Transitions of Care for Venous Thromboembolism
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Title: Patient Journey's in Venous Thromboembolism (VTE):
A Comprehensive Model of the Drivers of Self-Reported Patient Risks and Harms in the
Transition from Hospital to Home

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Abstract:

The **overall goals** of this project are to: (1) understand patients' venous thromboembolism (VTE) care experience during transitions of care (TOC) across various settings; (2) build a novel patient-centric statistical model of factors driving success and adversity in VTE care; (3) use this model to identify potential VTE care intervention targets; and (4) validate the model by implementing targeted VTE care interventions in the University of Utah Health Care (UUHC) Thrombosis Services and measuring associated care outcomes. Specific objectives include using themes from qualitative online interviews with VTE patients across the country (n=20) to inform a national survey of VTE sufferers (n=1000). This survey will quantify the TOC 'flow' in VTE across and between health care settings, and be used to build a comprehensive and novel statistical model of the drivers of TOC risks and harms and the role of adherence and other patient factors in exacerbating or mitigating risk of subsequent harm (VTE recurrence, bleeding, post-thrombotic syndrome, etc.). This model will be used to size and operationally prioritize patients most at risk of adverse outcomes during TOC, and provide a computer simulation to illustrate the potential reductions in harms achievable by changing care practices at key TOC points. This model will inform the implementation of empirically defined targeted interventions across inpatient and outpatient settings in UUHC Thrombosis Services, which will be evaluated by contrasting cohorts of patients in the UUHCS system on VTE harms (~n=500), leveraging electronic medical records and patient self-reports.

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Section C:

1. Overall Goal & Objectives

The RFP succinctly provides a rationale underlying the need for improved transitions of care (TOC) in venous thromboembolism (VTE), but it is worth reiterating that recurrent VTE is associated with significantly increased all cause per-patient-per year (PPPY) health-care costs.[1] Clearly, any interventions that can reduce the risk of VTE recurrence will benefit patient's personal lives, but also benefit society in terms of reduced health-care costs. The recent Institute of Medicine (IOM) report *Vital Signs: Core Metrics for Health and Health Care Progress*,[2] highlights the importance of evaluating quality of care by taking patient's self-reported care access and well-being into consideration. This proposed project takes a patient-centric approach to improving the quality of VTE transitional care. The **overall goals** of this project are to understand patients' self-reported VTE care experience as they transition to home across various care settings, build a novel patient-centric statistical model of factors driving success and adversity in VTE care that will identify targets for change (using a nationally representative survey), and validate and test that model by changing targeted care practices in the University of Utah Health Care (UUHC) Thrombosis Services that encompass hospital and community outpatient VTE patient services, with a pre/post analysis of patient surveys and chart reviews. Once the model is validated in the UUHC Thrombosis Services by demonstrating improved outcomes and patient satisfaction, it could then be used and evaluated in other healthcare systems and patient populations across the nation. **Specific objectives (OBJ)** are to:

OBJ# 1: Understand TOC in VTE from the perspective of patients using qualitative interviews, (*n*=~20) to hear patients' voices describing their VTE care journeys.

OBJ# 2: Use qualitative insights (from OBJ# 1), and appropriate patient-language, to refine a quantitative questionnaire and survey a large representative sample (n= 1000) of real-world VTE sufferers in order to quantify system and personal factors that may exacerbate the risk of harm during the TOC 'flow' in VTE (including experiences at acute care hospitals, outpatient/and ambulatory care facilities, and to and from home).

OBJ# 3: Understand patients' self-management and adherence to recommended VTE treatment regimens and patient and systemic factors that may elevate the risk of non-adherence

OBJ# 4: Build a comprehensive model of the drivers of TOC risks and harms and the role of adherence and other patient factors in exacerbating or mitigating risk of subsequent harm such as VTE recurrence, bleeding, post-thrombotic syndrome (PTS), etc.

OBJ# 5: Use the model to size and operationally define priority segments of patients most at risk of adverse outcomes during TOC.

OBJ# 6: Use the model to identify empirically grounded intervention targets and use computer simulation to illustrate the potential reductions in harms achievable by changing care practices at key TOC points.

OBJ# 7: Implement interventions *informed by our comprehensive model* (from OBJ# 6) across inpatient and outpatient settings in UUHC Thrombosis Services

OBJ# 8: Evaluate the impact of targeted intervention implementation in terms of improved patient outcomes and satisfaction by contrasting the self-report surveys and records of two cohorts of patients transitioning through UUHC Thrombosis Services, in pre-and post-intervention waves (*n*=~500, ~250 per wave).

