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The shifting care and outcomes for patients with endangered limbs – Critical limb ischemia (SCOPE-CLI) registry overview of study design and rationale

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ABSTRACT

Background: Critical limb ischemia (CLI), the most severe form of peripheral artery disease, is associated with pain, poor wound healing, high rates of amputation, and mortality (>20% at 1 year). Little is known about the processes of care, patients' preferences, or outcomes, as seen from patients' perspectives. The SCOPE-CLI study was co-designed with patients to holistically document patient characteristics, treatment preferences, patterns of care, and patient-centered outcomes for CLI.

Methods: This 11-center prospective observational registry will enroll and interview 816 patients from multi-specialty, interdisciplinary vascular centers in the United States and Australia. Patients will be followed up at 1, 2, 6, and 12 months regarding their psychosocial factors and health status. Hospitalizations, interventions, and outcomes will be captured for 12 months with vital status extending to 5 years. Pilot data were collected between January and July of 2021 from 3 centers.

Results: A total of 70 patients have been enrolled. The mean age was 68.4 ± 11.3 years, 31.4% were female, and 20.0% were African American.

Conclusions: SCOPE-CLI is uniquely co-designed with patients who have CLI to capture the care experiences, treatment preferences, and health status outcomes of this vulnerable population and will provide much needed information to understand and address gaps in the quality of CLI care and outcomes.

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1. Introduction

Critical limb ischemia (CLI), a devastating condition characterized by extreme pain, poorly healing wounds and potential amputation, has the poorest prognosis amongst all patients with peripheral artery disease (PAD) [1-5]. Significant variations in the management of CLI exist in the United States and are influenced by racial and ethnic disparities [6-10]. Although previous interventional registries and ongoing trials (including BEST-CLI [11], the BASIL-2 [12], and the BASIL-3 [13] trials) have and will provide guidance regarding appropriate treatment and follow-up in CLI, these studies have focused on clinical aspects of the disease. Beyond patency and amputation, patient-centered psychosocial and health status have rarely been assessed [14]. There is a paucity of data regarding patient-centered outcomes such as quality of life, ability to ambulate, pain control, and social acceptance.

There are critical gaps in knowledge including lack of insight into patients' perception of their disease and how socioeconomic, psychosocial, and economic variables impact prognosis. Moreover, there is a need for outcomes to support regulatory approaches to novel CLI treatments, reimbursement, and strategies to improve the cost-effectiveness of care. We also need a deeper understanding of current practice as it relates to CLI care.

Given the importance of understanding CLI patients' outcomes and the numerous existing gaps in knowledge, there is a pressing need to collect observational data on treatment patterns, adherence to performance measures, and outcomes that are relevant to patients and clinicians. To address this, the Shifting Care and Outcomes for Patients with Endangered Limbs – Critical Limb Ischemia (SCOPE-CLI) study was developed to study the CLI population at multiple centers throughout the nation. It seeks to provide preliminary information to identify areas of action that can be targeted in quality improvement programs for CLI. Most importantly, it will provide data on health status outcomes among patients with CLI, [15] while incorporating individual patient characteristics (demographics, socio-economic, psychosocial and clinical background) and treatments. The SCOPE-CLI study will also be well equipped to identify potential disparities in the provision of care and outcomes as a function of patient's characteristics. To address these goals, SCOPE-CLI was co-created with patients suffering from CLI to ensure the study encompasses relevant aspects of care and outcomes as seen from patients' perspectives.

The specific aims of SCOPE-CLI are (1) to generate additional evidence on the clinical characteristics, treatment patterns and outcomes of patients diagnosed with CLI; (2) to describe treatment patterns and variability across practices for the purposes of identifying gaps in quality care delivery; and (3) to perform a series of analyses to examine the associations of patient and treatment characteristics with a broad range of clinical and patient-centered outcomes. The central objective of SCOPE-CLI is to systematically quantify patients' CLI-specific health status and clinical outcomes and to perform subgroup analyses as a function of different PAD treatments and patient characteristics. Realizing these aims will allow us to improve the quality of medical decision making for CLI with patient-centered shared-decision frameworks. It will also allow us to better conceptualize and understand patient-centered endpoints that impact the experience of the disease, and subsequently allow us to design tailored disease management approaches from a holistic point of view.

2. Methods

2.1. Obtaining input from stakeholders

To design the SCOPE-CLI study, we engaged stakeholders with CLI experience to aid the research team in study development. Summary characteristics of the different stakeholders are shown in Table 1 with a full list of the stakeholder engagement planning sessions provided in Supplemental Table 1. A collaborative panel with expert physicians and patients (in whom a diagnosis of PAD had previously been made) was created to collect information on prioritization of outcomes and to define the screening and follow up processes. Individuals on this panel included six clinicians (four from interventional cardiology, two from vascular surgery) with expertise on various subsets of PAD to provide guidance on research aims, study design, and outcome measures. Six patient experts (three men and three women with an age range of 40 to 71 years) were included to help define patient-centered data points, identify the most relevant patient-centered outcomes, and to provide feedback on the overall study design.

