QALYs) for each treatment option.[16] The treatment with the greatest expected QALYs represented the recommended strategy. The research team administered the intervention before participants' appointment with their healthcare provider so that they could use this information to inform a final treatment decision.

Data collection

At the start of the interview, the research team documented participants' ages, levels of education, pregnancy status, pregnancy number, details regarding prior VTE, type and duration of treatment for prior VTE, and experience with LMWH. After completing the direct choice, preference elicitation exercises and receiving the results of their personalized decision analysis, participants made a preliminary treatment decision regarding LMWH. Subsequently, participants completed a self-administered questionnaire to evaluate decision quality using the Modified Decisional Conflict Scale,[17] Decision Self-Efficacy Scale,[18-20] and Satisfaction with Decision Scale.[21]

A member of the research team then conducted individual semi-structured interviews with all participants to explore their experiences and perceptions as they relate to: 1) the decision-making process; 2) the direct choice exercise; 3) the personalized decision analysis; and 4) their knowledge of LMWH. All interviews were audio recorded

and transcribed verbatim with identifying information removed. Spanish interview transcriptions were translated into English by an experienced bilingual translator.

Data analysis

We used descriptive statistics to summarize participants' ages, levels of education, pregnancy status, number and characteristics of previous VTE, and experience with LMWH. We assessed decision quality using the Decisional Conflict Scale, Self-Efficacy Scale, and Satisfaction with Decision Scale. Content analysis guided the data analysis from the individual interviews. Qualitative results were reported in the form of a descriptive synthesis, and supported by quotes.[22] We subsequently integrated the quantitative and qualitative data using a joint display, to enable an explicit comparison between datasets.[23]

Results

Recruitment

Figure 1 summarizes the recruitment process for the study (detailed information for each study site is available in Appendix A). Due to a delay in receiving ethics approval, only one of the planned study sites in Canada recruited participants. Among the 43 eligible patients identified through chart review, 27 agreed to participate in the study. The main reason for non-participation was the research team being unable to reach the patient via telephone (n = 9). Other reasons included lack of interest in the study (n = 5), refusal to take LMWH (n = 1) and no computer access (n = 1). After the study transitioned to an online platform in March 2021 due to the COVID pandemic, 12

patients who agreed to participate did not show up to the interview. A total of 15 patients who consented to participate completed the study.

Characteristics of participants

The mean age of participants was 32.5 years; most participants (9, 60%) had a university education, and nine (60%) were planning their pregnancy at the time of referral for counseling regarding prophylactic LMWH. The majority were considered to be at high risk for VTE (12, 80%) and had previous experience with LMWH (12, 80%). **Table 1** provides additional information on participants' previous experience with VTE and LMWH.

Patient-specific decision analysis and treatment decision

Table 2 presents the decision analysis treatment recommendation, participants' decision and the reasoning behind their decision. The decision model recommended prophylactic LMWH for 12 participants who were categorized as being at high risk for a recurrent VTE. For the three participants at low risk of VTE, the model recommended no LMWH. Four participants (27%) made treatment decisions that were discordant with the model recommendations.

In the qualitative interviews, participants explained that the results of the personalized decision analysis did not alter their treatment decision. Rather, their decisions were based on their previous experience with VTE, perceived risk of experiencing another event, and level of risk aversion. Because participants were either pregnant or planning pregnancy, there was an overwhelming concern about the impact that another VTE would have, not only on themselves but also on their baby. Participants

who had previous experience with LMWH explained that they thought the benefits of avoiding another VTE outweighed the inconveniences of taking daily injections of the medication throughout their pregnancy.

Perceptions of LMWH treatment decision

When asked to describe their decision-making process surrounding prophylactic LMWH, most participants stated that they assumed prior to referral, that they were going to have to take LMWH because of their history of VTE (**Table 3**). Due either to presentation of the need for LMWH by their primary healthcare provider, or misconceptions surrounding their actual risk of recurrent VTE – which they thought was much higher than available data suggest - participants were not always aware that this treatment decision was something to be discussed. Upon reviewing the clinical data presented during the direct choice exercise, some participants were surprised that, in previous discussions with healthcare providers, expectant management without LMWH was not presented as a treatment option. Participants expressed a desire to be informed about available treatment options. Most participants wanted to participate in the decision-making process but stated they would look to their provider to make a final treatment recommendation.

Experiences of shared decision-making intervention

Direct choice exercise

Participants found the content of the direct choice exercise to be appropriate and the information useful for their decision-making (**Table 3**). The format, which included numeric and graphic presentations of risk estimates, was acceptable. Some participants

referenced the risk estimates and/or low certainty of evidence to explain why they were (or were not) confident in their treatment decision and/or to justify their decision.

Preference elicitation exercises

The participants reported that the preference elicitation exercises helped them clarify their preferences, communicate their preferences, or think about outcomes they had not yet considered. Among the three exercises completed, the standard gamble exercise elicited the most diverse reactions from participants. Five participants (33%) reported difficulty understanding how to complete the exercise. Three of these participants (20%) also reported problems with having death as an anchor in the exercises because it scared them and was not something they were willing to risk. In contrast, four (27%) participants stated that they found the standard gamble to be the most useful of the three exercises. Having completed the ranking and visual analogue scale, these participants appreciated how the standard gamble inserted an element of uncertainty into their valuation of the health outcomes under consideration.

Personalized decision analysis

There were mixed reactions to the personalized treatment recommendation. Some participants reported that the decision analysis results validated what they were feeling (n = 3, 20%) or gave them a sense of comfort (n = 4, 27%) or confidence (n = 2, 13%) in their decision. Six (40%) participants stated that they were indifferent to the treatment recommendation. Four (27%) participants mentioned that they found neither the concept of quality adjusted life years nor the presentation of its results particularly useful. Overall, the personalized treatment recommendation appeared to be the least useful component.