2. Technical Approach
2.a. Current Assessment of Need in Target Area: A retrospective study of 15,000 medical records from <u>Utah and Colorado</u> estimated that 75,000 hospitalizations, 2839 permanent injuries, and 2587 deaths may occur annually due to preventable adverse events in outpatient care settings.[3] Each setting carries its own set of potential **patient harms**: Home to hospital - Misdiagnosis, medical errors, iatrogenic complications, non-patient centered care; Between Settings - Communication failures between providers; and Hospital to home - Failure to identify patient/caregiver needs and resources, non-adherence, confusing and/or contradictory discharge instructions, failure to recognize health literacy issues, lack of adequate support to implement or continue treatment instructions at home. <u>Patient factors</u> such as multiple comorbidities, age, gender, minority status, education or income level, underlying mental health issues, and satisfaction with care settings, are all important factors influencing the quality of interactions with the healthcare system and potential understanding of their disease and its treatment.[4-9] Medical errors including wrong or delayed diagnosis, incorrect drug treatment, miscommunication, or non-adherence to healthcare advice or treatment are the most common harms studied.[3,8,10-12] There is limited evidence from <u>patients' perspectives</u> on harms experienced across encounters with the healthcare system. This gap is important, as patients ultimately define experiences based on how their healthcare encounters have affected their health or quality of life. Negative perceptions of healthcare settings based on harms suffered may lead to healthcare underutilization, with associated adverse risk. Available studies are mainly retrospective medical record reviews focused on the actual visit, not the patients' experiences as they make their healthcare journeys to, from, and between different providers and settings. This study will be unique in understanding the challenges of VTE TOC, and the value of changing VTE services, from the patient's perspective.

The UUHC Thrombosis Services: Approximately 400 UUHC patients are newly diagnosed with VTE annually. Most VTE patients at UUHC are enrolled into pharmacist-managed anticoagulation services where they receive comprehensive education and anticoagulation therapy management. Most patients receive heparin-based initial therapy with transition to warfarin for maintenance therapy. However, the increasing use of direct oral anticoagulants (DOACs) [13] is simplifying the initial management of VTE but at the same time presenting another set of challenges for UUHC anticoagulation providers. At present the rates of use of DOACs within the UUHCS *hospital/ER* settings are still low relative to the level of warfarin prescriptions. In 2014, for all oral anticoagulants the proportions of orders written for each agent were warfarin (79.9%), rivaroxaban (17.3%), apixaban (2.4%), and dabigatran (0.4%). While various patient education practices have been shown to elevate DOAC adherence at the national level,[14] the levels of adherence in the UUHC system is not known at present. Dr. Witt (Co-Investigator in this application) and researchers from Kaiser Permanente have shown an association between the degree to which anticoagulation providers adhere to evidence based VTE treatment recommendations during the acute treatment of VTE, and rates of bleeding and recurrent VTE complications.[15] Anticoagulation providers in UUHC's Thrombosis Services use a systematic approach to VTE treatment and likely achieve a high degree of adherence to VTE treatment recommendations. Dr. Witt's group has also shown that patient non-adherence to anticoagulation therapy instructions increases the risk of adverse outcomes.[16] The UUHC

Thrombosis Service uses various approaches to address patient non-adherence to anticoagulation therapy, and compile annual **Quality Anticoagulation Metrics** using electronic data warehouses. For example: Time in Therapeutic INR Range (warfarin therapy) (61%); Clinically-Relevant Bleeding Complication Rate, per patient-year (~4.0%); and Thromboembolic Complication Rate, per patient-year (~1.5%). These metrics primarily measure the performance of anticoagulation providers and have focused on warfarin therapy. What is not known is how existing care transition pathways align with patient's expectations and needs, and the impact of these pathways on DOAC utilization, and self-reported adherence. Ready access to UUHC data metrics will provide an important means of validating clinical and educational/ communication changes identified and implemented within the context of this study (see Objectives 6-7).

2.b. Project Design and Methods: We propose 3 research phases over twenty-four months.
Phase 1. Qualitative Research **(OBJ# 1)**: The goals of this brief qualitative inquiry are to interview patients who have experienced VTE (either DVT or PE) to capture the likely universe of patient factors that can be assessed and then modeled in a large nationally representative survey. Pre-survey qualitative research is recommended in complex survey studies.[17] We will ask ~**20** VTE sufferers across the country to recall their VTE experience, the health care providers they interacted with, and treatments/advice received, as they made their "journey" to, from and between health care settings and home. Interviews will focus on communication, education, and accountability factors likely to elevate risk of patient harm (e.g., adverse events, VTE recurrence, and non-adherence to anticoagulation treatments) and beliefs and attitudes about VTE, its management and their own roles in maintaining adherence and disease self-management. Procedure: Patients will be interviewed using Online Bulletin Board (OBB) methods. Dr. Feehan has previously published research using OBBs to interview panels of healthcare decision-makers and developed analytic approaches for the interpretation of verbatim data derived from qualitative interviews.[18,19] Patients will be recruited and invited to participate in a day long online panel. Each respondent will engage for approximately **two hours** on the OBB over the course of the day, with including group interview/discussion questions and individual follow-up querying by the moderator. We will use a Pfizer preferred market research supplier, **The Modellers/Hall and Partners** (see section **D.b. Staff Capacity**) to screen respondents to verify study eligibility. Respondents will receive industry standard honoraria for their participation. Professional senior managers from The Modellers/Hall & Partners, who have conducted extensive in-depth-interviews with patients and health care providers, will moderate patient interviews. The investigator team will observe and listen to all interviews and provide suggestions for additional probes as required but will not directly interview respondents to avoid researcher-driven biases directly influencing the discussion.