After developing an initial framework, we then conducted patient focus groups and interviews with 28 patients. The patients involved in study development were from diverse backgrounds, with demographic information for all patients detailed in Supplemental Table 2. Interviews and focus group discussions were recorded, transcribed, and coded to identify priority themes to measure in the SCOPE-CLI registry. Qualitative content analysis was conducted by a multidisciplinary team consisting of three research nurses, a public health researcher, and a psychologist (KS, CD, CF, CP, KS) [16]. Interviews and focus groups were continued until content saturation was reached. Central themes that emerged included barriers to recognition and early diagnosis, escalation of disease and symptoms, education, coping, adjustment to a life with CLI, life impacts, regret, quality of care and readiness of health care system, symptoms, treatment goals, barriers to healing, and locus of control. Supportive quotes from each of these central themes are detailed in Supplemental Table 3.

2.2. Study design and data collection

2.2.1. Patient enrollment

Patients with CLI will be screened for enrollment at specialty PAD clinics including but not restricted to vascular surgery, podiatry, internal medicine, (interventional) cardiology settings, and during hospitalization as shown in Fig. 1. Trained study coordinators will screen patients from clinic lists, inpatient lists, and diagnostic testing queries including ankle-brachial index (ABI) and toe brachial index (TBI) results for eligibility. The enrollment target for the study is 816 patients. Enrollment began on August 1, 2021 and is anticipated to continue for 24 months.

Given the enrollment disparity of women and communities of color in clinical trials, the SCOPE-CLI registry will have enrollment targets of 40% women and 30% of patients from underrepresented racial and ethnic groups [17]. Enrollment numbers will be continuously monitored to ensure these targets are met.

Table 1
Summary of Demographics for Stakeholders Engaged in SCOPE-CLI Development.

Stakeholder Group	Group Members (n)	Number of Study Planning Meetings Attended	Number of Focus Groups Attended
SCOPE-CLI Study Team	Psychologist/Principle Investigator (1), Registered Nurse (2), Exercise Physiologist (1), Health Services Researcher (1)	48	4
Physician Expert Panel	Interventional Cardiologist (5), Vascular Surgeon (2)	29	0
Patient Expert Panel	Male Patients (4), Female Patients (2)	10	4
Patient Focus Group	Male Patients (17), Female Patients (11)	0	3

Table 2
Overview of SCOPE-CLI Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
1. Age ≥ 18 years	1. Acute limb ischemia
2. ABI and TBI performed within the last 6 months (if patient undergoes revascularization, patient can be enrolled if a pre-procedural ABI/TBI is available)	2. Currently a prisoner
3. Patient presents with current (within 30 days) Rutherford Class 4, 5, or 6 as defined as any of the following:	3. Unable to provide written informed consent
- Rutherford Classification 4 or ischemic rest pain or resting ankle pressure < 50 mmHg, flat or barely pulsatile ankle or metatarsal PVR or toe pressure < 40 mmHg	
- Rutherford Classification 5 or minor tissue loss; non-healing ulcer, focal gangrene with diffuse pedal ischemia or resting ankle pressure < 50 mmHg, or flat or barely pulsatile ankle or metatarsal PVR, or toe pressure < 40 mmHg	
- Rutherford Classification 6 or major tissue loss: extending above transmetatarsal level, functional foot no longer salvageable or resting ankle pressure < 50 mmHg, or flat or barely pulsatile ankle or metatarsal PVR, or toe pressure < 40 mmHg	
- CLI related ICD 10 code (reason for admission or indication for procedure)	
- Documentation of any of the following diagnostic evidence:	
i. SPP < 50 mmHg	
ii. TCPO2 < 50 mmHg	
iii. Angiographic evidence no straight line to foot or>70% stenosis in all 3 lower extremity arteries (AT, PT, peroneal)	
iv. ABI* ≤ 0.90	
v. Non-compressible ABI ≥ 1.40 AND TBI ≤ 0.70	
vi. TBI* ≤ 0.70	
4. English or Spanish speaking	

(*) These diagnostic testing results must be present to enter the study.
Abbreviations: ABI, Ankle Brachial Index; AT, anterior tibial; ICD, International Classification of Diseases; PT, posterior tibial, PVR, Pulse Volume Recording; SPP, skin perfusion pressure; TBI, toe brachial index; TCPO2, transcutaneous oximetry