Overall decision-making process

Despite the mixed reactions to the personalized decision analysis results, all participants confirmed that they liked the intervention, and found the process useful for their decision-making process. Some participants expressed appreciation for the opportunity to use an evidence-based decision support tool that took into account both clinical data and their personal values and preferences for managing VTE during pregnancy. Participants reported feeling more prepared for their upcoming consultation with their healthcare provider to discuss LMWH.

Decision quality

After going through the different components of the intervention, participants reported a high level of satisfaction with their treatment decision, with a mean score on the Satisfaction with Decision Scale was 25/30 (standard deviation [SD] = 4). This could reflect the use of the intervention, which provided participants with an opportunity to sit down with someone, review available clinical evidence, consider their preferences and discuss their decision-making process prior to the consultation with their healthcare provider. Participants with lower satisfaction scores also reported lower levels of decision self-efficacy and/or higher levels of decisional conflict. A table presenting the decision quality scores according to subgroups is available in Appendix B.

The mean score on the Self-Efficacy Scale was 82/100 (SD = 14), with a score of 100 indicating extreme confidence in making an informed decision. Two participants from the Spanish sites were identified as outliers, having lower self-efficacy scores compared to the rest of the sample. Their scores were 64 and 45, respectively. Both

participants were classified as high risk and made treatment decisions concordant with model recommendations (take LMWH). In both instances, the participants described their previous VTE as a traumatic experience. One participant, who was the youngest, expressed how they were uncomfortable with making decisions. The other participant was the oldest in the sample and described their fear of having a baby at an advanced age. Both participants had lower levels of education compared to the rest of the sample ("High School" and "Some University", respectively).

The mean score on the Decisional Conflict Scale was 22/100 (SD = 11), with a score of 100 indicating an extremely high level of conflict. Two participants (different from those who had the lowest Self-Efficacy scores) had Decision Conflict scores exceeding 37.5, reflecting a state of uncertainty about a course of action.[24] One participant described themself as being extremely risk averse. The other participant received a model recommendation of no LMWH. Despite being classified as low risk, they were experiencing symptoms of another clot and were told by their general practitioner that they would need to take LMWH. The experience of symptoms and the discordance between the model and physician recommendation could have increased their level of uncertainty towards this treatment decision.

Knowledge about LMWH

Participants reported the highest level of conflict for question #12 on the Decisional Conflict Scale ("This decision is easy for me to make"). Despite most participants having previous experience with LMWH and assuming they had to take LMWH, this remained a stressful and difficult treatment decision. Reasons include a lack

of studies providing high quality evidence, the need to consult with multiple healthcare providers, discrepancies between what their general practitioner previously told them (i.e., the need to take LMWH) versus what they were being told during this interview (i.e., there is an option to not take LMWH), as well as concerns regarding their unborn baby. Even though most participants (n = 12, 80%) had previous experience with LMWH, participants identified key gaps in knowledge surrounding this treatment decision – gaps that differed according to country. Participants from Spain reported unmet information needs surrounding LWMH dosage and administration techniques; participants from Canada reported surprise after learning about the increased risk of major bleed of which they were previously unaware. Participants from both countries reported being unaware about their actual risk of VTE, which data indicate was much lower than they believed.

Discussion

We have developed a shared decision-making intervention that uses decision analysis to produce individualized treatment recommendations regarding prophylactic LMWH in the antenatal period. Participants in the study appreciated the opportunity to use an evidence-based decision support tool that considered their personal values and preferences, and reported feeling more prepared for their upcoming consultation with their healthcare provider to discuss LMWH. While most participants liked the direct choice and preference elicitation exercises, there were mixed reactions to the standard gamble and personalized treatment recommendation.

A key issue was participants not understanding the standard gamble preference elicitation exercise. A third of participants in our study reported difficulty understanding

how to complete the exercise. Problems with the standard gamble are not infrequent; a randomized controlled trial of three decision support tools for atrial fibrillation discontinued the decision analysis intervention arm after six out of eight participants were unable to carry out the standard gamble.[25] A key component of shared decision-making is the incorporation of patient preferences into the decision. If patients do not understand the standard gamble, the values obtained from that exercise and entered into the decision analytic model may not accurately represent their preferences.

We opted to input the standard gamble values into our decision analytic model because it has demonstrated acceptability and reliability[26,27] as well as established theoretical underpinnings of expected utility theory.[14,15] Other decision analytic shared decision-making tools have used different methods of preference elicitation (e.g., VAS or time trade off technique – although the standard gamble construct validity may be superior)[28-34] or allowed patients, if they did not understand the exercise, the option to use population-based utility values.[35] The optimal way of eliciting patient preferences remains uncertain.

In addition to not understanding the standard gamble, many participants proved indifferent to the treatment recommendation produced by the decision analysis model. Although the literature offers considerable guidance on how to conduct the direct choice[36] and preference elicitation exercises,[37] there is hardly any information available on how to present the decision analysis results within the context of a shared decision-making encounter.

In this study, we presented participants with a figure displaying the expected QALYs for each treatment option and explained that the recommended treatment strategy was the one with the greatest QALYs (see published protocol for details).[12] It is possible that the QALY is not a metric that participants could easily understand and then use to inform their decision-making process, or that the interview scripts the research team used to explain the decision analysis results may have been too long or overly technical for participants.

Another explanation could pertain to how the decision analytic results were presented. Shared decision-making is often recommended in situations where there is uncertainty and/or a close tradeoff between the risks and benefits of treatment options, with the goal of helping patients orient themselves with the available evidence and decision options so that their values and preferences can be considered in the treatment decision.[38] Participants' reactions to the direct choice component of our intervention highlighted how understanding the certainty of evidence (or lack thereof) can inform decision-making regarding prophylactic LMWH during the antenatal period. The presentation of the decision analysis results did not explicitly reflect any of these uncertainties, both regarding the available research evidence and the patient's preferences.

