

Appendix 1 (as supplied by the authors): Supplemental material

Supplemental Methods

Covariates. We captured previous inpatient and outpatient peripheral revascularization procedures (open surgical or endovascular) using *Canadian Classification of Health Interventions* codes during a 3-year look-back window from the index amputation event. In addition, we captured prior major and minor lower limb amputations using this approach. The overall comorbidity burden was established using the Charlson Comorbidity Index (1). In addition, individual comorbid conditions were captured using validated coding algorithms in our databases. Immigration status was captured using the Immigration, Refugees and Citizenship Canada (IRCC)'s Permanent Resident Database, and long-term care residence prior to index amputation encounter was available from the Continuing Care Reporting System Database. To capture the use of sodium-glucose co-transporter 2 (SGLT-2) inhibitors at baseline, we examined individuals 66 years or older who had filled a prescription for a SGLT-2 inhibitor within 150 days prior to the index amputation date using the Ontario Drug Benefit Database.

Statistical Analysis. To fit exponential smoothing models (additive or multiplicative Winters), Akaike's Information Criterion and adjusted R^2 values were used to test for model fit. We used autocorrelation, partial autocorrelation, and inverse autocorrelation functions to model parameter appropriateness and seasonality. The augmented Dickey Fuller test and autocorrelation function were used to assess for stationarity (2). We assessed for the presence of white noise by examining the autocorrelation at various lags using the Ljung-Box X^2 statistic (3).

Supplemental Tables

Supplemental Table 1. Sources of data for the current population-level study.

Database	Description
Canadian Institute for Health Information Discharge Abstract Database	Records all hospitalizations in Ontario acute care hospitals
Ontario Health Insurance Plan Claims Database	Records data on physician and healthcare provider billing claims
Registered Persons Database	Records demographic and vital statistics data
National Ambulatory Care Reporting System	Records data on ambulatory and emergency department visits
Same Day Surgery	Records information on same day surgeries and procedures
Ontario Drug Benefits Database	Captures information on drug prescriptions filled among those 65 years or older, and those social assistance
Ontario Diabetes Database	Disease-specific ICES-derived cohort
Ontario Hypertension Database	Disease-specific ICES Sciences-derived cohort
Chronic Obstructive Pulmonary Disease Database	Disease-specific ICES-derived cohort
Congestive Heart Failure Database	Disease-specific ICES-derived cohort
Immigration, Refugees and Citizenship Canada (IRCC)'s Permanent Resident Database	Provides information on permanent and temporary residents as well as immigration and citizenship programs

Supplemental Table 2. Codes used to identify peripheral artery disease.

Peripheral Artery Disease – ICD-10-CA Codes

- I70.0 - Atherosclerosis of aorta
- I70.2 - Atherosclerosis of arteries of extremities
- I70.20 - Atherosclerosis of arteries of extremities without gangrene
- I70.21 - Atherosclerosis of arteries of extremities with gangrene
- I70.8 - Atherosclerosis of other arteries
- I70.9 - Generalized and unspecified atherosclerosis
- I73.9 - Peripheral vascular disease, unspecified (includes intermittent claudication)
- I74.0 - Embolism and thrombosis of abdominal aorta
- I74.3 - Embolism and thrombosis of arteries of lower extremities
- I74.4 - Embolism and thrombosis of arteries of extremities, unspecified (Peripheral arterial embolism)
- I74.5 - Embolism and thrombosis of iliac artery
- I74.8 - Embolism and thrombosis of other arteries
- I74.9 - Embolism and thrombosis of unspecified artery
- I79.2 Peripheral angiopathy in diseases classified elsewhere
- E10.50x - Type 1 diabetes mellitus with peripheral angiopathy
- E10.51x - Type 1 diabetes mellitus with peripheral angiopathy with gangrene
- E10.70x - Type 1 diabetes mellitus with peripheral angiopathy foot ulcer (angiopathic) (neuropathic)
- E10.71x - Type 1 diabetes mellitus with foot ulcer (angiopathic) (neuropathic) with gangrene
- E11.50x - Type 2 diabetes mellitus with peripheral angiopathy
- E11.51x - Type 2 diabetes mellitus with peripheral angiopathy with gangrene
- E11.70x - Type 2 diabetes mellitus with foot ulcer (angiopathic)(neuropathic)
- E11.71x - Type 2 diabetes mellitus with foot ulcer (angiopathic) (neuropathic) with gangrene
- E13.50x – Other specified diabetes mellitus with peripheral angiopathy
- E13.51x - Other specified diabetes mellitus with peripheral angiopathy with gangrene
- E13.70x - Other specified diabetes mellitus with foot ulcer (angiopathic) (neuropathic)
- E13.71x - Other specified diabetes mellitus with foot ulcer (angiopathic) (neuropathic) with gangrene
- E14.50x - Unspecified diabetes mellitus with peripheral angiopathy
- E14.51x - Unspecified diabetes mellitus with peripheral angiopathy with gangrene
- E14.70x - Unspecified diabetes mellitus with foot ulcer (angiopathic) (neuropathic)
- E14.71x - Unspecified diabetes mellitus with foot ulcer (angiopathic) (neuropathic) with gangrene

Abbreviations: ICD-10-CA, International Statistical Classification of Diseases, Tenth Revision, Canadian Version.

Supplemental Table 3. Coding definitions for identifying patients, procedures, and comorbid conditions.

