Quality of Care and Outcomes in Patients with Critical Limb Ischemia: Derivation of a Nationwide Cerner Health Facts Vascular Datamart

April 28, 2021

Jeremy B Provance, MS

Faculty advisors: Kim G Smolderen, PhD & Carlos Mena-Hurtado, MD

Vascular Medicine Outcomes Program

Yale University
School of Medicine

Outline

- Overview of contemporary clinical databases
- Key opportunities and aims
- Critical limb ischemia (CLI) background and quality of care
- 30-day amputations after endovascular intervention
- Variability in guideline directed medical therapy
- Future work

Contemporary Clinical Databases

- Highest quality clinical research databases are clinical registries
  - Pre-specified data points curated through point-of-care electronic data capture, electronic health record abstraction, or both
  - Participants are enrolled and followed for a specified time window
  - Greater generalizability through multi-site collaboration
  - Developed with clinical research as the primary use
- Clinical registries have important limitations
  - Use only pre-specified study variables for participants at enrolling sites
  - Registry enrollment will end; individual patient follow-up will end
  - Difficulty validating current data and linking future data due to de-identification
  - Highly specified inclusion criteria (for example, only patients undergoing a procedure)
- Electronic health record data warehouses offer a unique opportunity to provide adaptable databases for clinical research

Outline

- Overview of contemporary clinical databases
- Key opportunities and aims
- Critical limb ischemia (CLI) background and quality of care
- 30-day amputations after endovascular intervention
- Variability in guideline directed medical therapy
- Future work

Opportunity using EHR Data Warehouses

- Electronic health records can be extracted (transformed) and loaded into a research database
  - All patients, data fields (both structured and unstructured), and time points
  - Often follow conventional data ontologies

- If transformed into a common data model:
  - Aggregated into multi-site databases
  - EHR-provider agnostic
  - Present the opportunity for global scale clinical research

- Because records are re-identifiable, data can be:
  - Validated
  - Refreshed with additional follow-up and supplemented with new data

- Electronic health records are not developed with clinical research as the primary use; requires a multi-disciplinary approach to create high-quality research warehouses

Current Initiatives for PAD

ELSEVIER

Journal of Vascular Surgery

Education corner

The use ... identifica... and futu...

Elsie Gyang Ross MD, MSc ..., Nigam H. Shah MBBS, PhD ..., Ronald L. Dalman MD ..., Kevin T. Nead MD, MPhil [c], John P. Cooke MD, PhD [d, e], Nicholas J. Leeper MD [a]

OPEN ACCESS

RESEARCH ARTICLE

PDF/EPUB

Tools Share

Jump to

Leveraging the Electronic Health Record to Create an Automated Real-Time Prognostic Tool for Peripheral Arterial Disease

Adelaide M. Arruda-Olson, Naveed Afzal, Vishnu Priya Mallipeddi, Ahmad Said, Homam Moussa Pacha, Sungrim Moon, Alisha P. Chaudhry, Christopher G. Scott, Kent R. Bailey, ... See all authors

Originally published 1 Dec 2018 | https://doi.org/10.1161/JAHA.118.009680 | Journal of the American Heart Association. 2018;7:e009680

EHR data warehouses can:

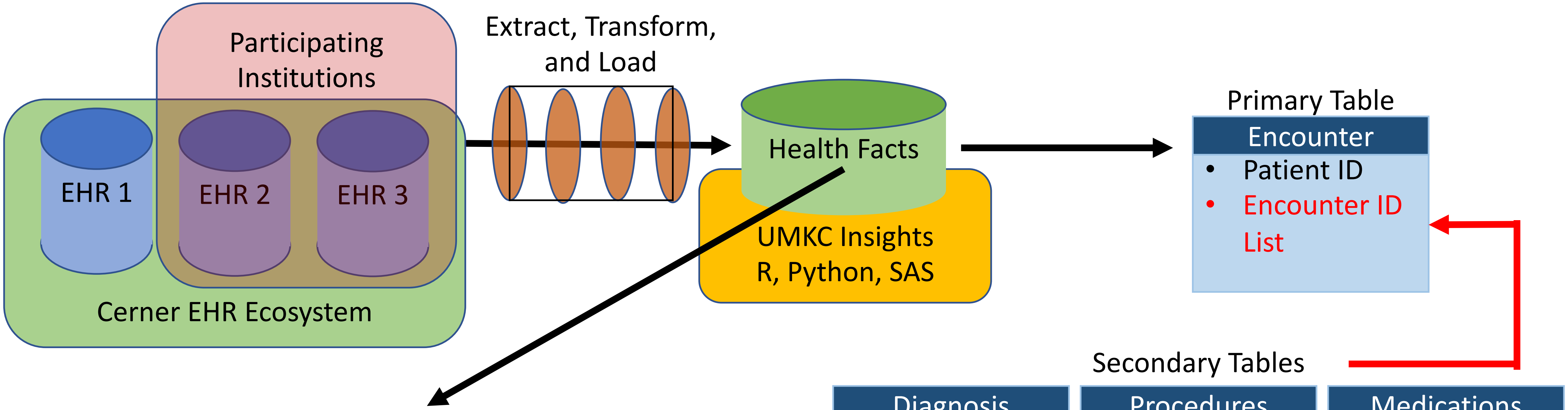
- identify PAD and risk of mortality
- predict risk of mortality

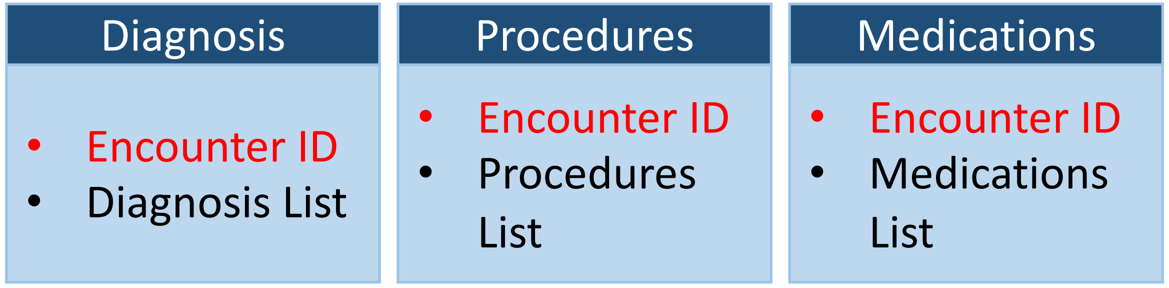
Aims

1. Develop methods to create a high-fidelity data warehouse from the national Cerner Health Facts electronic health record database for use in cardiovascular outcomes research

2. Apply the warehouse examining quality of care and outcomes in patients with critical limb ischemia
   a. 30-day amputation outcomes after endovascular PVI
   b. Variation in guideline directed medical therapy (GDMT) after amputation

Cerner Health Facts EHR Database





- >69 million unique patients, 782 sites, year 2000-2017
- Inpatient, outpatient, emergent patient records
- Encounter level data with demographics, site characteristics, diagnoses, procedures, medications

Deriving Data Set Variables

Variable Creation Function

1. Store Variable Definition
2. Scan Diagnosis Column for Match
3. Create new variable; 1 = Match, 0 = Not Match
4. Join new variable columns to patient table by Encounter ID

Diabetes Definition
• Diabetes Mellitus = 250.0, 250.1…

Diagnosis	Diabetes	Encounter
895.0	0	101
S98.1	0	102
730.0	0	103
250.0	1	104

***For patient level variables, encounters were grouped

Outline

- Overview of contemporary clinical databases
- Key opportunities and aims
- Critical limb ischemia (CLI) background and quality of care
- 30-day amputations after endovascular intervention
- Variability in guideline directed medical therapy
- Future work

Critical Limb Ischemia Background

- CLI is the severe form of peripheral artery disease
  - ~170,000 people in the Unites States have CLI[1]
  - Symptoms include rest pain, ulceration, or gangrene
  - High risk for amputation, death, and other cardiovascular adverse events[2]

- CLI treatment includes[3]:
  1. Vascular medicine referral
  2. Peripheral diagnostic testing to confirm inadequate perfusion
  3. Guideline directed medical therapy
     - Statin
     - Anti-platelet
     - Anti-hypertensive (where hypertension is indicated)
  4. Revascularization as appropriate

Metric	**Critical Limb Ischemia**		
ABI	≤0.40		
TBI	≤0.30		
Rutherford[4]	4	5	6
	Rest pain	Ulceration	Gangrene

1. Nehler 2014 in *J Vasc Surg* 2. Farber 2018 in *NEJM* 3. Conte 2019 in *J Vasc Surg* 4. Rutherford et al. 1999 in *J Vasc Surg*