The developers of other decision analytic shared decision-making tools have structured the presentation of the decision analysis results to allow patients and/or healthcare providers to conduct sensitivity analyses to explore how changes in clinical data or preferences impact the treatment recommendation.[33,39-43] This level of engagement

with the decision analysis model could enable a better understanding of key factors that drive a treatment decision and, as a result, a more robust discussion among patients and providers.

Another explanation for the perceived indifference to the decision analytic model output was that we did not provide participants with enough information on the model structure. To avoid getting too technical, we did not go into detail regarding key elements of the model structure. For example, one important consideration was that was not communicated to participants was that we used a lifetime time horizon for the QALY calculation. Within the context of treatment decisions for VTE and pregnancy, patients are more likely to focus on the immediate future than consider a lifetime time horizon. Therefore, it is less likely that their decision will be consistent with the decision analytic model. While there is guidance on how to use decision analytic models to inform reimbursement recommendations for health technologies,[44] there is a lack information on how to construct a model to support shared decision-making.

Mistrust of the black box nature of a decision analytic model represents another possible explanation for their perceived indifference to the decision analysis results. Conducting sensitivity analyses with the patient and/or presenting a simplified decision tree and folding it back might enhance patients' understanding of the model, and thus trust in the procedure. The failure of decision analysis to have an important impact on clinical practice guideline production suggests, however, that mistrust may extend beyond patients to expert health professionals, guideline development methodologists and other actors in the guideline development process.

The small sample size, high level of education among participants and the recruitment of participants from two high-income countries limit the generalizability of our pilot findings. In addition, there were some issues with recruitment where a high number of patients did not show up to the scheduled online interviews once the study transitioned online during the COVID-19 pandemic. It was not possible for the research team to compare non-participants' and participants' characteristics and examine non-participants' reasons for declining to take part in the pilot study. Since a decision analysis approach to shared decision-making may not be suitable for all decision-making contexts and patient groups, further research is required to determine whether certain subgroups of patients (i.e., those at low risk of VTE) are more suited to benefit from this type of decision support tool.

Conclusion

The results of this mixed methods pilot study suggest that the use of a decision analysis intervention is acceptable and beneficial among patients who must decide whether to take LMWH during the antenatal period. Participants appreciated the opportunity to use an evidence-based decision support tool that considered their personal values and preferences, and reported feeling more prepared for their upcoming consultation with their healthcare provider to discuss LMWH. However, this mixed methods pilot study identified several issues that require resolution prior to further evaluation of its effectiveness. These issues are likely to arise in other applications of personalized decision-analysis for shared decision-making.

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Tables and figures

Table 1. Sociodemographic and clinical characteristics of participants

	N	(%)
Demographic Characteristics		
Age, mean (SD)	32.5	(6.3)
Level of education		
High school	1	(7)
College	3	(20)
Some university	2	(13)
University	9	(60)
Country of residence		
Canada	7	(47)
Spain	8	(53)
Clinical Characteristics		
Pregnancy status		
Pregnant	6	(40)
Planning pregnancy	9	(60)
Risk of recurrent VTE		
High*	12	(80)
Low	3	(20)
Previous VTE Experience		
Number of previous events		
1	12	(80)
2	3	(20)
Type of previous event**		
Leg	9	(60)
Lung	7	(47)
Other	2	(13)
Complete recovery from event***		
Yes	8	(53)
No	7	(47)
Previous LMWH Experience		
Previous use of LMWH		
Yes	12	(80)
No	3	(20)
LMWH difficult or troublesome		
Yes	7	(47)
No	5	(33)
Not applicable	3	(20)
Fear of needles		
Yes	2	(13)

No	10	(67)
Not applicable	3	(20)

* High risk defined as patients with thrombophilia and/or without a major transient risk factor (leg casting, major surgery, hospital admission, immobilization, active cancer)
** Categories not mutually exclusive due to participants experiencing multiple thrombi
*** Recovery from any of the following symptoms: residual leg pain, leg swelling, change in leg color, chest pain or discomfort, or shortness of breath
Abbreviations: SD, standard deviation; VTE, venous thromboembolism; LMWH, low molecular weight heparin

Table 2. Decision analytic model recommendation and participants' treatment decision regarding LMWH during pregnancy

Participant number	VTE Risk*	Model recommendation	Participant decision	Quotes from semi-structured interviews illustrating reason for decision
1	High	Take LMWH	Take LMWH	*"I am a very risk averse person. If I weren't to take it and then ended up getting a clot, that would put more stress on me. Knowing that I had an option, and I chose not to do it."*
2	High	Take LMWH	Take LMWH	*"My preference would be to not experience any blood clots. But since it did happen, I will do whatever is necessary [to avoid another clot]."*
3	Low	No LMWH	Take LMWH	*"I mean, I always knew that it was going to be not a big deal. Like I said before, not a huge inconvenience in my life."*
4	High	Take LMWH	Take LMWH	*"Being healthy for my kids was the main factor. I would rather take the injections throughout my pregnancy and go through that than risk having complications."*
5	Low	No LMWH	Take LMWH	*"I knew I'd have to take the injections [after experiencing symptoms]… Even though I have the risk of a major bleed. I believe that can be handled at that time."*
6	High	Take LMWH	Take LMWH	*"I've experienced a DVT and I don't want to again. But at least I know what to expect. A pulmonary embolism? That's very scary. It would put a lot of stress on my body and the baby. So, I just don't like that option."*
7	High	Take LMWH	Take LMWH	*"The seriousness of my previous clots makes me very afraid… By taking heparin I am avoiding a risk. It's not a guarantee but at least I am being more careful."*