2.2.2. Inclusion/Exclusion Criteria

Study coordinators will use a standardized screening form to verify inclusion and exclusion criteria detailed in Table 2. Inclusion criteria include: (1) Age ≥ 18 years; (2) an ABI/TBI within the past 6 months (without a revascularization procedure since the test was performed) showing the following results: ABI ≤ 0.90 and TBI ≤ 0.70, or if the ABI is non-compressible (ABI ≥ 1.40) the TBI must be ≤ 0.70; (3) evidence of current (within the past 30 days) Rutherford Class 4, 5, or 6 CLI; and (4) English or Spanish speaking. Patients will be excluded if they (1) present with acute limb ischemia; (2) are currently incarcerated; or (3) are unable to provide written informed consent.

2.2.3. Patient interviews

The SCOPE-CLI is uniquely designed to collect a variety of patient reported outcomes. A primary outcome for SCOPE-CLI is PAD-specific health status as determined by the 20-item Peripheral Artery Questionnaire (PAQ) [18]. Items are answered on a Likert scale with the following domains addressed: physical limitation, symptoms, social function, treatment satisfaction, and quality of life. A summary score ranging from 0 to 100 is generated from the combination of scores for each domain, with higher scores indicating better health status. Due of the unique manifestations of CLI, above and beyond PAD, SCOPE-CLI will test and validate a pool of disease-specific questions related to patients' CLI symptoms and functioning. These questions were generated from the qualitative input gathered as part of the SCOPE-CLI preparatory work. Depending on the disease stage that is applicable to them, patients with CLI will receive additional questions for the subdomains of (1) functional status (e.g. balance, physical exhaustion); (2) symptoms (e.g. pain, wound discomfort, phantom pain related to amputation); (3) treatment satisfaction (e.g. satisfaction with provider communication, confidence in provider abilities, confidence in appropriate treatment for wounds and amputation); (4) quality of life (e.g. social isolation, dependance on others, fear of wounds and amputation, prosthesis use); and (5) social limitation (e.g. ability to live independently). They are answered along various Likert scales and will form the foundation for a disease-specific health status supplement to the PAQ for patients with CLI. Other measures of health status will include the EQ-5D [19] and information on prosthesis use.

In addition to health status outcomes, SCOPE-CLI will also collect a variety of patient-centered data points using the unique measures shown in Table 3. Measures were selected for inclusion based on those which addressed central themes and areas of importance as expressed by patients during the preparatory pilot work. These measures span the following domains: psychosocial (including mood symptoms [20-24], stress [25], loneliness [26], illness perception [27], discrimination [28], and personality [29-31]), lifestyle (including nutritional status [32-34] and tobacco use [35]), and decision-making [36-38]. Economic factors, including lost productivity, will be measured by collecting information on patients' missed workdays, hours of care given to each patient, and missed workdays for caregivers [39]. A single-item health literacy screener will also be included [40].

A complete schedule of events for the study period is shown in Table 3. Some health status assessments will be repeated at each follow up visit, while other measures will be limited to a single assessment point (either at baseline or dispersed across follow up visits) to minimize response burden. Experienced clinical research assistants will be responsible for conducting structured follow-up patient interviews over the phone at 1, 2, 6, and 12 months. This will be centrally organized at the coordinating center.

2.2.4. Medical record Abstraction

In addition to the information obtained from the interview, patients will have their demographic information and medical history (including cardiac history, peripheral vascular history, wound history, non-cardiac history, vitals, and labs) abstracted at baseline from chart review by trained data collectors. Other diagnostic information collected at baseline will include angiography, skin perfusion pressure (SPP), transcutaneous oximetry ($TCP0^2$), duplex ultrasound testing, and CT and MRI results using data elements as previously established in the PORTRAIT registry [41].

Wound information will be collected at baseline and will include wound location, pain, debridement history, and wound assessment using the Bates-Jensen Wound Assessment Tool of the three most significant wounds [42]. This validated tool describes 13 characteristics of a wound, including size, edge characteristics, presence of necrotic tissue, exudate, skin color, and epithelialization.

Other medical information (including hospital admissions, cardiovascular events, and peripheral vascular interventions) will be abstracted from patients' medical records at 6 and 12 months.