Outline

- Overview of contemporary clinical databases
- Key opportunities and aims
- Critical limb ischemia (CLI) background and quality of care
- 30-day amputations after endovascular intervention
- Variability in guideline directed medical therapy
- Future work

Creating a Health Facts CLI Database: A Two-Step Process

Health Facts Database: 69,117,801 Patients 460,732,189 Encounters 782 Sites

Step 1: Patient Exclusions

1. Patient age < 18 at encounter
2. Encounter not for 1 or more code for ALI
3. Encounter for 1 or More of 155 ICD-9/10 codes for CLI

→

CLI Patient Cohort
N = 51,794 patients
N = 295,676 encounters
N = 404 sites

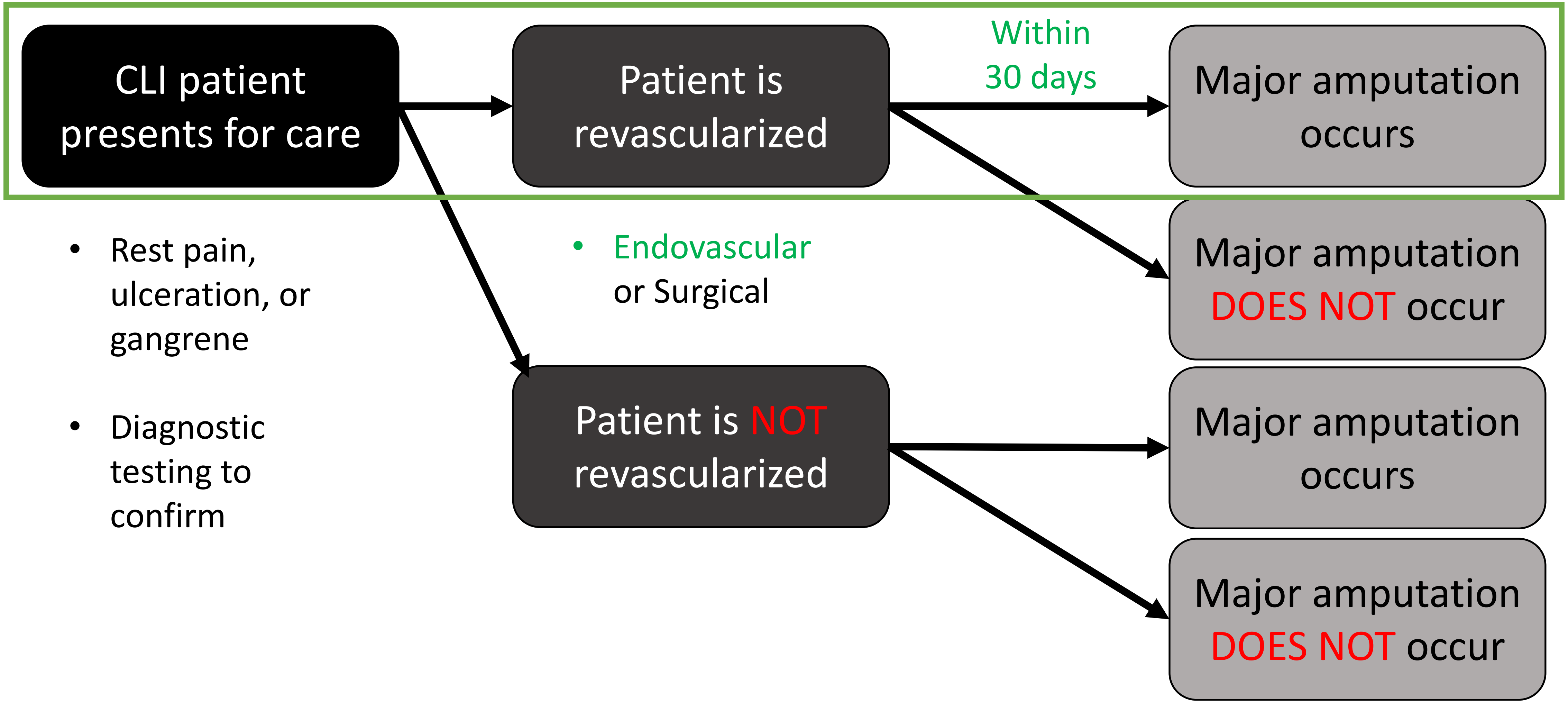
Step 2: Database Quality Exclusions

1. Encounter Year < 2010
2. Overall Site Patient Encounters < 100, *or*
3. Overall Site Diagnosis Encounters < 100, *or*
4. Overall Site Procedure Encounters < 100, *or*
5. Overall Site Medication Encounters < 100

→

High Fidelity CLI Patient Cohort
N = 31,490 patients
N = 79,359 encounters
N = 233 sites

30-Day Amputations: a CLI care quality metric[1,2]