Phase 2: National Quantitative Survey **(OBJ# 2)**. A representative online survey of VTE sufferers will quantitatively verify the key patient identified factors carried in from the qualitative phase including "nodes" in the TOC pathway (hospital and outpatient care utilization and interaction), and factors that may elevate the risk of harm (e.g., demographics, illness and comorbidities, support systems, adherence, self-care, reading comprehension, mental health, insurance, attitudes and beliefs about VTE, etc.). The survey will be used to develop a *Structural Equation Model (SEM)* that will gauge the relative impact of a host of patient factors on the risk of

adverse VTE outcomes from poor TOC including bleeding episodes, VTE recurrence, and PTS.) Sample Size: We propose to conduct a representative online survey of up to **1,000** adult patients aged 18 years or over, across the country, screened to have at least one VTE admission to an acute care hospital within the previous 2 years. This sample size will also will be sufficiently powered to output prevalence of harm results for meaningful subgroups of interest, such as those experiencing DVT versus PE. We intend to use root mean square error of approximation (RMSEA)[20] as one of the primary statistics to assess overall model fit. Our approach is to determine a sample that would be sufficient to enable us to distinguish models that fit the data given accepted thresholds (RMSEA = .05) and models that don't (RMSEA > .07)[21] We calculated the minimally acceptable sample size of 630, assuming the following: alpha = .05, power = .80, 30 *df*, null RMSEA = .07, alternative RMSEA = .05. Survey Recruitment and Online Survey Procedure: Respondents will be recruited from a panel of patients who previously elected to participate in patient-oriented research studies, and will receive industry-standard honoraria for participating. **Pfizer** and other pharmaceutical companies frequently utilize these panels in research. The investigators have previously partnered with these panel firms to conduct large-scale quantitative studies for publication.[22-24] Respondent screening and invitation: An invitation letter will be sent electronically to panel members describing the study and inviting them to enter the survey to answer screening questions. If qualified they will give consent electronically by checking a consent box, and then move immediately on to the full survey. Survey Duration: It is anticipated that each survey will take **45 minutes** to complete. This is quite standard given the comprehensiveness of the survey we are proposing and the online survey provides an engaging and user-friendly platform for administering the questions. Survey Measures: The patient survey will focus on the primary outcome of self-reported VTE related harms (recurrent VTE, bleeding, mental health issues, PTS, lost productivity, etc.) as mediated by experiences in various care settings during VTE treatment. Factors associated with these outcomes will be assessed in three broad domains of Patient Factors; Self-Reported Environmental Factors; and Demographics. While recognizing that descriptors of key attitudes and behaviors will be gleaned from the Phase 1 Qualitative research, the survey will include at a minimum the following: 1. *Self-reported medication therapy experience and adherence* (**OBJ# 3**). A critical component of the survey will focus on patients' use of IV, SQ, and oral anticoagulation therapies in the transition from the hospital, emergency department, or clinic to outpatient settings. Each respondent will report on therapies received in the initial (first 7 days), long-term (7 to 90 days) and extended (90+ days) phases of VTE treatment.[25] Suboptimal anticoagulation during the first 90 days of VTE treatment has been associated with increased risk of recurrent VTE (see McRae, 2014 for a review).[26] Patients will be asked about their use of medications *vis a vie* the American College of Chest Physician Guidelines (ACCP).[25] Patients will be asked about their experiences with and adherence to low-molecular-weight heparin [LMWH] (i.e., enoxaparin, dalteparin), fondaparinux, unfractionated heparin [UFH], warfarin, and/or direct oral anticoagulants (i.e., rivaroxaban, apixaban, edoxaban and dabigatran) as they transitioned to home. Multiple measures will be used to assess adherence including standard instruments modified for patient use such as the SMAQ [27] or the Adherence Estimator.[28] Attitudinal questions will assess perceptions of instructions received from health care providers in various settings and personal beliefs about adherence to anticoagulant medications in the initial, long-term, and extended treatment