2.2.5. Clinical endpoints

Vital status (including date and cause of death) will be assessed by medical record abstraction and patient report through at least 1 year of follow-up for all participants. After 1 year, yital status will be assessed annually for an additional 5 years using the National Death Index (NDI). Other clinical endpoints (including CLI-specific and cardiovascular events) will be adjudicated at 1 year. CLI-specific events include lower extremity diagnostic procedures and interventions (angioplasty/stenting, surgical procedures, amputation, peripheral bypass graft, atherectomy, endarterectomy, and thrombectomy), and intra or post-procedure events. Cardiovascular events include cardiovascular procedures

(coronary angioplasty/stenting, coronary artery bypass grafting, carotid artery revascularization, and associated bleeding complications), myocardial infarction, unstable angina, congestive heart failure, cardiac arrest, cardiogenic shock, embolism, and cerebrovascular disease (transient ischemic attacks, hemorrhagic stroke, and ischemic stroke).

2.3. Statistical analysis

Patient characteristics will be described for the overall sample. Continuous variables means, medians, and interquartile ranges will be described (as appropriate). Categorical data will be summarized as counts and percentages. Two-group comparisons will be tested with independent Student *t*-test or Mann-Whitney *U* test for continuous variables and Chi square tests for categorical variables.

The analytic models that will be used to handle the continuous health status data and the time to event data (for Major Adverse Limb Events and Amputation Free Survival) will be accommodated by various regression frameworks, so as to adjust for potentially confounding covariates. Finally, with regards to the potential of having missing data (due to incomplete patient interviews, study drop-outs, and deaths) multiple imputation will be used to account for missing-data bias attributable to observed characteristics, or by inversely weighting the observed data by the propensity to participate in follow-up and to correct standard errors, confidence intervals and p-values to account for uncertainty due to missingness [29]. Additional hypotheses and power calculation are detailed in Supplementary Tables 4 and 5.

Table 3
Overview of Information Collected via Enrollment, Patient Interview, and Medical Record Abstraction in SCOPE-CLI.

		Baseline	1 Month	2 Month	6 Month	12 Month
	Screening Information					
Enrollment	Informed Consent	x				
	Inclusion/Exclusion Criteria	x				
	Contact Information	x				
	Referring Provider Information	x				
	Demographics	x				
Patient Interview	**Health Status Measures**					
	Maximum Walking Distance	x	x	x	x	x
	Peripheral Artery Questionnaire + Critical Limb Ischemia (PAQ-CLI) module	x	x	x	x	x
	EuroQol-5D	x	x	x	x	x
	Prosthesis Questions	x	x		x	x
	Functional Status	x	x		x	x
	Patient Assessment of Improvement in Health Status		x	x	x	x
	Psychosocial Measures					
	Patient Health Questionnaire 8-item version (PHQ-8)	x			x	x
	Patient Health Questionnaire 2-item version (PHQ-2)		x	x		
	Generalized Anxiety Disorder 2 (GAD-2)		x			
	Primary Care PTSD Screen (PC-PTSD)					x
	Perceived Stress Scale (PSS)	x	x	x	x	x
	Loneliness Screener	x				
	Brief Illness Perception Questionnaire (IPQ)	x				
	Discrimination in Medical Settings (DMS) Scale	x				
	Relationship Questionnaire (RQ)	x				
	Life Orientation Test-Revised (LOT-R)		x			
	Big 5 Inventory (BFI-44)		x			
	General Self Efficacy Scale (GSE-6)		x			
	Lifestyle Measures					
	Malnutrition Screening Tool (MST)			x		
	Hunger Vital Sign			x		
	Brief Screener to Estimate Fast Food and Beverage Consumptions			x		
	Question Inventory on Tobacco (QIT)	x	x	x	x	x
	Decision Making Measures					
	Deber-Kraetschmer Problem-Solving Decision-Making Scale	x				
	Decision Regret Scale (DRS)	x			x	
	SURE Instrument	x				
	Other Information					
	Socioeconomic Status	x	x		x	x
	Quality of Care Questions	x				
	CLI Knowledge and Preference Questions	x				x
	Health Literacy	x				
	Caregiver Status	x			x	x
	Financial Barriers to Care	x				x
	Interval Hospitalization History		x	x	x	x
Medical Record Abstraction	**Medical History**					
	Wound Ischemia and Foot Infection (WIFI) Score	x				
	Cardiac and Risk Factor History	x				
	Non-Cardiac History	x				
	Peripheral Vascular History	x				
	Vital Signs	x				
	Pulse Exam	x				
	Diagnostic Testing (ABI/TBI, Ultrasound, Angiography)	x				
	Laboratory Testing	x				
	CLI Risk Management Strategies	x				
	Hospitalization Information	x	x	x	x	x
	Medication History	x	x	x	x	x
	Wound Assessment (Bates-Jensen Wound Assessment Tool)	x	x			

Abbreviations: ABI, Ankle Brachial Index; CLI, Critical Limb Ischemia; TBI, Toe Brachial Index

2.4. Data sharing

Data sharing is supported through contacting the study principal investigator (corresponding author). Collaborators interested in working on the data set can request a proposal form. Research proposals will undergo a predefined review and approval process by the SCOPE-CLI publications committee. The publications committee is comprised of site investigator representatives and the steering committee.