1. Conte 2009 in *J Vasc Surg*, 2. Jaff 2015 in *Ann Vasc Dis*

CLI Patients Post Endovascular Intervention

High fidelity CLI cohort:	31,490 Patients	79,359 Encounters	233 Sites

Procedure Exclusions

1. Patient does not have one of 148 ICD-9, ICD-10, or CPT-4 codes for endovascular peripheral vascular intervention

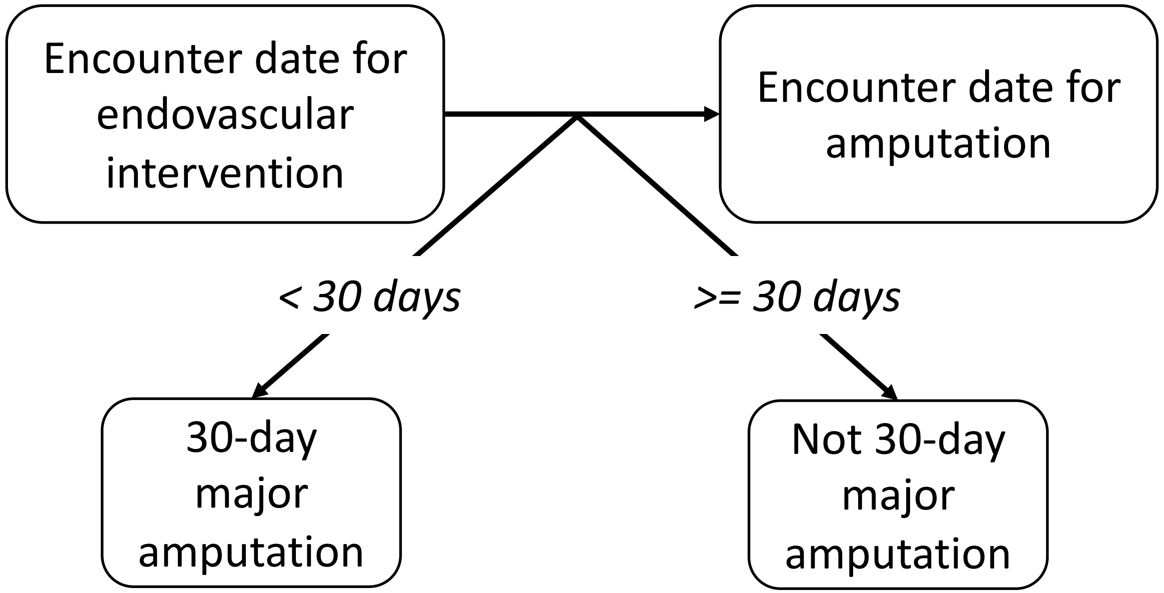
→

<u>CLI Endovascular PVI Cohort</u>

N = 16,173 patients

N = 20,111 encounters

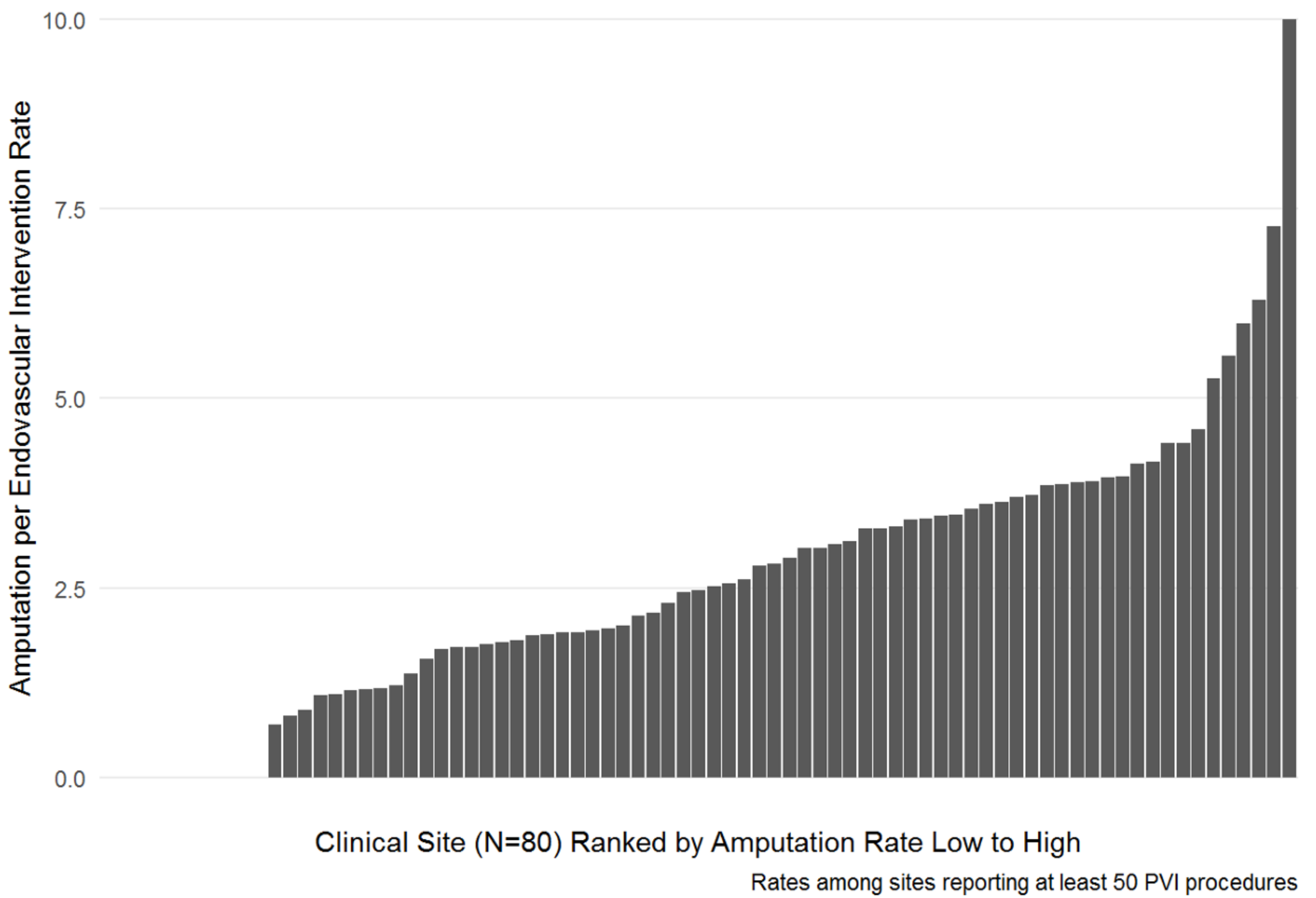
N = 179 sites



<u>Patient characteristics</u>

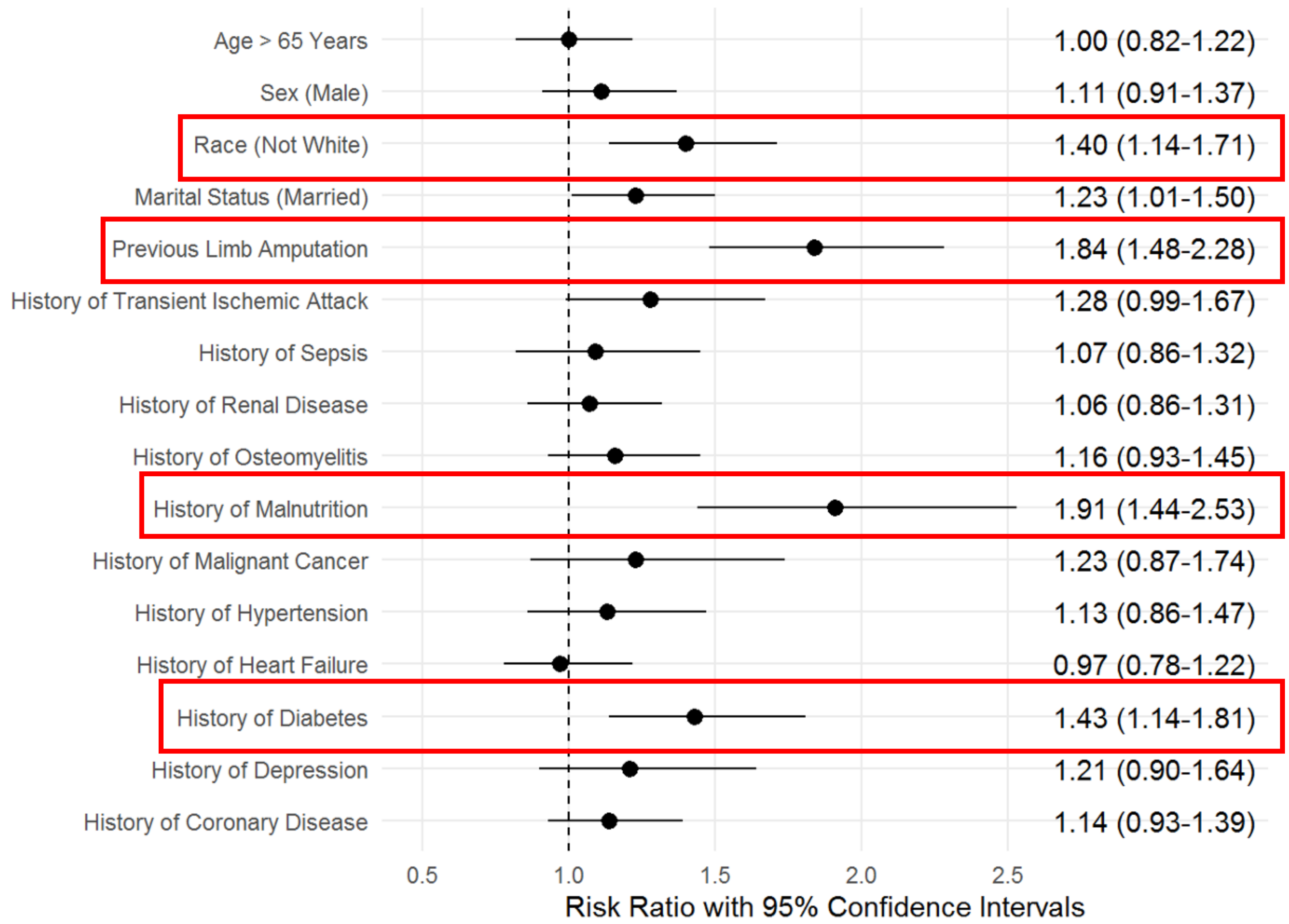
- Mean age 69.0 (± 12.6) years
- 58.0% male
- 29.6% non-white

Variability in 30-Day Amputation Rates



- 2.8% overall rate
- 2.5% median rate; IQR, 1.29%-3.63%)
- Rate ranged 0.0%-10.0% by site
- Unadjusted MRR: 1.40 (1.35-1.46)
- Fully adjusted MRR: 1.11 (1.09-1.13)