phases, and perceptions relating to the risks of recurrent VTE, bleeding, and death. 2. *Demographics*: Will include common demographic indicators, ethnicity, age, income, rural vs suburban/urban location etc. 3. *Environmental Factors*: Self-reported external factors hypothetically associated with adherence to VTE treatment including: (a) health system engagement indicators (e.g., availability of primary care, hematology, and thrombosis services); (b) indicators of satisfaction with various healthcare providers (e.g., 'likelihood to recommend' using the Net Promotor Score (NPS) [29,30] a loyalty and advocacy metric previously used by the applicants;[22,31] (c) Insurance status (form and level of coverage) and perceived ability to pay for services/ medications; (d) other support availability (e.g., family support, patient support programs); and (e) self-reported chronic conditions and other comorbidities that increase the disease/ adherence burden. 4. *Internal Patient Factors*: Self-reported personal factors impacting VTE regimen adherence, including: (a) Health Locus of Control Scales (HLC): The level of HLC (person's beliefs they have personal control over their illness and its management) is associated with stronger adherence and better patient outcomes;[32,33] (b) Psychological Distress and Cognitive Function: Current and past distress can impact self-management and adherence. Standard measures including the 12 item General Health Questionnaire,[34] or the Mini-Mental State Examination [35,36] will be used; (e) Health literacy: Valid but brief screening instrument to gauge respondent's ability to comprehend and act on written health information;[37] (f) Level of computer literacy and patient comfort with the use of health technologies (e.g., use of reminders and alerts).

Statistical Modeling (OBJ# 4). 1. Structural Equation Modeling (SEM): SEM [38] will be used to identify the characteristics that most strongly predict the likelihood of VTE medication regimen non-adherence and self-reported harm outcomes. The patient self-report data will be included in a driver model of non-adherence (see Figure 1; only a subset of potential measures are shown). For ease of readability the sample SEM as *illustrated* here is simplified graphically, with error terms (ξ), intercorrelations amongst observed indicator variables, and dummy factor loadings (λ) and parameter estimates (β) not shown. The underpinning conceptualization of the model is that there is a direct relationship between the two *latent* prime outcome constructs: L1: VTE Medication Non-Adherence and L2: VTE Harm. Observed indicator variables will be included in the model and their relative association with the latent constructs estimated. SEM elegantly takes into account the error inherent in all forms of self-reported data along with the intercorrelations between any measures in the survey. Moreover these indicators are likely to be correlated, as those experiencing harms (such as VTE recurrence and bleeding or are also more likely to report non-adherence to their VTE regimens). The SEM will simultaneously incorporate those error terms and the intercorrelations in estimating the model. SEMs have been widely used in modeling causal pathways of numerous health and disease states [38-42] and in health services research.[43-45] While applying SEM to VTE outcomes in this application is unique, studies have demonstrated the utility of the SEM analytic approach in cardiovascular disease patient self-management and the development of associated metrics,[46] and the role of self-monitoring of symptoms and improved adherence and outcomes in heart failure.[47]

Figure 1. Structural Equation Model – *Illustrative*
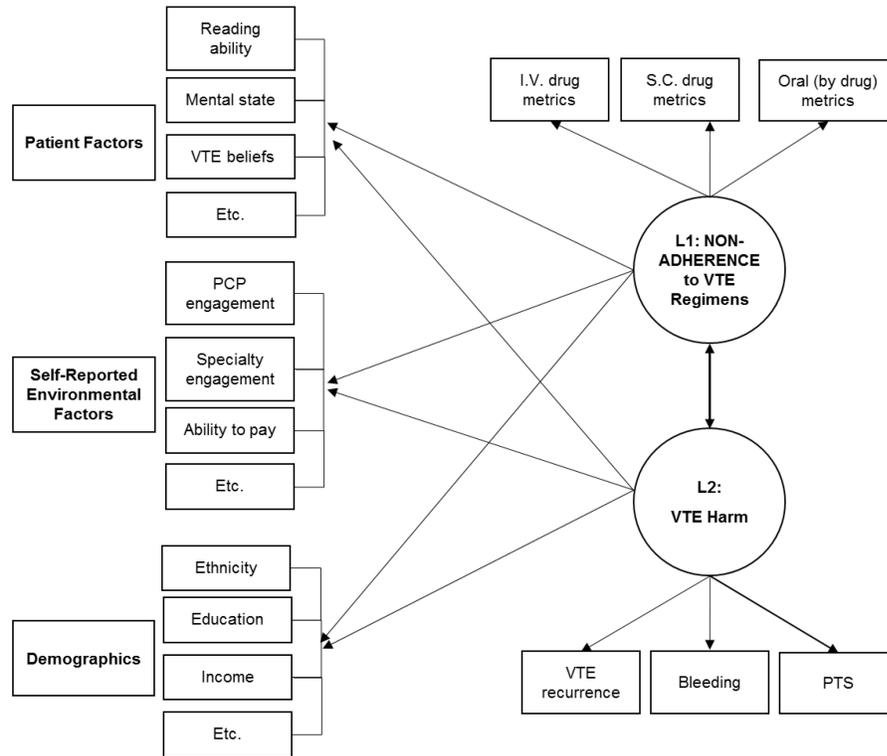
2. Patient Segmentation **(OBJ# 5):** The quantified TOC "flow" and SEM parameters, will also allow sizing and characterization of VTE population sub-segments most at risk of harm in their TOC. These may represent particular targets for intervention, or may be differentially responsive to subsequent interventions tested in the UUHC Thrombosis Services. Dr. Feehan has previously modeled distinct sub-types of patients with AMD on their environmental, cardiovascular status, and genetic vulnerability.[48] 3. Change Tables and Adverse Outcome Reduction Simulation (**OBJ# 6)**: To ensure the practical utility of the developed SEMs, we will develop an Excel-based "SEM simulator" that will input model parameters and output improvements in VTE adverse outcomes based on a change of any significant predictor variable by a set amount, as if a targeted intervention successfully modified a given risk factor. This will input key metrics from the measurement models and give the unit change in the VTE outcomes that would result from a one-unit change in any model factor.[49,50] For example in the proposed study, a hypothetical 10 % improvement in "*patients' confidence in self-managing their VTE medications*" could result in a 10 % improvement in "*oral anticoagulant adherence*," resulting in a potential 6% reduction in "*VTE recurrence*" (% illustrative).