8	High	Take LMWH	Take LMWH	*"They did a genetic test and seeing that I had Factor V Leiden, it was useful to know that I was high risk... Having the option of administering heparin calmed me down because in this way I could prevent a clot."*
9	High	Take LMWH	Take LMWH	*"For me it is enough that 46 cases [out of 1,000] decrease. It is true that it is not 0% but the risk does drop a lot taking heparin... In my case, I am not being treated but preventing, so I would recommend taking it."*
10	High	Take LMWH	No LMWH	*"The risk of presenting a thrombus is very low and with heparin the risk reduction is very small. It's like having a car accident, what are the odds? That's why I'm not going to take heparin."*
11	Low	No LMWH	No LMWH	*"Because what prevents the thrombus is so small; if you told me, for example, that it [the risk of a clot] decreases by half, then I would understand; but it is so little that I prefer not to prick myself."*
12	High	Take LMWH	Take LMWH	*"My fear of pulmonary emboli is very big... I am very influenced by my previous experience of having pulmonary embolism... For me it was a very traumatic event."*
13	High	Take LMWH	No LMWH	*"My previous experience; I had such a bad time, and I was so scared. Now seeing that the risk is so low and also that the benefit is not that much, I would consider not taking it [LMWH]."*
14	High	Take LMWH	Take LMWH	*"My gynecologist told me I am high risk…so I didn't think about it. Before taking any risk, I prefer to use heparin."*
15	High	Take LMWH	Take LMWH	*"To me, the risk of not taking it [LMWH] appears more significant."*

* High risk defined as patients with thrombophilia and/or without a major transient risk factor (leg casting, major surgery, hospital admission, immobilization, active cancer)
Abbreviations: LMWH, low molecular weight heparin; DVT, deep vein thrombosis; VTE, venous thromboembolism

Table 3. Participants' perceptions and experiences

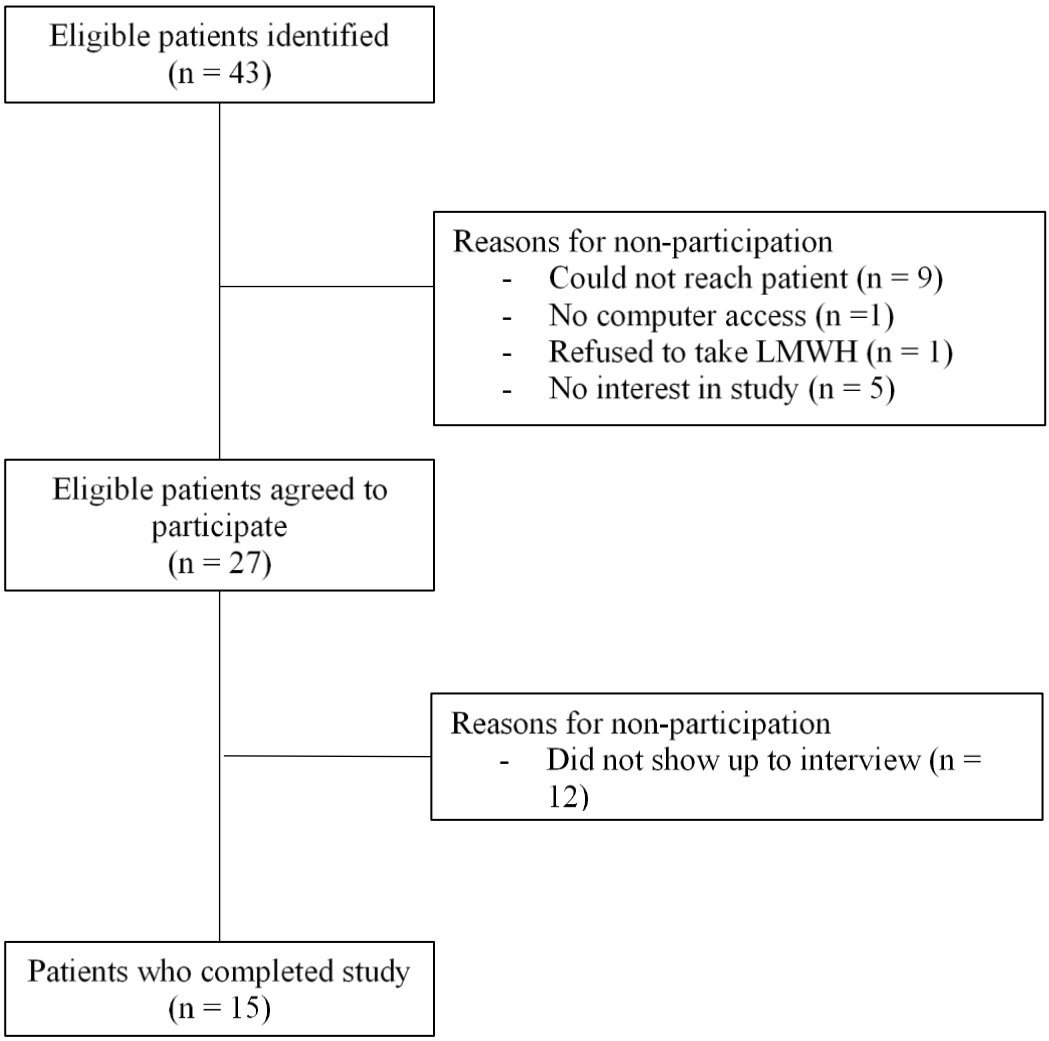
	Description	Supporting Quotes
Perception of the LMWH decision	● Most participants assumed that they were going to have to take LMWH ● Participants were not aware that the decision to take or not take LMWH was something to be discussed ● Given that expectant management was not offered as a treatment option, several participants were surprised at the low risk of experiencing another clot	*"Taking it is something that I kind of expected."* - Participant #2 *"I was not confused at any time, I did not consider not taking it. Even now when my doctor has recommended taking it, it does not cross my mind not doing so."* – Participant #12 *"I was surprised to learn that the probability of having a clot in pregnancy is very low. I thought that since I had a previous clot I was going to have a clot in my next pregnancy and that is why I had to take heparin."* – Participant #13
Preferred level of involvement in decision-making	● Participants want to make an informed treatment decision ● Most participants are interested in participating in the decision-making process with their healthcare provider ● Participants look to their healthcare provider to provide a final treatment recommendation	*"I like to do my homework but I like to take this decision together [with healthcare provider]. I feel more comfortable that way, the doctor has more knowledge than me."* – Participant #5 *"Definitely more my health provider makes the decision but I like to do some research and make sure that I'm informed."* – Participant #6 *"I prefer the doctor to make the decisions for me, but to be able to ask questions about it."* – Participant #8
Experience with direct choice exercise	● Participants found the direct choice exercise to be appropriate and useful ● The format was acceptable ● Some participants referenced the low certainty of evidence to explain why they	*"Very useful because I am a visual learner and seeing those things helped me."* – Participant #4 *"Even just having the numbers, like a 5.5 compared to a 0.9 percent risk – I know those are small numbers – but there is still a significant difference."* – Participant #6