Patient Predictors of 30-Day Amputation



30-Day Amputation General Summary

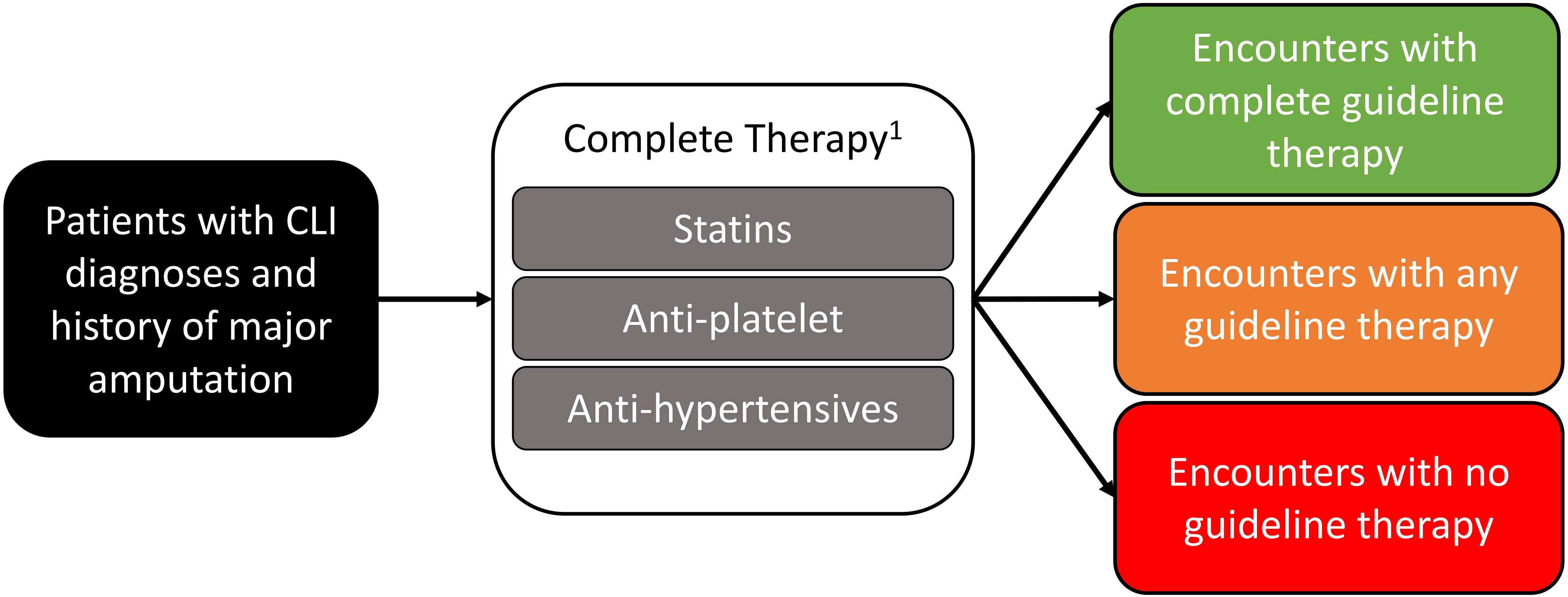
- Rates of 30-day amputation remain low and are within set bounds (2-6%)[1,2] for high quality intervention evaluation
- Site-level factors account for substantial variability in rates
- Modifiable patient and site level factors offer opportunity to reduce 30-day amputations after endovascular PVI
- 30-day amputation may be a useful marker of post-PVI CLI care

1. Davies 2015 in *J Vasc Surg*, 2. Vierthaler 2015 in *J Vasc Surg*

Outline

- Overview of contemporary clinical databases
- Key opportunities and aims
- Critical limb ischemia (CLI) background and quality of care
- 30-day amputations after endovascular intervention
- Variability in guideline directed medical therapy
- Future work

Guideline Directed Medical Therapy in CLI[1]