2.c. Evaluation Design (OBJ# 7-8): The third phase of the proposed study will involve utilizing the expertise of Drs. Witt, Fleming and Johnson to operationalize changes in TOC practices within the UUHC system that are empirically justified from the earlier predictive model and measure the resultant impact on patient outcomes. The model will be used to prioritize changes in how the UUHC Thrombosis Services prepare, communicate with, and educate patients as they transition to home. By basing change in clinical/educational practices on a

robust empirical model, the likelihood of seeing significant improvements in patient outcomes will be enhanced. The SEM simulator will be used to select target interventions with high likelihood of impacting outcome measures (e.g., recurrent VTE, bleeding, resource utilization, patient satisfaction); the feasibility of potential intervention targets will be evaluated to determine whether they can be readily implemented and tied to measurable outcomes in UUHC Thrombosis Services with potential application to other institutions. The suitability of a given intervention target (e.g., standardized education of newly diagnosed VTE patients prior to transitioning to home; use of motivational interviewing techniques; reminders for key events such as medication refills, dosing transitions for direct oral anticoagulants, INR test reminders for warfarin; etc.) will be carefully considered with input from Thrombosis Services staff. <u>Phase 3: Quantitative Intervention Evaluation</u> **(OBJ# 8)**: Evaluation will comprise multiple components. First, at an overall level the system-wide *Quality Anticoagulation Metrics* (see **2.a. Current Assessment of Need in Target Area** above) for the overall UUHC Thrombosis services will be contrasted pre and post intervention. Second, we will compare and contrast the <u>records and patient surveys of two cohorts of VTE patients</u> using the UUHC Thrombosis services, pre- and post-intervention initiation. At the time of the National Survey conducted in year one, we will also survey a pre-intervention prospective wave of ~250 UUHC patients online using the UUHC Thrombosis Service. These patients will be informed about the survey by UUHC clinical staff, and be directed to the same website for the National Survey, go through the same screening and consent procedures (with an additional consent request to access their electronic medical record for chart review), and complete the same 45 minute survey. In year 2, a second prospective wave of post-intervention initiation patients will be invited to participate and complete the same consent and survey as the first pre-intervention wave. In each wave patients will be invited to complete the survey after they have completed 90-days of therapy, and will be asked to report their experience of VTE, and associated harms and other key metrics as per the National Survey (e.g., likelihood to recommend the UUHC Thrombosis Service using the NPS measure). For both pre and post-intervention waves key metrics of TOC harms (bleeding, VTE recurrence, unscheduled clinic or ED visits related to VTE symptoms, etc.) will be abstracted from the patients' records and coded for analysis (across all UUHC hospital and outpatient services). The Modellers / Hall and Partners will link individuals' abstracted record data to individual survey responses. Pre-post intervention evaluation analyses will comprise: (1) EMR analyses - examine the prevalence of harms (recurrence, bleeding, etc.) in the records of the two cohorts pre- and post; (2) Self-report analyses - use results from the patient survey's pre- and post-intervention waves to identify changes in self-reported outcomes and satisfaction measures; (3) VTE Harm concordance - analyses will also be done to determine the associations between patient self-reported of VTE harms contrasted with the harms abstracted from the patient's EMR, to determine the level of over-or-underreporting in both data sources: (4) Bias analyses - contrasting the self-report of patients in the UUHC with the prior national model survey results, to identify any biasing factors that may contribute to greater or lesser intervention effectiveness in this Utah cohort.