2.5. Pilot phase design

The above-described screening mechanism was developed and tested to identify patients with CLI at three pilot sites including the St. Luke's Mid America Heart Institute/University of Missouri-Kansas City (Kansas City, Missouri), Yale New Haven Hospital/Yale School of Medicine (New Haven, CT), and University Hospitals Cleveland Medical Center/Case Western University (Cleveland, OH). Enrollment started in 2020 and is currently ongoing. An additional 8 multidisciplinary centers (Fig. 2) will be joining the enrollment efforts for the SCOPE-CLI registry in 2022. Participating sites include academic medical centers with multidisciplinary site investigators including interventional cardiologists, vascular surgeons, and podiatrists. One international center in Australia (University of Adelaide) is also participating.

Characteristics of the enrolling sites were collected including institution characteristics (institution type and academic affiliation), details regarding the CLI care team (including specialty type, dedicated wound care teams), specifics regarding diagnostic procedure availability and annual volumes, peripheral revascularization procedure volume and specialist distribution, information on multi-disciplinary conferences, supervised exercise therapy, smoking cessation programs, quality improvement initiatives, and medical record information.

3. Results

3.1. Site characteristics

Site characteristics for the institutions participating in SCOPE-CLI detailed in Table 4. Nine of the 11 sites were in urban settings (81.8%), with three (27.3%) located in suburban areas. No sites were in rural areas. Regarding insurance coverage for > 30% of the patient population that will be enrolled in SCOPE-CLI, 10 of the 11 sites have Medicare patients (90.9%), 8 have private insurance patients (72.7%), 5 have Medicaid patients (45.5%), 4 have Managed Care patients (36.4%), and 2 have indigent care patients (18.2%). Of the 11 institutions, all but one (90.9%) were not-for-profit and all (100.0%) were categorized as teaching hospitals. Five of the 11 sites that responded (45.5%) endorsed having a cardiovascular fellowship program and two (18.2%) had a peripheral vascular-specific advanced fellowship program. Four of the hospitals participating (30.8%) had a Limb Salvage Clinic and all but one (90.0%) had a designated CLI Care Team. The median annual volume of institutional peripheral percutaneous angioplasties was 350 [200.0 – 302.0], open surgical bypass was 51.0 [44.0 – 79.5], and non-traumatic amputations was 73.0 [50.0 – 190.0].

3.2. Pilot patient data

Pilot data were collected between January 2020 and July 2021 from three centers. A total of 70 patients were enrolled. The baseline interview took on average 45 to 60 min to complete. Baseline patient characteristics for the pilot patient sample are detailed in Table 5. The mean age for patients was 68.4 ± 11.3 years with 31.4% female, 20.0% African American, and 4.4% Hispanic. At enrollment, 43.3% were presenting with new symptoms and 56.7% were presenting with an exacerbation of symptoms. According to Rutherford Classification, patients were 10.0% Rutherford Class 4, 88.6% Rutherford Class 5, and 1.4% Rutherford Class 6. The mean baseline ABI (from the lower of the two extremities) was 0.64 ± 0.35 and for TBI was 0.36 ± 0.0.32.

4. Discussion

The SCOPE-CLI academic research consortium brings together a robust network of collaborators from vascular surgery, interventional cardiology, vascular medicine, podiatry, wound care, behavioral health, and patient advocates to phenotype patients – including their socioeconomic, psychosocial, and ischemic and wound profiles – who are currently navigating a diagnosis of CLI. It does so from a whole-patient