1. Conte 2019 in *J Vasc Surg*

GDMT in CLI Patients with Amputations

High fidelity CLI cohort: 31,490 Patients 79,359 Encounters 233 Sites

Amputation exclusions

1. No documented non-traumatic, major amputation, classified by ICD-9/10 and CPT codes

→

CLI Amputation Cohort
N = 10,192 patients
N = 74,669 encounters
N = 213 sites

ALI and patient type exclusions

1. Documented acute limb ischemia classified by ICD-9/10 codes
2. Patient type not "Inpatient"

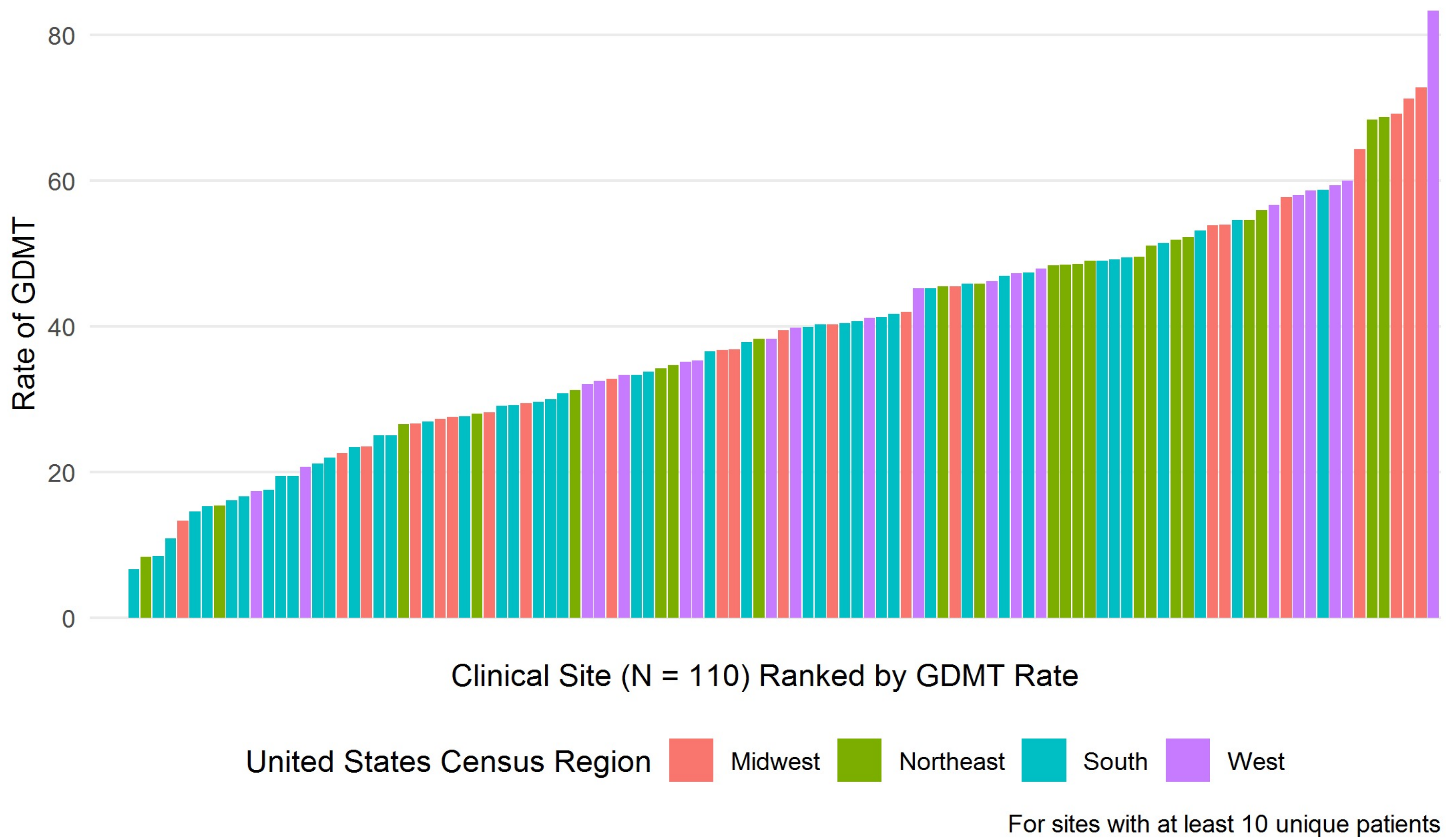
→

CLI Amputation Cohort
N = 9,272 patients
N = 30,856 encounters
N = 196 sites

Patient characteristics

- Mean age 66.8 (± 12.3) years
- 63.5% male
- 62.7% white race

Guideline Medication Therapy Site Variability



- 27.2% complete GDMT rate

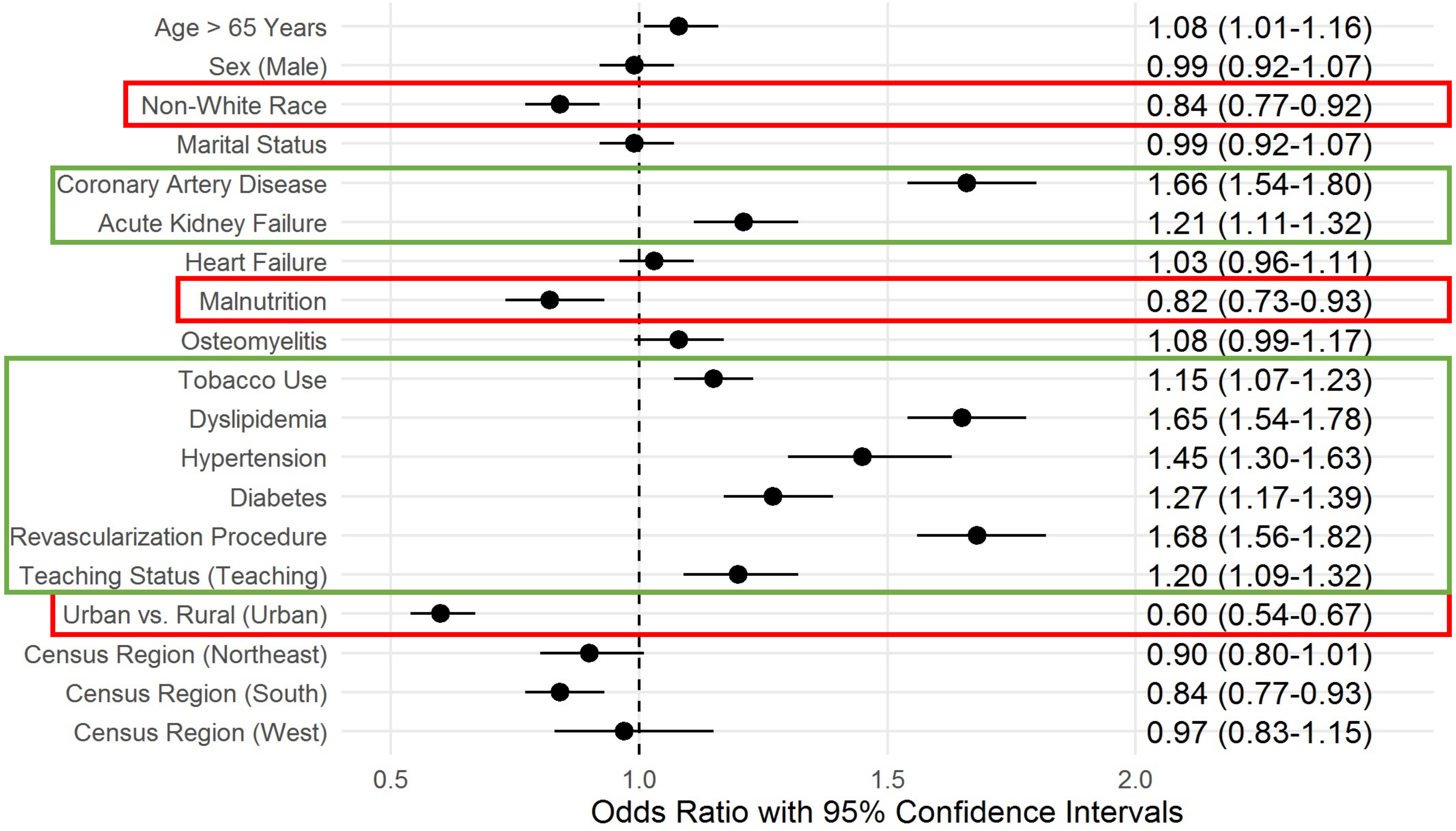
- 72.4% any GDMT rate

- 49.8% statin
- 55.5% anti-platelet
- 49.6% anti-hypertensive

- Unadjusted MOR: 2.32 (2.19-2.45)

- Fully adjusted MOR: 2.07 (1.96-2.18)

Factors Predicting Guideline Medical Therapy



GDMT Variability General Summary

- Only one in four encounters for patients with CLI and a history of major amputation documents complete guideline directed medical therapy
- Variability in guideline directed medical therapy in patients with CLI between clinical care sites is substantial
- Patients with comorbid cardiovascular diseases more often have GDMT documented
- Further study to understand variation among patients and sites for this key quality of care metric[1] is warranted

1. Conte 2019 in *J Vasc Surg*

General Discussion

- We provide a new and reproducible workflow to use electronic health record databases to conduct high-fidelity cardiovascular outcomes research
- We document variability in 30-day amputation rates in CLI after endovascular PVI and associated patient and site-level factors
- We document guideline directed medical therapy rates in CLI patients after amputation at a national level using contemporary data
- By examining contemporary quality of care in CLI patients at a national level, we can begin to inform national quality initiatives in CLI care

Key Limitations

- Health Facts is an observational database
  - Includes data from only Cerner customers who volunteer to share data
- Health Facts is de-identified for the end user
  - Future work to validate results requires re-identification
- Health Facts does not include unstructured data (such as clinical notes or images)

Outline

- Overview of contemporary clinical databases
- Key opportunities and aims
- Critical limb ischemia (CLI) background and quality of care
- 30-day amputations after endovascular intervention
- Variability in guideline directed medical therapy
- Future work

Future work with the VAMOS group

- Initial results from the VISION VQI-Medicare linked database highlight that ***only* 61.6% of PVI encounters documented complete guideline directed medical therapy at discharge**

- At Yale New Haven Health, the VAMOS group hopes to utilize EHR warehouse data to examine vascular medicine outcomes
    - Identified records provides opportunity to validate results using unstructured data (such as clinical notes)
    - Vascular medicine would benefit from automated insights for quantification of risk, diagnosis prior to peripheral diagnostics, and heterogeneity of treatment effects

Questions & Discussion

Supplementary

Guideline Directed Medical Therapy Evidence

Global vascular guidelines on the management of chronic limb-threatening ischemia by Conte et al. 2019 in *J Vasc Surg*				
Medication	Indication	GRADE[1]	Level of Evidence	Key References
Moderate or high intensity statin	Reduce all-cause and cardiovascular mortality	1 (Strong)	A (High)	Leng 2000 in *Cochrane Review* Heart Protection Study Collaborative 2002 in *Lancet*
Anti-hypertensives (where appropriate)	Reduce hypertension	1 (Strong)	B (Moderate)	Accord Group 2010 in *NEJM* Bavry 2010 in *Hypertension*
Anti-platelet therapy	Treat all CLI patients	1 (Strong)	A (High)	Anti-thrombotic Trialists 2002 in *BMJ* Anti-thrombotic Trialists 2009 in *Lancet*

1. Balshem 2011 in *J Clin Epidemiol*

Future Directions

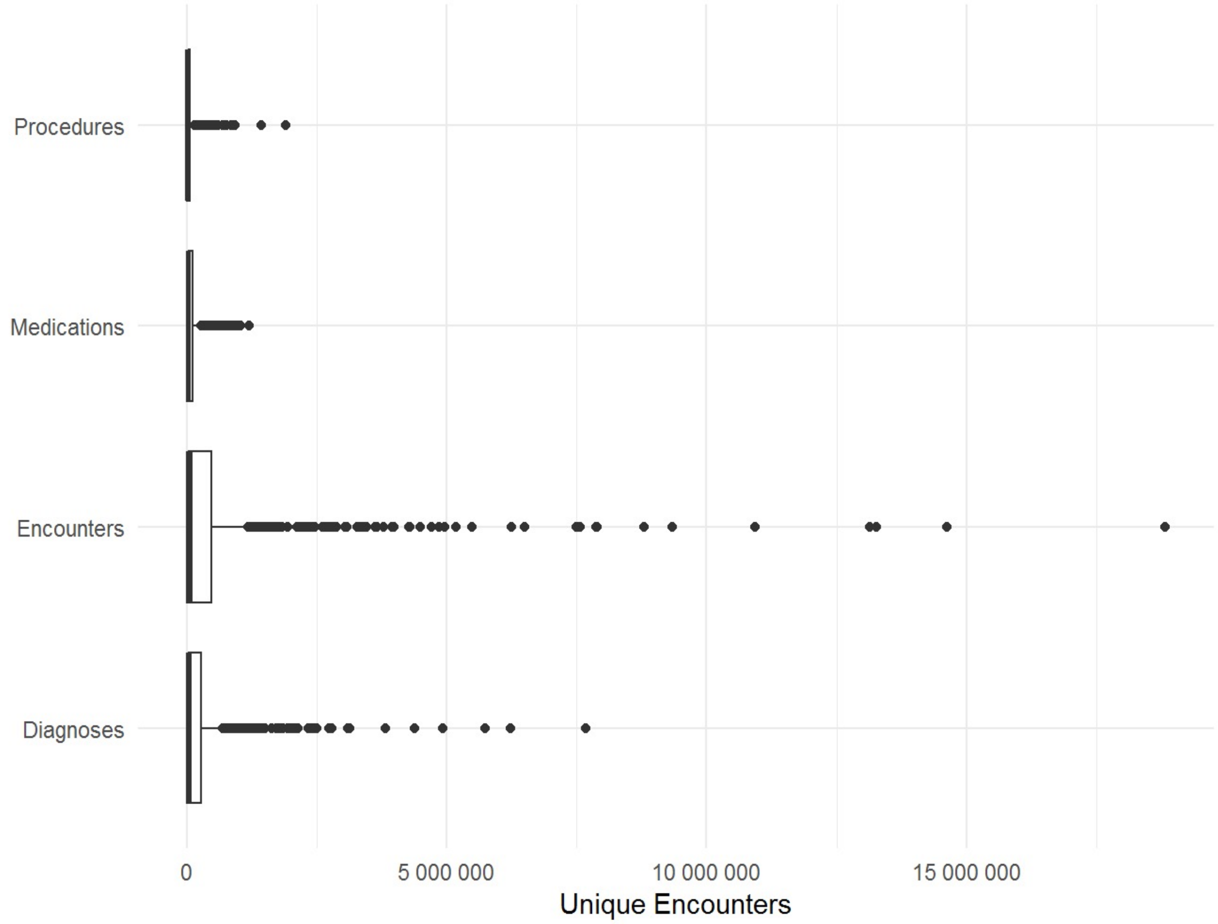
1. Continued development of methods for use of EHR warehouses for high-quality, contemporary, adaptable clinical research

2. Include unstructured data (such as clinical notes) for analysis and validation of results

3. Advanced analytics: machine learning algorithms for cardiovascular outcomes research
   a. Automated phenotype identification
   b. Disease risk and prognosis scoring
   c. Heterogeneity of treatment effects

Why choose N < 100 for site exclusion?