3. Detailed Workplan and Deliverables Schedule: The three stages of the research can be completed <u>within 24 months</u>. We are confident that the considerable volume of work involved in this project will be accomplished as we will leverage a current **Pfizer Preferred Market**

Research Supplier (under our close direction) to conduct the exploratory qualitative research and the subsequent national survey/structural equation model and the statistical analysis of the pre-post intervention EMR and survey data to evaluate the intervention <u>extremely</u> quickly with extraordinary high quality standards.

1/Months 1-3	Overall design finalization, IRB approval, data collection agency contracting, design of Phase 1 qualitative discussion guides
1/ Months 4-6	Qualitative recruitment/ interviews, draft Phase 2 quantitative survey
1/ Months 7-9	Survey national cohort & UUHCs' pre-intervention patient wave, build SEM and develop change table simulator
1/ Months 10-12	Publish Phase 1 <u>qualitative</u> findings, identify intervention targets from the model, and develop targeted interventions in TOC practice
2/ Months 1-3	Implement interventions
2/ Months 4-6	Continue interventions, publish <u>quantitative</u> model research findings, survey post-wave of patients
2/ Months 7-9	Evaluate interventions by analyses of EMR data and pre-post patient surveys
2/ Months 10-12	Publish and disseminate <u>intervention evaluation</u> findings

<u>Deliverables</u>**:** Study findings will be disseminated through published research papers in medical and scientific peer-reviewed journals that focus on transitions of care and thrombosis (e.g., JAMA Internal Medicine, Blood, Journal of Internal Medicine, Chest, Journal of Thrombosis and Haemostasis); in national and local community press; University of Utah Health Care system websites, workshops with VTE service providers, and key national conferences (e.g., International Society on Thrombosis and Haemostasis Congress, Thrombosis and Hemostasis Societies of North America and the American Society of Hematology).

References:

1. Lefebvre P, Laliberté F, Nutescu EA, Duh MS, LaMori J, Bookhart BK, Olson WH, Dea K, Hossou Y, Schein J, Kaatz S. All-cause and disease-related health care costs associated with recurrent venous thromboembolism. Thromb Haemost. 2013 Dec;110(6):1288-97. doi: 10.1160/TH13-05-0425. Epub 2013 Oct 2.
2. Blumenthal D, McGinnis JM. Measuring Vital Signs: an IOM report on core metrics for health and health care progress. JAMA. 2015 May 19;313(19):1901-2. doi: 10.1001/jama.2015.4862.
3. Woods DM, Thomas EJ, Hall JL, Weiss KB, Brennan TA. Ambulatory care adverse events and preventable adverse events leading to a hospital admission. Qual Saf Health Care. 2007;16:127-31.
4. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients: results of the Harvard Medical Practice Study 1. New England J Med 1991;324:370-6.
5. Zandieh SO, Goldmann DA, Keohane CA, Yoon C, Bates DW, Kaushal R. Risk factors in preventable adverse drug events in pediatric outpatients. J Pediatric 2008;152(2):225-31.