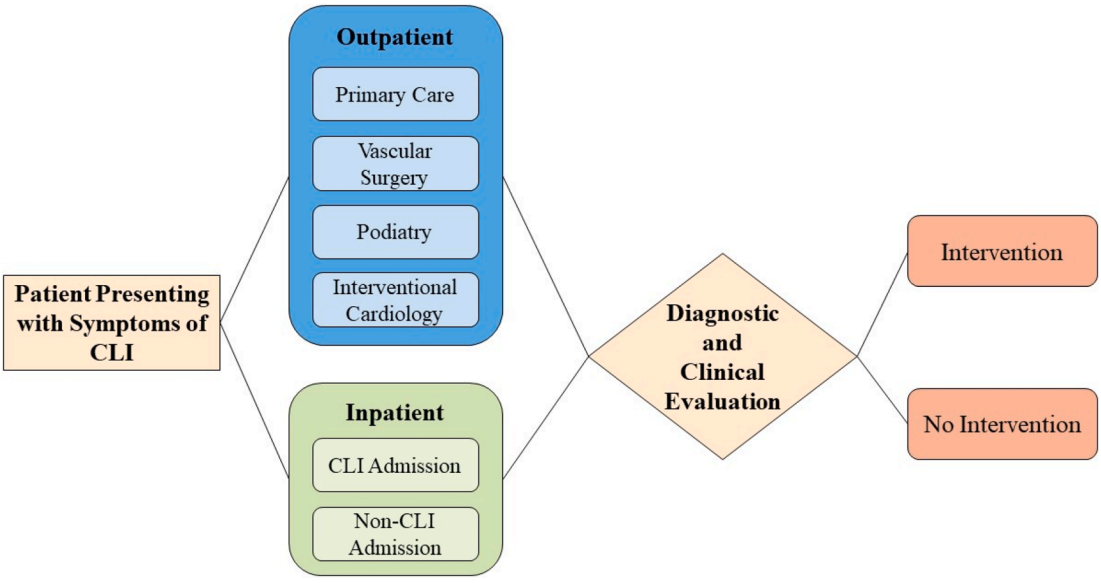

Fig. 1. CLI Clinical Pathways for Identifying Eligible Patients for Enrollment in SCOPE-CLI. The clinical pathway for patients who will be enrolled in SCOPE-CLI is shown in Fig. 1. Patients presenting with symptoms of Rutherford Class 4–6 critical limb ischemia (CLI) will be enrolled in the outpatient setting including primary care, vascular surgery, podiatry, and interventional cardiology clinical as well as the inpatient setting either during a CLI-related or non-CLI related admission. Patients will undergo diagnostics and clinical evaluation per the standard of care. Based on the standard of care of the treating team, patients either will or will not undergo intervention. Intervention status does not determine eligibility into the study.

Table 4
Summary of SCOPE-CLI Participating Site Characteristics.

Institutional Characteristics (n = 11)		Value
Patient Population (>30%)	Indigent Care	2 (18.2%)
	Managed Care	4 (36.4%)
	Medicare	10 (90.9%)
	Medicaid	5 (45.5%)
	Private/Group/Non-HMO	8 (72.7%)
Institution Type	For Profit	1 (9.1%)
	Not for Profit	10 (90.9%)
	VA	0 (0.0%)
	Other Government	0 (0.0%)
Institutional Programs	Teaching	11 (100.0%)
	Non-Teaching	0 (0.0%)
	Residency Program	7 (63.6%)
	CV Fellow Program	5 (45.5%)
	Specialty Hospital	2 (18.2%)
	PAD Specialty Fellowship Program	2 (18.2%)
Institution Academic Affiliation	University	8 (72.7%)
	University-affiliated	3 (27.3%)
	Non-academic	0 (0.0%)
Site Location	Urban	9 (81.8%)
	Suburban	2 (18.2%)
	Rural	0 (0.0%)
Presence of a CLI Care Team	Yes	10 (90.0%)
Presence of Limb Salvage Clinic	Yes	4 (30.8%)
Annual Volumes (2017)	Resting ABI	1050.0 [681.0 – 1826.0]
	Exercise ABI	175.0 [150.0 – 203.0]
	Open surgical bypass	51.0 [44.0 – 79.5]
	PTA	250.0 [200.0 – 302.0]
	Non-traumatic amputations	73.0 [50.0 – 190.0]
Supervised CLI-Specific Exercise Program	Yes	3 (33.3%)
In-Person Smoking Cessation Program	Yes	7 (70.0%)

All values listed as n (%) or median [interquartile range].
Abbreviations: ABI, Ankle Brachial Index; CLI, Critical Limb Ischemia; CV, Cardiovascular; HMO, Health Maintenance Organization; PAD, Peripheral Artery Disease; PTA, Percutaneous Angioplasty; VA, Veteran's Affairs.

Table 5
Baseline Characteristics of First 70 Patients Enrolled into the SCOPE-CLI Pilot Study.