	are not confident in their decision or to justify their decision	*"How is it possible that there is no more information about all this? Because there are very few studies perhaps and that is why the certainty is low."* – Participant #10
Experience with preference elicitation exercises	● The exercises helped participants clarify their preferences, communicate their preferences, or think about preferences for outcomes they had not considered ● Several participants mentioned that the exercises did not include other outcomes important to them were not addressed (e.g., health of baby) ● Reactions to the standard gamble exercise were mixed	"*I was already clear about was important to me, this has helped me to speak about it."* – Participant #7 "*The gamble was interesting for me because I could see more visually the risks and benefit of how it really would affect me as the percentages changed*." – Participant #2 "*The ranking and the thermometer helped me clarify what is most important to me. The last exercise [gamble] talking about death scared me a little… under no circumstances would I choose death.*" – Participant #8
Experience with personalized decision analysis	● For some participants, the decision analysis results validated what they were feeling or gave them confidence in their decision. For others, their reaction to the results was indifferent ● Several participants explained that they don't respond to the concept of quality adjusted life years ● Participants said that more informative ways of presenting the decision analysis results are required	"*I don't think it really changed [my decision]. But knowing I'm going to have a 0.2 increase in my quality of life [laughs] At least it makes you a little more comfortable that you're making an OK decision*." – Participant #1 "*I think it was just helpful to have that additional numerical value to confirm what I suspected. It was just that confirmation that I am making the right choice."* – Participant #6 "*With the model I see that it is practically the same to take heparin as not... It is not a result that is very conclusive for me*." – Participant #10
Perception of overall shared decision-making process	● Participants appreciated an evidence-based intervention that considered their	"*I knew what my decision was but now I know what kind of questions I am going to ask when I have my appointment. And I have a better understanding of the different side effects. I've only thought about it*

	personal values and preferences for managing VTE during pregnancy ● Participants felt more prepared for their consultation	*from a PE perspective. I've never thought about DVT or major bleeding."* – Participant #1 "*All information is useful, although I would not change my decision."* – Participant #12 "*I liked these exercises, although the quality of life was less useful to me. For me, the important thing is to be able to have information and to help me think about the risks and benefits."* – Participant #8

Abbreviations: LMWH, low molecular weight heparin; DVT, deep vein thrombosis; VTE, venous thromboembolism