6. Gandhi TK, Burstin HR, Cook EF, et al. Drug complications in outpatients. J Gen Intern Med. 2000;15(3):149-54.
7. Field TS, Gurwiatz JH, Harrold LR, et al. Risk factors for adverse drug events among older adults in the ambulatory setting. J Am Geriatr Soc. 2004;52(8):1349-54.
8. Kuzel AJ, Woolf SH, Gilchrist VJ, et al. Patient reports of preventable problems or harm in primary health care. Ann Fam Med 2004;2(4):333-40.
9. Anderson LA, Zimmerman MA. Patient and physician perceptions of their relationship and patient satisfaction: a study of chronic disease management. Patient Educ Cons. 1993;20(1):27-36.
10. Dovey SM, Meyers DS, Phillips RL, et al. A preliminary taxonomy of medical errors in family medicine. Q Safe Health Care. 2002;11:233-8.
11. Mohr JJ, Lannon CM, Thoma KA,et al. Learning from errors in ambulatory pediatrics (LEAP). Advances in patient safety: From research to implementation. 2004;1:355-68.
12. Fernald DH, Pace WD, Harris DM, et al. Event reporting to a primary care patient safety reporting system: A report from the ASIPS collaborative. Ann Fam Med 2004;2:327-32.
13. Gómez-Outes A, Terleira-Fernández AI, Lecumberri R, Suárez-Gea ML, Vargas-Castrillón E. Direct oral anticoagulants in the treatment of acute venous thromboembolism: a systematic review and meta-analysis. Thromb Res. 2014 Oct;134(4):774-82. doi: 10.1016/j.thromres.2014.06.020. Epub 2014 Jul 6.
14. Shore S, Ho PM, Lambert-Kerzner A, Glorioso TJ, Carey EP, Cunningham F, Longo L, Jackevicius C, Rose A, Turakhia MP. Site-level variation in and practices associated with dabigatran adherence. JAMA. 2015 Apr 14;313(14):1443-50. doi: 10.1001/jama.2015.2761.
15. Martinez K, Kosirog E, Billups SJ, Clark NP, Delate T, **Witt DM**. Clinical Outcomes and Adherence to Guideline Recommendations During the Initial Treatment of Acute Venous Thromboembolism. Ann Pharmacother. 2015 Apr 30. pii: 1060028015583892.
16. **Witt DM**, Delate T, Clark NP, Garcia DA, Hylek EM, Ageno W, Dentali F, Crowther MA. Nonadherence with INR monitoring and anticoagulant complications. Thromb Res. 2013 Aug;132(2):e124-30. doi: 10.1016/j.thromres.2013.06.006. Epub 2013 Jun 22.
17. Clark MD, Determann D, Petrou S, Moro D, de Bekker-Grob EW.Discrete choice experiments in health economics: a review of the literature. Pharmacoeconomics. 2014. 32: 883–902.
18. Mesure P, McGouran O, & **Feehan M**. Using Online Bulletin Boards to Develop High Value Corporate Strategy. Proceedings of the ESOMAR Congress 2010.
19. **Feehan M**, Ilangakoon C, Mesure P. Three Steps to Clarity: A structured approach for qualitative verbatim analysis. Quirk's Marketing Res Rev. 2013 October: 48–55.
20. Hooper D, Coughlan J, Mullen MR. Structural Equation Modelling: Guidelines for Determining Model Fit. EJBRM. 2008;6(1):53-60.
21. Steiger JH. Understanding the limitations of global fit assessment in structural equation modeling. Personality and Individual Differences. 2007;42(5):893-898.
22. **Munger M**, Eliot G, Hartman J, Vincent K, **Feehan M**. Community pharmacists' occupational satisfaction and stress: a profession in jeopardy. JAPhA. 2013;53:282-296
23. Oderda GM, Shiozawa A, Walsh M, Hess K, Brixner DI, **Feehan M**, Akhras K. (2014) Physician Adherence to ACR Gout Treatment Guidelines: Perception vs. Practice. Postgrad Med. 2014 May;126(3):257-267.

24. **Munger M**, Ruble JH, Nelson SD, Ranker L, Petty RC, Silverstein S, Barton E, **Feehan M**. National Evaluation of Prescriber Drug Dispensing. Pharmacother. 2014 Oct;34(10):1012-21. doi: 10.1002/phar.1461. Epub 2014 Jul 23.

25. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S-e494S. doi:10.1378/chest.11-2301.

26. McRae S. Treatment options for venous thromboembolism: lessons learnt from clinical trials. Thrombosis Journal. 2014;12:27. doi:10.1186/s12959-014-0027-8.

27. Knobel H, Alonso J, Casado JL, Collazos J, González J, et al. Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study. AIDS. 2002;16:605–613.

28. McHorney CA. The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease. Curr Med Res Opin. 2009;25: 215–238. doi:10.1185/03007990802619425.

29. Reichheld FF. The one number you need to grow. Harv Bus Rev. 2003;81: 46–54, 124.

30. Reichheld FF. The Ultimate Question: Driving Good Profits and True Growth. Harvard Business Press. 2006:235 p.

31. **Feehan M**, Ilangakoon C, Mesure P. Keeping score: is the Net Promoter Score a reliable tool in a global recessionary environment? Marketing Research. 2010;Winter: 6–10.

32. Härkäpää K, Järvikoski A, Mellin G, Hurri H, Luoma J. Health locus of control beliefs and psychological distress as predictors for treatment outcome in low-back pain patients: results of a 3-month follow-up of a controlled intervention study. Pain. 1991;46: 35–41.

33. Govindarajan P, Larkin GL, Rhodes KV, Piazza G, Byczkowski TL, et al. Patient-centered integrated networks of emergency care: consensus-based recommendations and future research priorities. Acad Emerg Med. 2010;17: 1322–1329. doi:10.1111/j.1553-2712.2010.00939.x.

34. Banks MH, Clegg CW, Jackson PR, Kemp NJ, Stafford EM, et al. The use of the General Health Questionnaire as an indicator of mental health in occupational studies. Journal of Occupational Psychology. 1980;53: 187–194. doi:10.1111/j.2044-8325.1980.tb00024.x.

35. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12: 189–198.

36. Velayudhan L, Ryu S-H, Raczek M, Philpot M, Lindesay J, et al. Review of brief cognitive tests for patients with suspected dementia. Int Psychogeriatr. 2014;26: 1247–1262. doi:10.1017/S1041610214000416.

37. Wallace LS, Rogers ES, Roskos SE, Holiday DB, Weiss BD. Brief report: screening items to identify patients with limited health literacy skills. J Gen Intern Med. 2006;21: 874–877. doi:10.1111/j.1525-1497.2006.00532.x.

38. McHorney CA, Zhang NJ, Stump T, Zhao X. Structural equation modeling of the proximal-distal continuum of adherence drivers. Patient Prefer Adherence. 2012;6: 789–804. doi:10.2147/PPA.S36535.

39. Williams GC, Niemiec CP, Patrick H, Ryan RM, Deci EL. The importance of supporting autonomy and perceived competence in facilitating long-term tobacco abstinence. Ann Behav Med. 2009;37: 315–324.doi:10.1007/s12160-009-9090-y.

40. Tann SS. Implications for quality of life research in Latino populations. J Transcult Nurs. 2005;16:136–141. doi:10.1177/1043659604273552.
41. Metz SM, Wyrwich KW, Babu AN, Kroenke K, Tierney WM, et al. Validity of patient-reported healthrelated quality of life global ratings of change using structural equation modeling. Qual Life Res. 2007;16:1193–1202. doi:10.1007/s11136-007-9225-1.
42. Kapetanovic S, Griner R, Zeldow B, Nichols S, Leister E, et al. Biomarkers and neurodevelopment in perinatally HIV-infected or exposed youth: a structural equation model analysis. AIDS. 2014;28:355–364. doi:10.1097/QAD.0000000000000072.
43. Hossain MM, Laditka JN. Using hospitalization for ambulatory care sensitive conditions to measure access to primary health care: an application of spatial structural equation modeling. Int J Health Geogr. 2009;8:51. doi:10.1186/1476-072X-8-51.
44. Agiro A, Wan TTH, Ortiz J. Organizational and Environmental Correlates to Preventive Quality of Care in US Rural Health Clinics. J Prim Care Community Health. 2012;3: 264–271. doi:10.1177/2150131911434804.
45. Fischer KE. Decision-making in healthcare: a practical application of partial least square path modelling to coverage of newborn screening programmes. BMC Med Inform Decis Mak. 2012;12: 83.doi:10.1186/1472-6947-12-83.
46. Steca P, Greco A, Cappelletti E, D'Addario M, Monzani D, Pancani L, Ferrari G, Politi A, Gestra R, Malfatto G, Parati G. Cardiovascular Management Self-efficacy: Psychometric Properties of a New Scale and Its Usefulness in a Rehabilitation Context. Ann Behav Med. 2015 Mar 17. [Epub ahead of print]
47. Vellone E, Riegel B, D'Agostino F, Fida R, Rocco G, Cocchieri A, Alvaro R.Structural equation model testing the situation-specific theory of heart failure self-care. J Adv Nurs. 2013 Nov;69(11):2481-92. doi: 10.1111/jan.12126. Epub 2013 Mar 21.
48. **Feehan M**, Hartman J, Durante R, Morrison MA, Miller JW, et al. Identifying subtypes of patients with neovascular age-related macular degeneration by genotypic and cardiovascular risk characteristics. BMC Med Genet. 2011;12:83. doi:10.1186/1471-2350-12-83.
49. Dillon W, White J, Rao V, Filak D. "Good Science": Use structural equation models to decipher complex customer relationships. Marketing Research. 1997;9:22–31.
50. VanderWeele TJ, Hawkley LC, Thisted RA, Cacioppo JT. A marginal structural model analysis for loneliness: implications for intervention trials and clinical practice. J Consult Clin Psychol. 2011;79:225–235.doi:10.1037/a0022610.
52. Durante R, Casey B, **Feehan M**. The mutual blame game: how physicians and patient perceptions of non-adherence contribute to the problem. PBIRG Perspective. 2014, Spring 16(1), 12-14.
53. **Munger MA**, Van Tassell, B, Lafleur J. Medication noncompliance: An unrecognized cardiovascular risk factor. Medscape General Medicine 2007; Sept 19(9)3:58. 2007;http://medgenmed.medscape.com/medgenmed.
54. Durante R, Wong D, Griffen R, **Feehan** M. Doing More with Less: Leveraging Multi-Dimensional Modeling for Cost-Effective Global Research and Marketing Strategy. Marketing Insights. 2014, March: 29-33.