Demographics	n = 70
Age (years), mean ± SD	68.40 ± 11.29
Female Sex	22 (31.4%)
Race	
Asian	0 (0.0%)
Black	14 (20.0%)
Native American or Pacific Islander	0 (0.0%)
White	56 (80.0%)
Other	0 (0.0%)
Hispanic Ethnicity	3 (4.4%)
Socio-Economic Factors	
Marital Status - Married	35 (57.4%)
Insurance Status - Medicare	37 (52.9%)
Cardiovascular History	
Congestive Heart Failure	20 (28.6%)
Hypertension	50 (71.4%)
Prior CAD	33 (47.1%)
Smoking History	39 (55.7%)
Non-Cardiac History	
Chronic Kidney Disease	21 (30.0%)
Depression (requiring treatment)	7 (10.0%)
Obstructive Sleep Apnea	13 (18.6%)
Diabetes	38 (54.3%)
Cancer (other than skin)	5 (7.1%)
Peripheral Vascular History	
Carotid Disease	2 (2.9%)
AAA History	1 (1.4%)
History of Non-Healing Ulcer	24 (34.3%)
History of Major Amputation	17 (24.3%)
History of Claudication	12 (17.1%)
Family History of Peripheral Artery Disease	1 (1.4%)
Current PAD Status	
Symptoms on Presentation	
New Onset	26 (43.3%)
Exacerbation	34 (56.7%)
Rutherford Class 4	7 (10.0%)
Rutherford Class 5	62 (88.6%)
Rutherford Class 6	1 (1.4%)
WIFI Score, mean ± SD	
Wound Grade	1.17 ± 0.81
Ischemia Grade	1.45 ± 1.17
Foot Infection Grade	0.51 ± 0.82
Lowest ABI Value, mean ± SD	0.64 ± 0.35
Lowest TBI Value, mean ± SD	0.36 ± 0.32

All values are presented as n (%), unless otherwise indicated.
Ab breviations: AAA, abdominal aortic aneurysm; ABI, ankle brachial index; CAD, coronary artery disease; SD, standard deviation; TBI, toe brachial index; WIFI, Wound Ischemia and Foot Infection.

perspective with data-elements that have been prioritized by patients themselves. The SCOPE-CLI study is unique in that it prioritizes outcomes beyond limb preservation – i.e. patients' symptoms, functioning, and quality of life – as primary outcomes of interest. It will also test an item bank of questions that will generate a CLI-specific health status instrument, a much-needed tool to better capture patients' experiences. SCOPE-CLI will also make an inventory of the current state of the quality of care accessible to patients with CLI. Evaluation of site variability in care practices, delivery of quality care metrics, and outcomes for those with CLI is a key objective sure to advance the field to the benefit of patients, health systems, and payors.

Concentrating on the patient experience is crucial because the majority of patients with CLI survive 1 year following their diagnosis after receiving medical management and revascularization approaches [43]. While patients' health status (symptoms, functioning, and quality of life) is an outcome of utmost importance to patients, to date there are few data about the health status outcomes for patients with CLI [15]. The care goals and outcomes that matter most to patients with CLI are poorly understood. Moreover, it is only recently that there have been calls for CLI outcomes studies to shift from studying 'limbs' to 'patients' when looking at revascularization outcomes following a diagnosis of CLI [44]. Along with this shift from 'limb' to 'patients', is a need to understand current presentation forms of CLI, the patient profiles and the quality of care they have access to, and to develop better risk stratification methods. It will also lay the groundwork for enabling the development of patient-centered tools that allow for shared decision making approaches, decision support tools, and disease management programs that are patient-centric, an area for which there is a great need as no such instruments are currently existing.

Significant variability and disparities of PAD outcomes by race and ethnicity and/or socio-economic status have been widely published. Specifically, Black, Hispanic, Native American patients experience higher rates of amputation compared to white patients, often these disparities are seen amongst patients in the lowest income groups [45,46]. Various explanations have been posited for these findings including structural systemic inequities, healthcare insurance coverage, access to healthcare and racial bias by healthcare providers and health care systems, and complex associations with social determinants of health [47]. Little has been written about the patient experience, the impact on patients' mental health, barriers in navigating the care system, and getting timely and quality care for PAD. SCOPE CLI will be able to investigate these complex mechanisms that may explain delays in care and suboptimal care and outcomes most often seen amongst socio-economically disadvantaged populations, and in African American populations. The SCOPE-CLI study will be well equipped to identify potential disparities and underlying mechanisms of action (e.g. discrimination experiences in the health care setting, financial barriers