Figure 1. Recruitment process



Appendix A. Study recruitment

Figure 1. Recruitment process at Canadian sites

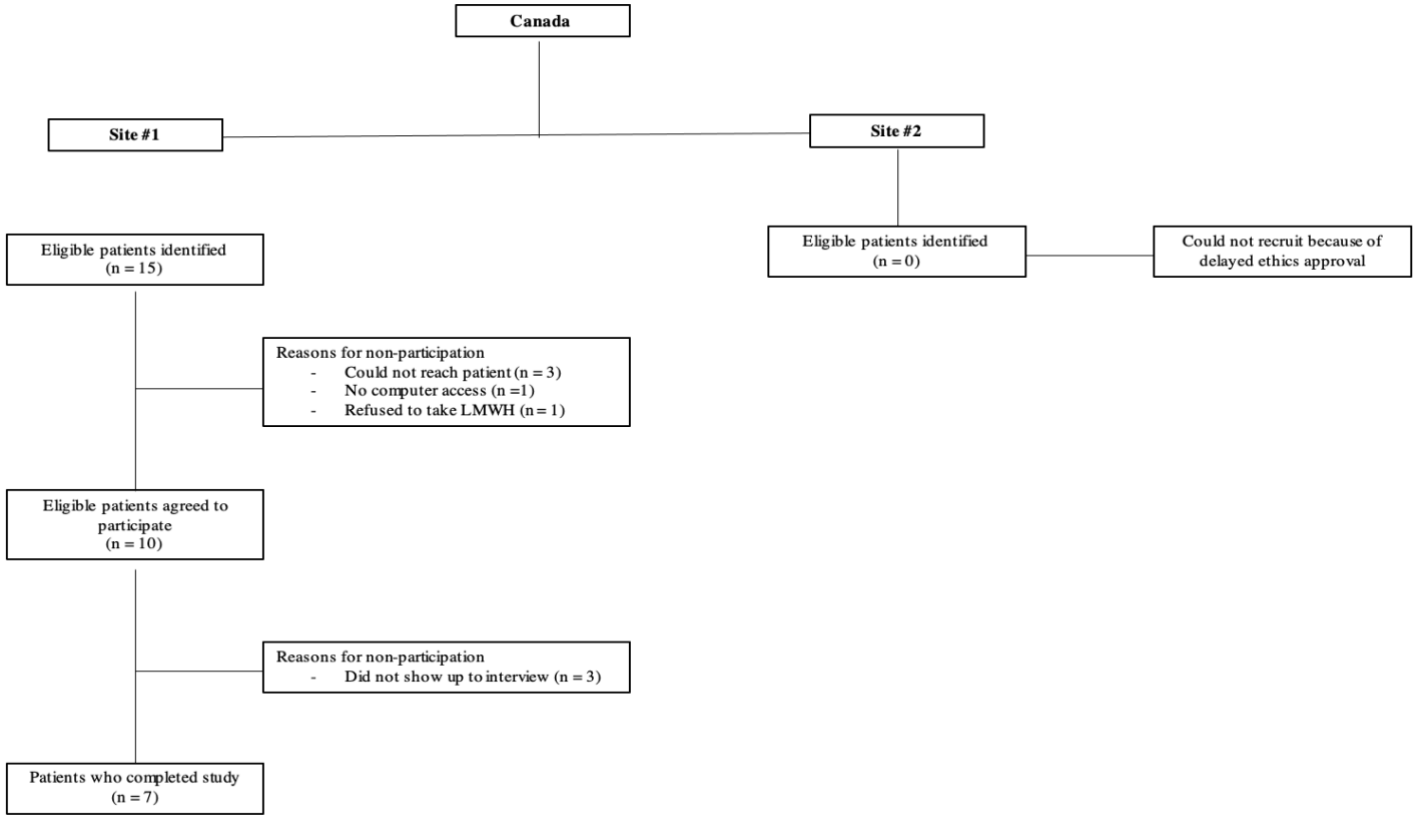
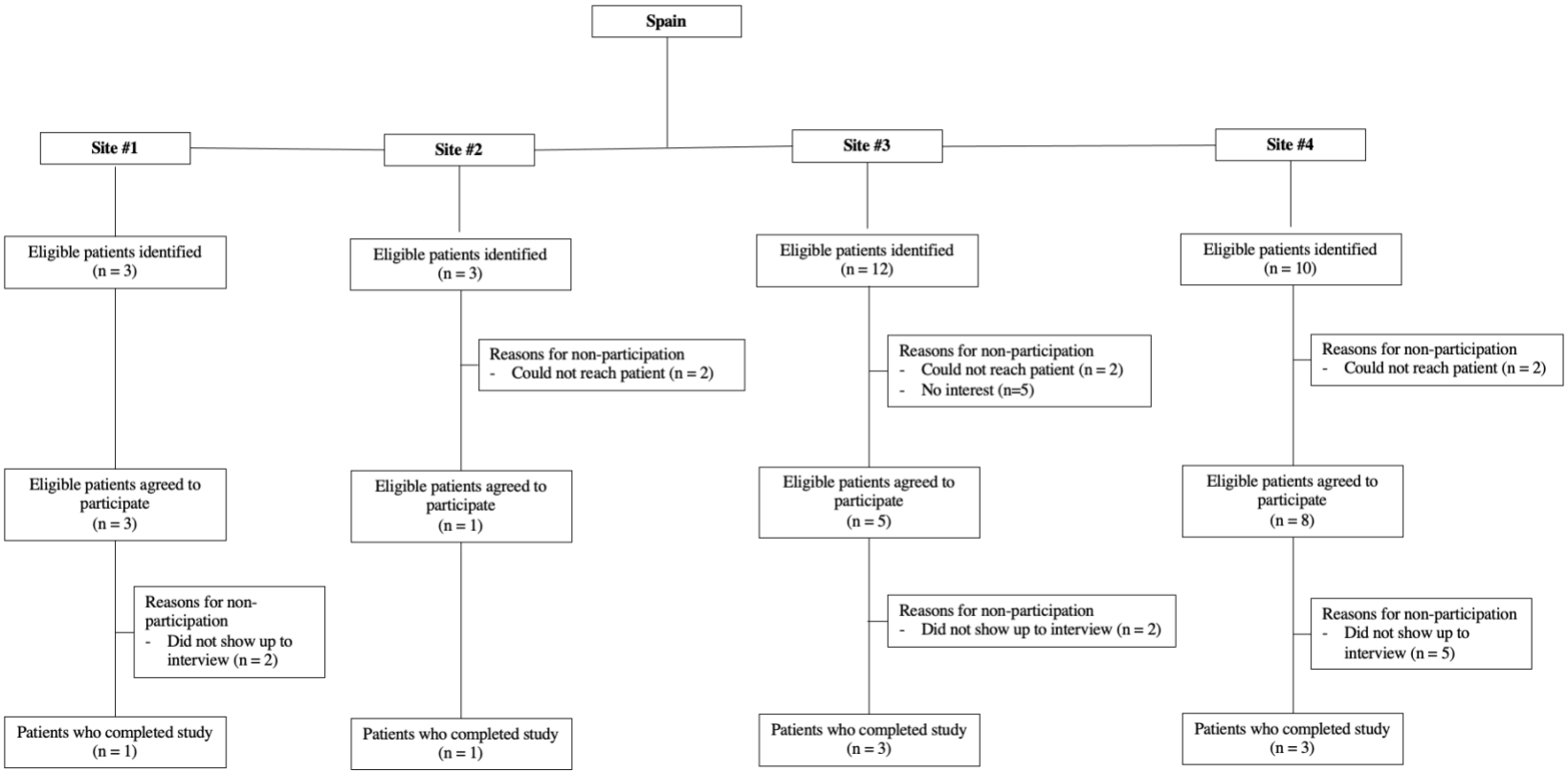


Figure 2. Recruitment process at Spanish sites



Appendix B. Decision quality

Table 1. Decision quality according to subgroup

	Satisfaction with Decision		Decision Self-Efficacy		Decisional Conflict	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Entire sample (N = 15)	25.4	(3.8)	82.3	(14.2)	21.8	(11.2)
Subgroups						
VTE risk						
High Risk (n = 12)	25.7	(3.7)	80.9	(15.4)	19.1	(9.6)
Low Risk (n = 3)	24.3	(4.7)	87.9	(6.6)	32.3	(13.0)
Country of residence						
Canada (n = 7)	24.3	(4.3)	89.6	(7.7)	23.7	(14.1)
Spain (n = 8)	26.4	(3.2)	75.9	(15.8)	20.1	(8.6)
Participant decision and model recommendation						
Concordant (n = 11)	25.5	(3.8)	80.0	(15.9)	19.2	(9.8)
Discordant (n = 4)	25.0	(4.1)	88.6	(4.9)	28.9	(13.1)
Type of event						
Leg (n = 9)	25.1	(3.9)	84.6	(12.0)	21.2	(13.0)
Lung (n = 7)	26.4	(3.9)	77.3	(17.4)	22.8	(8.4)
Other (n = 2)	24.5	(2.1)	90.9	(9.6)	16.4	(7.7)

Abbreviation: SD, standard deviation; VTE, venous thromboembolism

CHAPTER 5. CONCLUSION

Overview

This thesis explored the use of decision analysis in shared decision-making for thromboprophylaxis during pregnancy. This chapter summarizes the key findings and future directions arising from the work that was conducted as part of the DASH-TOP study and contributed to this thesis.