- Health Facts sites have a wide distribution of unique encounter numbers by site
    - Many in 0-100
    - Some in the millions
- We considered lower quartile exclusions and, although successful, this penalizes sites classified as smaller bed size (<5 beds vs. 500+ beds) due to relative encounter numbers
- We considered a ratio approach: # diagnosis encounter:# of overall encounters
    - Not all sites will use every module the same way (i.e. procedures at outpatient sites) thus this does not proportionally generalize to all sites
- Many sites that did not utilize a specific EHR module (for example: procedures) would have zero encounters—this is an easy exclusion
- Upon investigation, some sites with millions of encounters in one module had low (N=67, for example) but non-zero numbers in another
- To account for low and no module usage, N < 100 per module was selected



Variability in 30-Day Amputation by Site

Model	Number of Sites	Median Risk Ratio (95% Confidence Intervals)
Model 1: Unadjusted	N = 179	1.40 (1.35-1.46)
Model 2: Adjusted for Patient Characteristics[1]		1.30 (1.26-1.34)
Model 3: Adjusted for Patient[1] and Site[2] Characteristics		1.14 (1.12-1.16)
Model 4: Adjusted for Patient,[1] Site,[2] and US Census Region		1.11 (1.09-1.13)

1. Patient characteristics include dichotomous age greater than or less than 65 years, biological sex, white race vs. non-white race, marital status, documented coronary artery disease, depressive disorder, diabetes, heart failure, previous lower limb amputation, malignant cancer, hypertension, kidney disease, malnutrition, osteomyelitis, sepsis, and previous transient ischemic attack.

2. Site characteristics include teaching vs. non-teaching site, urban vs. rural status, and bed size classification.

Variation in Guideline Medical Therapy by Site

Model	Number of Sites	Median Odds Ratio (95% Confidence Intervals)
Model 1: Unadjusted	N = 196	2.32 (2.19-2.45)
Model 2: Adjusted for Patient-level Covariates[1]		2.31 (2.18-2.44)
Model 3: Adjusted for Revascularization Procedure		2.25 (2.13-2.38)
Model 4: Adjusted for Site-level Covariates[2]		2.11 (1.99-2.23)
Model 5: Adjusted for US Census Region		2.07 (1.96-2.18)

1. Patient-level encounter characteristics included age over 65, sex, race, history of diabetes, history of coronary artery disease, history of hypertension, history of heart failure, and history of myocardial infarction.
2. Site-level encounter characteristics included teaching vs. non-teaching status and urban vs. rural rurality classification.

Health Facts Human Subjects Protection

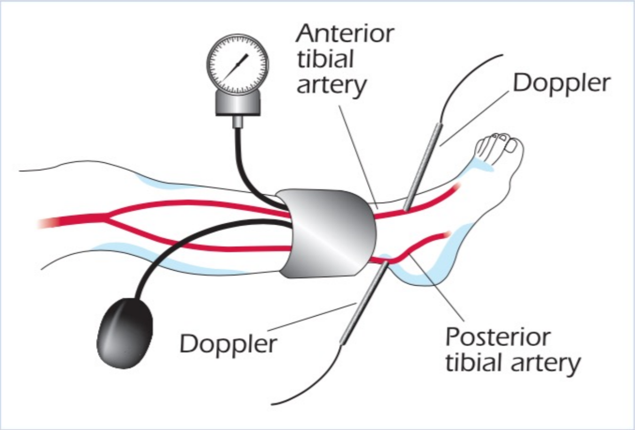
- Health Facts is fully de-identified for research purposes
- Non-Human Subjects designation by the UMKC IRB (protocol 14-567)

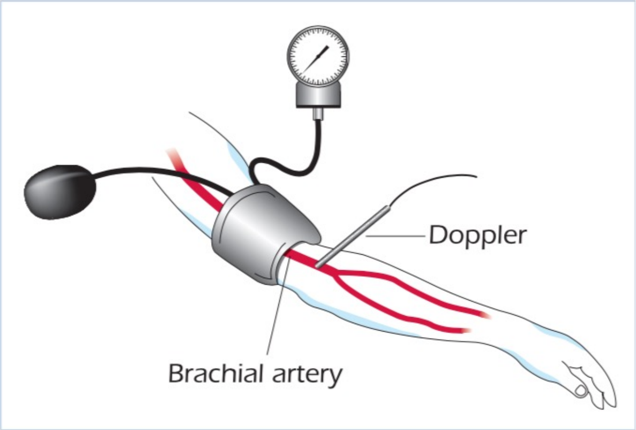
PAD Diagnosis & Staging

Metric	Normal	Peripheral Artery Disease			Critical Limb Ischemia		
ABI	>0.90	≤0.90			≤0.40		
TBI	>0.70	≤0.70			≤0.30		
Rutherford[1]	0	1	2	3	4	5	6
	No Claudication	Mild Claudication	Moderate Claudication	Severe Claudication	Ischemic Rest Pain	Minor Tissue Loss	Major Tissue Loss

1. Rutherford et al. 1999 in *J Vasc Surg*

Ankle Brachial Index (ABI)





From Tendera, M. et al. 2011 in *Eur. Heart J.*

$$\frac{\text{Higher Systolic Pressure Between Posterior Tibial Artery or Dorsalis Pedis Artery}}{\text{Higher Systolic Pressure Between Left and Right Brachial Arteries}} = \text{ABI; ratio} \leq 0.90 \text{ indicates PAD}$$

Feigelson et al. 1994 in *Am J Epidemiol*

Toe Brachial Index (TBI)

Higher Systolic Pressure Between
Left and Right Big Toes
―――――――――――――――――――――――
Higher Systolic Pressure Between
Left and Right Brachial Arteries

= TBI; ratio ≤0.70 indicates PAD

Romanos et al. 2010 in *J Foot Ankle Res*

ABI versus TBI

- Both tests measure peripheral blood flow and indicate vessel occlusion
- Both tests have acceptable sensitivity, specificity, PPV, and NPV
- TBI is the more appropriate test when:
  - Peripheral arteries become calcified and non-compressible
  - Micro-vasculature in the foot becomes occluded but peripheral arteries are not
- TBI may be better at indicating CLI than ABI—see Shishehbor et al. 2016 in *J Vasc Surg*