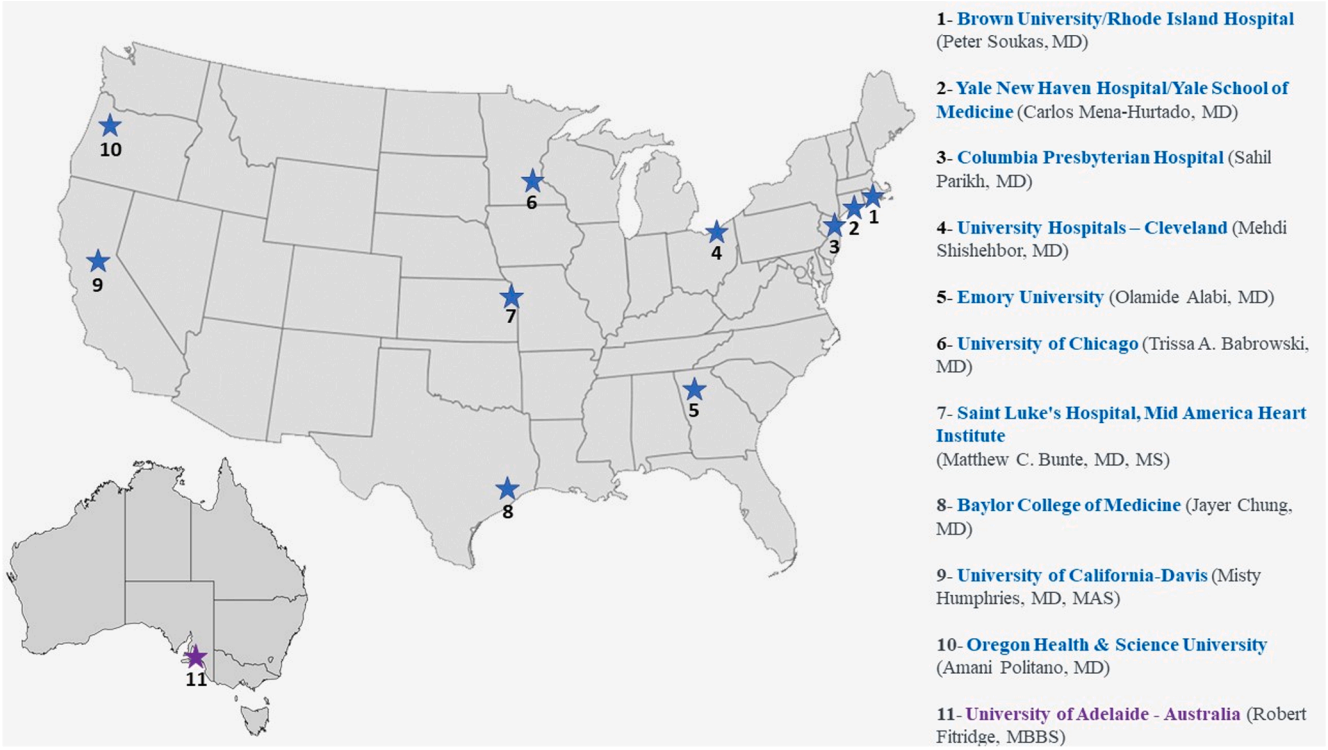

Fig. 2. Map of Sites Participating in SCOPE-CLI in the United States and Australia. The eleven sites enrolling patients in SCOPE-CLI are shown on the map in Fig. 2. These include various academic institutions across the United States and one site in Australia.

in accessing care) in the provision of care and patients' outcomes as a function of patient's characteristics, as its glaring racial inequities have been a reality for too long [48].

CLI admission rates in the US have been on the rise over the past decade, underscoring the need to better understand this population. Increasingly, younger populations (<65 years) are driven by surging rates of obesity and an epidemic of diabetes mellitus [48]. Survival and amputation rates have barely decreased,[48] and medical management surrounding procedural interventions have been well-documented to be poor [48]. Data that are available are becoming quickly outdated and have typically suffered from large dropout rates [4,49]. Moreover, much of the data came from clinical trials, [4,49] raising additional concerns of representativeness to the broader CLI population. As such, there is an urgent need for high-quality prospective studies with a focus on the patient-centered outcomes in patients with CLI. SCOPE-CLI will serve that need and will systematically quantify patients' CLI-specific health status and clinical outcomes and to perform subgroup analyses as a function of different PAD treatments and patient characteristics.

As this is an observational effort, limitations related to residual confounding will remain and larger questions of comparative-effectiveness will have to be supported by propensity-matched analyses. Further randomized clinical trial evidence dedicated to the population of CLI would be beneficial, as CLI cohorts are underrepresented in class I recommendations for PAD in general. Targeted comparative effectiveness research in CLI will have to be developed to address this gap. Another limitation is that SCOPE-CLI currently has only large academic centers represented in their consortium, and the practices described in this network may not extend to other practices. On the other hand, the current SCOPE-CLI hub creates the ideal environment to map out models of CLI care and study their associations with outcomes with highly specialized expertise coming from top-level vascular surgery, interventional cardiology, and podiatry experts, as conceptual frameworks that can then be tested and replicated in other settings.

In conclusion, the SCOPE-CLI study will seek to extend prognostic outcomes models for outcomes of interest to patients beyond traditional cardiovascular risk factors, including socio-economic factors, psychological profile data, and wound risk models such as the WIfI score [50,51] that are prospectively collected in the study. It will also provide preliminary information to identify areas of action that can be targeted in sustainable quality improvement programs and patient-centered decision-making and outcomes assessment platforms for this population.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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