Key findings

In Chapter 2, we report the results of a scoping review exploring studies that have used decision analysis within shared decision-making encounter. We found that personalized decision analysis has been used to help patients and clinicians engage in shared decision-making in a variety of clinical contexts, including pregnancy.[1] Most studies reported that the decision analysis interventions were broadly beneficial. However, it was difficult to synthesize results across studies since a range of outcomes were used to evaluate the effectiveness and acceptability of the decision analysis interventions. Adding to this challenge was the lack of an agreed-upon framework for the design and execution of these type of complex studies, which must evaluate a multicomponent intervention against the backdrop of a shared decision-making encounter – the concept itself being highly debated, with one review identifying 21 separate conceptual definitions of shared decision-making.[2]

In Chapter 3 we present the protocol for a sequential explanatory mixed methods pilot study to evaluate the DASH-TOP tool, followed by the study results in Chapter 4. Participants appreciated the opportunity to use an evidence-based decision support tool

that took into account their personal values and preferences and reported feeling more prepared for their upcoming consultation with their healthcare provider to discuss LMWH. While participants liked the direct choice and preference elicitation exercises, there were mixed reactions to the personalized treatment recommendation. Some participants reported that the decision analysis results validated what they were feeling or gave them a sense of comfort or confidence in their decision. Others stated that they were either indifferent to the treatment recommendation or they did not find concept of quality adjusted life years (QALYs) particularly useful to their decision-making process.

Despite the compelling rationale of having an individualized treatment recommendation that combines patients' unique values and preferences with available research evidence, the results from our pilot study point to three questions that must be answered before we can fully understand the potential of decision analysis in supporting a shared decision-making encounter for prophylactic LMWH in the antenatal period.

Unanswered questions

Question #1: How should utilities be elicited from patients?

A key issue of the DASH-TOP pilot study was participants not understanding the standard gamble preference elicitation exercise. We opted to input the standard gamble method to elicit utility values because it has demonstrated acceptability and reliability[3,4] as well as established theoretical underpinnings of expected utility theory.[5,6] However, a third of participants in our study reported difficulty understanding how to complete the exercise. If participants did not understand the standard gamble, then the values obtained from that exercise and inputted into the decision analytic model are unlikely to accurately

represent how they value the health states relevant to the LMWH treatment decision. While the standard gamble is the most commonly used method of preference elicitation for decision analytic shared decision-making tools, our scoping review noted the use of other methods (e.g., VAS or time trade off technique).[7-12] Yet these are not without their own limitations.

The VAS is a method of preference elicitation in which individuals are asked to rate each health outcome along a feeling thermometer that has a scale of 0 (dead) to 100 (perfect health). While the VAS is easier to understand than the standard gamble, it lacks a theoretical foundation and is elicited in a choiceless context that does not require individuals to make trade-offs or consider uncertainty.[13] The VAS is also subject to end scale bias, where individuals will avoid the ends of the scale, and spacing-out bias, where individuals tend to spread out health outcomes along the scale regardless of what the outcome actually is.[14]

The time trade-off is another common form of preference elicitation used for decision analysis shared decision-making tools. Unlike the VAS, both the time trade off and standard gamble include an element of uncertainty that requires individuals to make trade-offs in their assessment of health outcomes and, thus, arguably provide a more accurate estimation of preferences.[15] The time trade off method was initially developed to address the cognitive difficulties people have with processing probabilities in the standard gamble. In a time trade off exercise, individuals are asked to make trade-offs between duration of life and health status.[15] Unlike the standard gamble, the time trade off method is riskless and assumes a linear utility for duration. Studies have shown that the time trade

off method is subject to bias from time preferences (people do not always value health in future years the same as health at the current time) and individuals' different life expectancies.[15]

There is empirical evidence that the VAS, time trade off and standard gamble yield systematically different estimates of preferences.[16] Whether one method produces estimates that are more consistent with patients' preferences is unclear. In addition to the challenge of selecting the most appropriate method of preference elicitation, our pilot study highlighted additional considerations that are specific to the patient population in the DASH-TOP pilot study.

Several participants in our study reported being traumatized by their previous VTE and many more described how that experience weighed heavily on their decision-making process. This likely impacted their risk perception during the standard gamble exercises. When completing such an exercise, it's one thing to ask participants to consider how they would feel about possibly living with chronic condition or experiencing a hypothetical health state - but another matter entirely to ask them to consider an acute and life-threatening event that they have already experienced. The desire to avoid re-experiencing trauma may have affected participants' level of risk aversion.