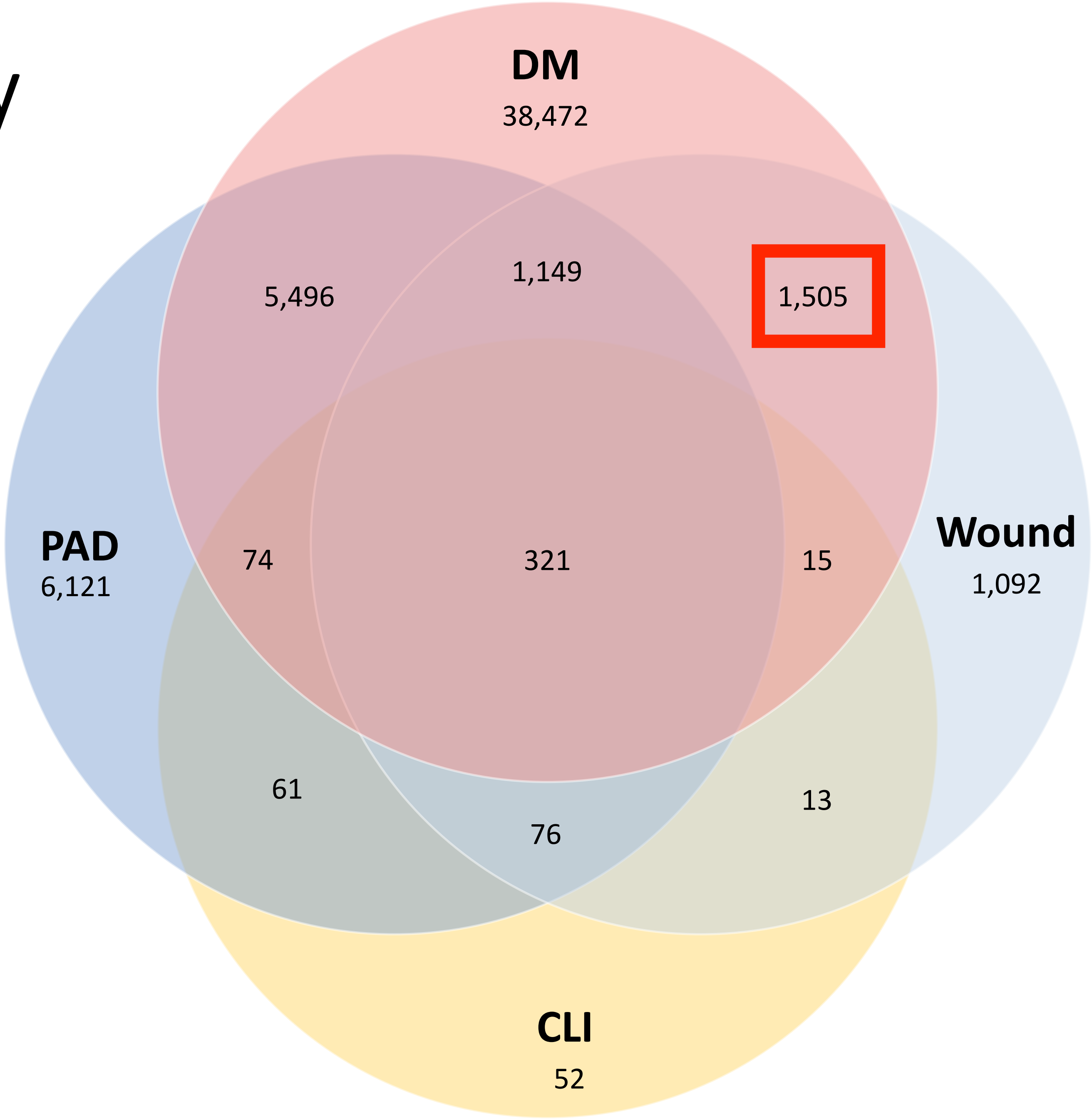
Preliminary Data

Unique patients with:
PAD: 13,598
DM: 47,057
Wounds: 4,471
CLI: 637

Data from Cerner i2b2 installation at Truman Health Systems as of Apr 2020

Unique patients as of Fall 2019

Total N> 812,881



Included vs. Excluded Health Facts Sites

Characteristic	Overall Health Facts Site Counts (Percent) N = 782	Included Health Facts Site Counts N = 348 (44.5%)	Excluded Health Facts Site Counts N = 434 (55.5%)
Unique Encounters (Mean [SD])	589,172 (1,571,564)	1,090,427 (1,915,309)	187,245 (1,072,906)
Unique Diagnosis Encounters (Mean [SD])	302,555 (697,892)	558,520 (903,412)	45,111 (157,796)
Unique Procedure Encounters (Mean [SD])	68,879 (168,711)	109,697 (204,296)	3,720 (20,792)
Unique Medication Encounters (Mean [SD])	101,281 (185,686)	141,233 (208,875)	8,593 (32,034)

Encounter Characteristics in a Derived CLI Cohort

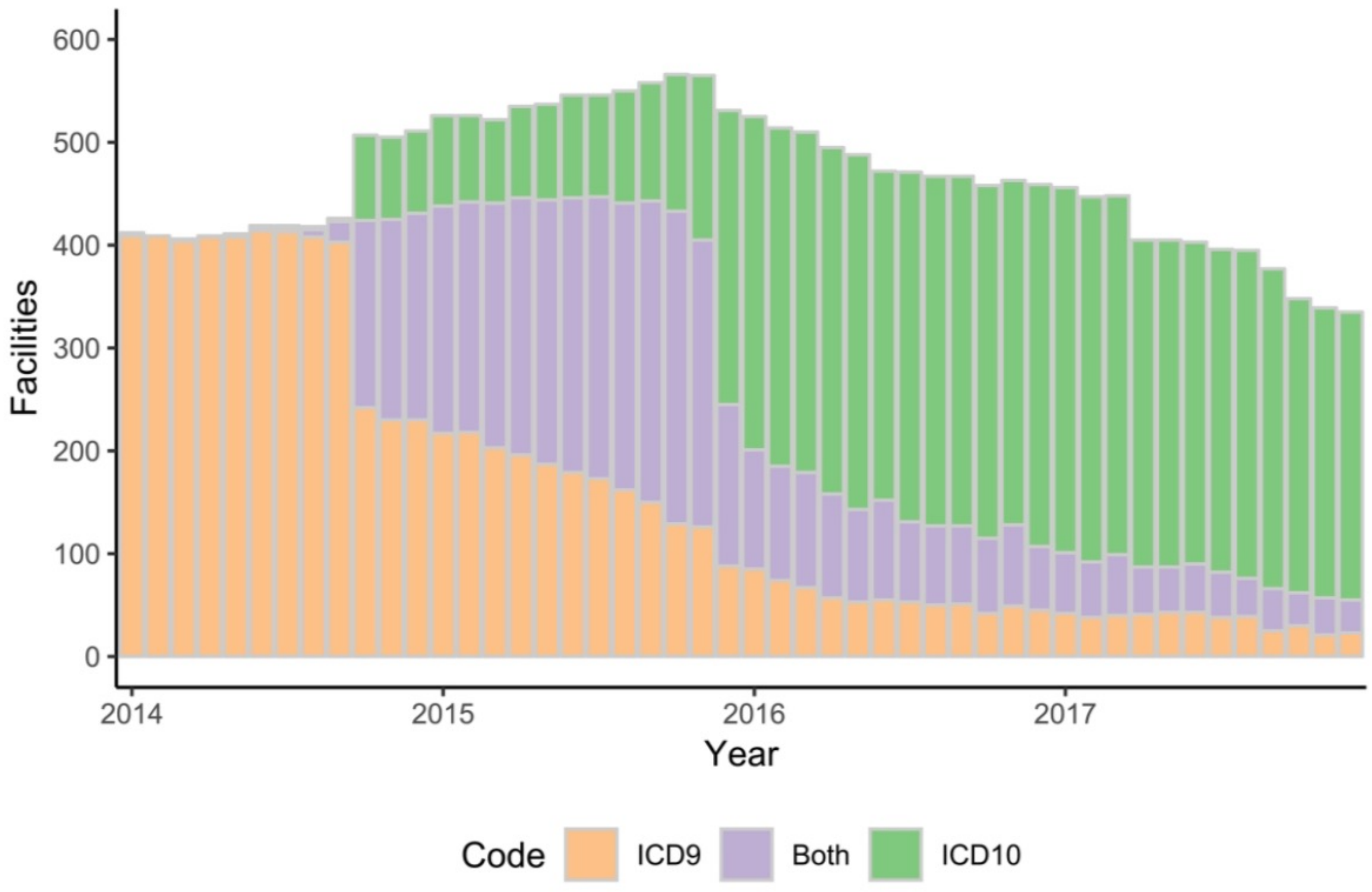
Characteristic	Patient Encounters (Percent) Total N = 79,413
Mean Age (Standard Deviation)	68.7 (12.4)
Race (White)	52,048 (69.6)
Marital Status (Married)	45,923 (58.9)
Census Region	
Midwest	16,854 (21.2)
Northeast	17,535 (22.1)
South	35,372 (44.5)
West	9,652 (12.2)
Site Teaching Status (Teaching)	46,948 (77.5)
Site Urban vs. Rural Status (Urban)	63,024 (79.4)

Clinical History in a Derived CLI Cohort

Characteristic	Patient Encounters (Percent) Total N = 79,413
Acute Kidney Failure	16,520 (20.8)
Atrial Fibrillation	17,038 (21.5)
Back Pain	1,122 (1.4)
Chronic Kidney Disease	35,180 (44.3)
Chronic Wound	34,760 (43.8)
Coronary Artery Disease	44,583 (56.1)
Depressive Disorder	9,911 (12.5)
Diabetes	50,994 (64.2)
Dyslipidemia	42,586 (53.6)
Heart Failure	28,722 (36.2)
Lower Limb Amputation	15,675 (19.7)
Malignant Cancer	6,568 (8.3)
Hypertension	65,802 (82.9)
Malnutrition	6,519 (8.2)
Myocardial Infarction	5,069 (6.4)
Obesity	12,104 (15.2)
Osteomyelitis	11,318 (14.3)
Sepsis	10,547 (13.3)
Thyroid Disorder	9,991 (12.6)
Tobacco Use	35,297 (44.4)
Transient Ischemic Attack	10,829 (13.6)