Because the participants in our study were either pregnant or planning pregnancy at the time of completing the standard gamble exercise, there was also an overwhelming concern about the impact that each hypothetical health state would have on their unborn baby. The health state descriptions for PE, DVT and major bleed did not directly address

the possibility of miscarriage or other facets of their baby's health, which participants expressed was a major concern for them. It is possible that some of the perceived indifference to the personalized treatment recommendation was because participants felt as though the preference elicitation exercises and/or decision analytic model did not include outcomes that were important to them. The LMWH treatment decision includes a number of short- and long-term outcomes for both mother and baby, raising the question of how to obtain utility scores for combined maternal/fetal health states.[17]

Another pregnancy-related issue with the preference elicitation exercises pertained to the concept of death, which was used as an anchor in the standard gamble exercise. Some participants in our study mentioned that even a small possibility of death was an unacceptable risk for them because of it would also mean death for their baby. This type of thinking contributed to a high level of loss aversion whereby participants were more sensitive to the losses involved in the standard gamble (i.e. death) than the gains (i.e. perfect health). For risk-averse individuals, the standard gamble is not an ideal method of deriving utility scores because it biases the estimates upward.[18] It is possible that another anchor might be more appropriate for eliciting preferences among this patient population. The use of alternative anchors has been explored in other patient groups, such as ophthalmic diseases.[19]

Question #2: How should decision analysis results be presented to patients?

In addition to not understanding the standard gamble exercise, many participants were indifferent to the treatment recommendation produced by the DASH-TOP

intervention. While there is much guidance in the literature on how to conduct the direct choice[20] and preference elicitation exercises,[21] there is less information available on how to present the decision analysis results within the context of a shared decision-making encounter. In this study, we presented participants with a figure displaying the expected QALYs for each treatment option and explained that the recommended treatment strategy was the one with the greatest QALYs.[22]

It is possible that the QALY is not a metric that participants could easily understand and therefore use to inform their decision-making. The QALY was initially developed to inform top-down decision-making processes and was presented to decision-makers in the context of a cost-utility analysis.[23] As a result, most patients are unaware that QALYs exist and, although providers may be aware of them, many are skeptical or perplexed by them.[23] Although providers and patients may be interested in incorporating information on quality and quantity of life in their clinical decision-making process, improving the relevance of the QALY as a shared decision-making metric involves improving its interpretability for this audience.[23] The interview scripts that the DASH-TOP team developed to explain the decision analysis results to participants may have been too long or overly technical.

Another explanation for the perceived indifference to the decision analytic model recommendation was that we did not provide participants with enough information on the model structure. To avoid getting too technical, we did not go into detail regarding key elements of the model structure. For example, one important consideration was that was not communicated to patients was that we used a lifetime time horizon for the QALY

calculation. Within the context of treatment decisions for VTE and pregnancy, patients are more likely to focus on the immediate future than consider a lifetime time horizon. Therefore, it is less likely that their decision will be consistent with the decision analytic model.

Mistrust of the black box nature of a decision analytic model that participants could not understand represents another possible explanation for participants' perceived indifference to the decision analysis results. The manner in which a personalized treatment recommendation is interpreted and incorporated into a decision depends on how the model and its results are understood.[24] Participants' reactions to the direct choice component of our tool highlighted how understanding the certainty of clinical evidence (or lack thereof) can inform decision-making regarding prophylactic LMWH in the antenatal period. Yet our presentation of the decision analysis results did not incorporate any uncertainty regarding the clinical data or patient preferences. The developers of other decision analytic shared decision-making tools structured their presentation of the decision analysis results in a way that allowed patients and/or healthcare providers to fold back the decision tree or conduct sensitivity analyses to explore how changes in clinical data or preferences in the model impact the treatment recommendation.[12,25-29] Conducting sensitivity analyses and/or presenting a simplified decision tree and folding it back with patients might enhance their understanding of the model, and thus trust in the procedure.

Question #3: How should the impact of decision analysis on a shared decision-making encounter be evaluated?

A final unanswered question is how to evaluate the impact of decision analysis on a shared decision-making encounter. Four participants (27%) in our study made treatment decisions that were discordant with the model recommendation and, in the qualitative interviews, participants explained that the results of the personalized decision analysis did not alter their treatment decision.

These results suggest that patients' treatment decisions might be better explained by other theories of health behaviour than expected utility theory. There is substantial empirical evidence that an individual's choice and/or behaviour does not align with the assumptions of expected utility theory,[15,30-35] which form the basis of personalized decision analysis. People value their health and make clinical decisions in dynamic ways, so it is not surprising that participants in the DASH-TOP study did not act as rational decision-makers seeking to maximizing their total expected QALYs.

Even though decision analysis did not alter participants' treatment decisions, it does not mean there is no impact on shared decision-making; there are other ways decision analysis can support a shared decision-making process. In our scoping review, we identified a plethora of outcomes used to evaluate the application of decision analysis to shared decision-making encounters. The most common outcomes assessed were the impact of decision analysis on patients' treatment decisions and the consistency between the treatment decision and decision analysis recommendation. However, the studies also evaluated many other outcomes, including the impact of decision analysis interventions on decisional conflict, participation, self-efficacy, knowledge, anxiety, satisfaction with

the decision-making process, satisfaction with the provider, treatment adherence, consultation length and treatment costs.[1]

This diversity in outcomes indicates that there is no consensus on what measure of effect should be used when evaluating the impact of decision analysis on shared decision-making encounters. Although participants in our study stated that the personalized treatment recommendation did not alter their decision, they did express appreciation for the opportunity to use an evidence-based tool that incorporates their individual values and preferences and reported feeling more prepared for their consultation. Like other studies, we did not take into account any outcomes related to the provider – a key actor in the shared decision-making process.[1] Further reflection is required to determine how we should conceptualize the added benefit of decision analysis to shared decision-making.

Concluding remarks

This thesis explored the application of a decision analytic intervention to support shared decision-making for prophylactic thromboprophylaxis in the antenatal period. The results from a scoping review and the DASH-TOP pilot study highlight both the potential for decision analysis to support shared decision-making as well challenges facing those who wish to implement such a tool in a clinical context. The DASH-TOP team is currently developing an online integrated version of the decision analytic tool presented in this thesis. Prior to conducting a randomized controlled trial of the online tool to evaluate the added benefit of using decision analysis for shared decision-making, there remain three, critical, unanswered questions that must be addressed.

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