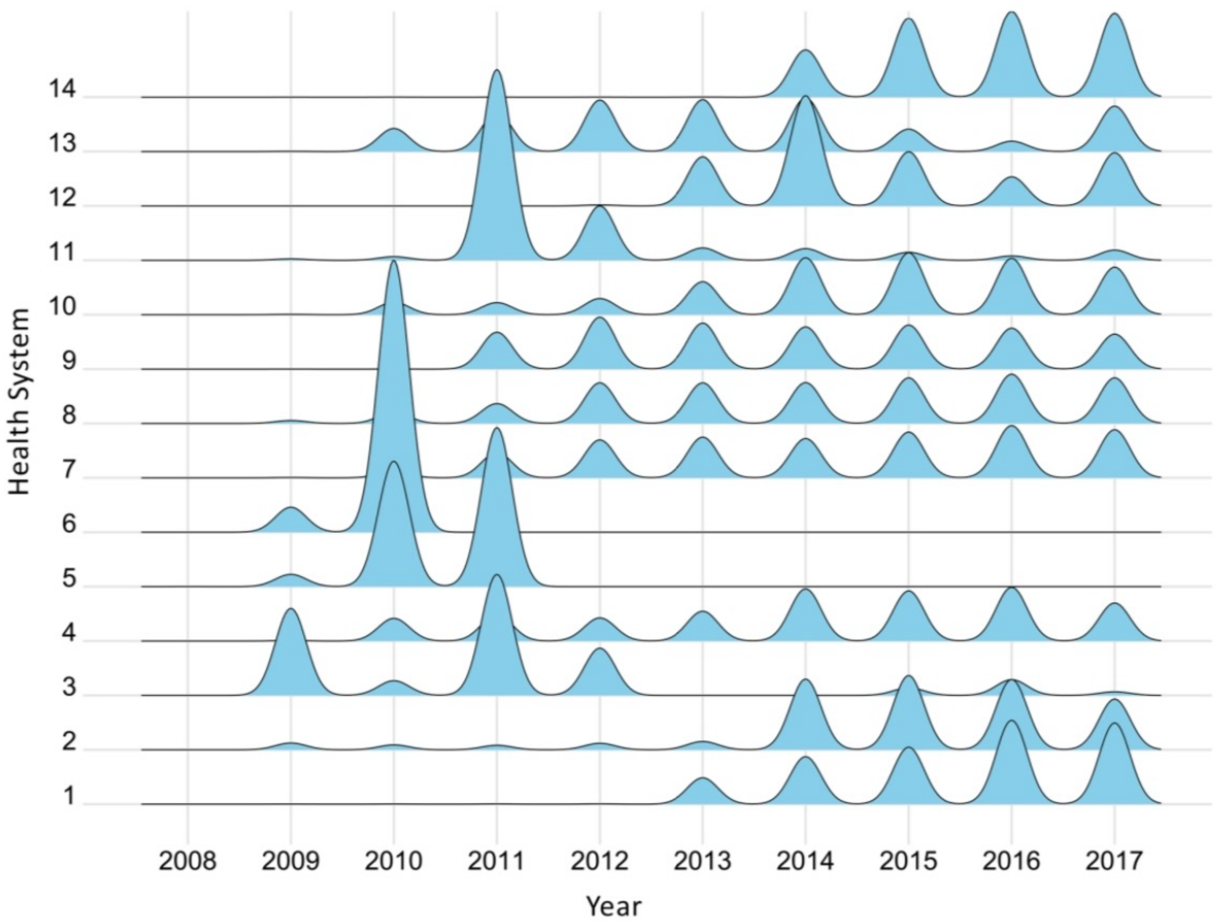
Glynn & Hoffman 2019

Figure 3 – Transition from ICD-9 to ICD-10



Glynn & Hoffman 2019

Figure 4B – Annual smoking history documentation by health system



Specific Aims

- **SPECIFIC AIM 1.** Examine contemporary temporal trends and geographic variation in non-traumatic, lower-extremity amputations for patients with PAD in the Health Facts Database

- **SPECIFIC AIM 2.** Examine the variability in quality of clinical care given to patients with PAD and documented critical limb ischemia

- **SPECIFIC AIM 3.** Develop predictive models of social and clinical predictors of adverse outcomes for patients with PAD and documented critical limb ischemia

Impact

- Provide contemporary, national estimates of non-traumatic amputations for patients with PAD and CLI
- Describe variability in the quality of care patients receive (particularly care prior to an amputation)
- Understand and predict which patients will experience an adverse outcome

AIM 1. Examine contemporary temporal trends and geographic variation in non-traumatic, lower-extremity amputations for patients with PAD in the Health Facts Database

1. Construct a data mart from the Cerner Health Facts EMR database for all patients with a PAD or CLI diagnosis between 2010 and 2018

2. Characterize prevalence of amputations by describing temporal trends, patient-specific factors, site-specific factors, and differences between census divisions

Aim 1 Methods

- Primary outcome: non-traumatic, lower-extremity amputation
- Overall rates of amputation will be calculated within the data mart (Amputation PAD Patients/All PAD Patients)
- Patient demographics, clinical history, and encounter-level site characteristics will be compared for patients with and without an amputation
- Hierarchical logistic regression will be fit to understand temporal trends of amputation over time

Aim 1 Expected Results

- Report contemporary rates of amputations in a national cohort of patients
- Compare previous rates of amputation to current rates

Aim 1 Possible Limitations

- Later years (>2010, >Q32015) may have better quality data; may need to restrict analysis to later years

AIM 2. Examine the variability in quality of clinical care given to patients with PAD and documented critical limb ischemia

1. Describe contemporary rates of cardiovascular risk management, perfusion testing, and revascularizations completed for all encounters post-CLI diagnosis

2. Compare rates of non-invasive cardiovascular risk management to rates of major amputation procedures by site

3. Compare rates of revascularization procedures to rates of major amputation procedures within each patient with variability across sites

Aim 2 Methods

- Primary outcomes: (1) hemodynamic diagnostic testing, (2) revascularization procedures, and (3) adherence to guideline medication therapy
- Overall rates of peripheral diagnostic testing, revascularization, and optimal medication therapy will be calculated for all CLI patients
- Median Odds Ratios (MOR) will be utilized to understand variability in care between clinical sites and census divisions

Aim 2 Expected Results

- Show national rates of quality of care testing among PAD and CLI patients over time
- Describe the variability in quality of care utilization between care locations
- Report gaps in quality of care where the largest improvements can be made

Aim 2 Possible Limitations

- Health Facts does not include provider type
- Initial exploration shows rates of diagnostic testing is low
- Some clinical sites may need to be filtered out

AIM 3. Develop predictive models of social and clinical predictors of adverse outcomes for patients with PAD and documented critical limb ischemia

1. Develop a hierarchical, logistic regression model to predict Major Adverse Limb Events and Major Adverse Cardiac Events

Potential Additional Statistical Exercises:

A. Develop a Bayesian limited dependent variable model to predict Major Adverse Limb Events and Major Adverse Cardiac Events, compare model performance to logistic regression model

B. Use a machine learning approach to identify non-linear artifacts of the data that could contribute variance to models

Aim 3 Methods

- Primary outcomes: (A) major adverse limb events (MALE; amputation, major intervention, inclusive of new bypass surgery, major graft revision, thrombectomy/thrombolysis) and (B) major adverse cardiac events (MACE; myocardial infarction, stroke, and death)

- Parametric survival analysis will be utilized to perform time-to-event analysis to understand significant differences between patient- and site-level groups that might experience a MACE or MALE event

- Additional Aim 3 Statistical Exercises:
  - Bayesian survival analysis will be conducted and model performance compared to parametric methods
  - Machine learning modeling will be conducted to identify non-linear artifacts of the data

Aim 3 Expected Results

- Provide a comprehensive risk model for patients who might experience a MALE or MACE event, including lower extremity amputation.

- Additional Exercises
  - Compare logistic regression analysis methods to contemporary Bayesian methods
  - Utilize machine learning to identify potential non-linear predictive elements in the Cerner Health Facts database

Aim 3 Possible Limitations

- Health Facts only includes patient mortality if the patient expires as an inpatient, no death index reconciliation occurs so analysis may have to be limited to non-mortality events

Costs of Amputation

- Average cost of an amputation per patient: $45k[1]; $11k/year after that in follow-up costs[2]
- Amputations cost $250M/year in US health care spending[3]
- Intangible costs: reduction in mobility, physical pain, and psychological impact of losing a limb[4]

1. Kurichi et al. 2013 in *Am J Phys Med Rehab*; 2. Visser et al. 2003 in *Eur J Vasc Endovasc Surg*; 3. *Amputee Coalition of America*, 4. Suckow et al. 2015 in *Ann Vasc Surg*