	Database	Codes	Validity
PAD and Diabetes Characteristics			
PAD	CIHI-DAD	See Supplemental Table 2	
Diabetes	Ontario Diabetes Database	Diagnosis date in Ontario Diabetes Database that precedes the index date	80% PPV, 86% sensitivity, 97% specificity (4)
Peripheral revascularization	CIHI-DAD SDS	CCI Open: 1KA57LA, 1KA76MZ, 1KE57LA, 1KE76MZ, 1KG57LA, 1KG76MI, 1KT57LA, 1KT76MZ, 1JM76MI Endovascular: 1KA50GQ, 1KA57GQ, 1KE35, 1KE50, 1KE57GQ, 1KG35, 1KG50, 1KG57GQ, 1KT50, 1KT57GQ	88% PPV, 87% sensitivity (5) for 1KG76
Major limb amputation	CIHI-DAD SDS	CCI Major: 1VC93, 1VG93, 1VQ93	96% PPV, 98% sensitivity (5) for 1VQ93
Minor limb amputation	CIHI-DAD SDS	CCI Minor: 1WA93, 1WE93, 1WI93, 1WJ93, 1WK93, 1WL93, 1WM93, 1WN93	
Comorbid Conditions			
Coronary artery disease	CIHI-DAD OHIP	ICD-10-CA I20, I21, I22, I23, I24, I25, Z95.5, Z95.8, Z95.9, R93.1, T82.2 CCI 1IJ54, 1IJ57, 1IJ50, 1IJ76 OHIP R741, R742, R743, G298, E646, E651, E652, E654, E655, G262, Z434	Codes based on previous study (6)
Cerebrovascular disease	CIHI-DAD	ICD-10-CA G45, G46, H34.0, I60-I69	As defined in the calculation of Charlson Comorbidity Index by ICES
Congestive heart failure	Congestive Heart Failure Database	Diagnosis date in Congestive Heart Failure Database that precedes the index date	85% sensitivity, 97% specificity (5)
Hypertension	Hypertension Database	Diagnosis date in Ontario Hypertension Database that precedes the index date	87% PPV, 73% sensitivity, 95% specificity, 88% NPV (7)
Chronic obstructive pulmonary disease	COPD Database	Diagnosis date in Ontario COPD Database that precedes the index date	85% sensitivity, 78% specificity, 94% NPV (8)
Chronic kidney disease	CIHI-DAD	ICD-10-CA N032-N037, N052-N057, N18, N19, N250, Z490-Z492, Z940, Z992	As defined in the calculation of Charlson Comorbidity Index by ICES
Dialysis	OHIP	OHIP Hemodialysis: R849, R850, G325, G323, G326, G860, G333, G862, G863, G865, G866 Peritoneal dialysis: G330-G333, G861, G864 Continuous renal replacement therapy: G083, G085, G295, G326, R849, G082, G090-G096, G294	91%-99% accuracy (9)

Abbreviations: PAD, peripheral artery disease; CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database; CCI, Canadian Classification of Health Interventions; PPV, positive predicative value; ICD-10-CA, International Statistical Classification of Diseases, Tenth Revision, Canadian Version; OHIP, Ontario Health Insurance Plan; NPV, negative predictive value; COPD, chronic obstructive pulmonary disease.

Supplemental Table 4. Codes used to exclude patients with amputations related to malignancy, trauma/injury, or other non-peripheral artery disease and non-diabetes related diagnoses.

Malignancy – ICD-10-CA Codes

- C40.2 Malignant neoplasm of long bones of lower limb
- C40.3 Malignant neoplasm short bones of lower limb
- C41.8 Overlapping malignant lesion of bone and articular cartilage
- C41.9 Malignant neoplasm bone and articular cartilage, unspecified
- C43.7 Malignant melanoma of lower limb, including hip
- C47.2 Malignant neoplasm of peripheral nerves of lower limb, including hip
- C49.2 Malignant neoplasm of connective and soft tissue of lower limb, including hip
- C76.5 Malignant neoplasm of lower limb
- C79.5 Secondary malignant neoplasm of bone and bone marrow
- C90.0 Multiple myeloma
- C90.20 Plasmacytoma of bone
- D16.2 Benign neoplasm of long bones of lower limb
- D16.3 Benign neoplasm of short bones of lower limb
- D21.2 Other benign neoplasm of connective and other soft tissue of lower limb, including hip
- C44.7 Malignant neoplasm skin of lower limb, including hip
- C46.^ Kaposi's sarcoma
- C47.^ Malignant neoplasm of peripheral nerves and autonomic nervous system
- D36.1^ Benign neoplasm of peripheral nerves and autonomic nervous system

Trauma/Injury – ICD-10-CA Codes

- S70-79, S80-89, S90-99: lower extremity trauma
 - T01.3^ Open wounds of multiple regions of lower limb(s)
 - T02.3^ Fractures involving multiple regions of one lower limb
 - T02.5^ Fractures involving multiple regions of both lower limbs
 - T04.3-T04.9 Crush injury including lower limbs
 - T05.3-T05.9 Traumatic amputation including foot or lower limb
 - T12.0 Fracture of lower limb, level unspecified, closed
 - T12.00 Fracture of lower limb, level unspecified, closed
 - T13.0 Superficial injury of lower limb, level unspecified
 - T13.1 Open wound of lower limb, level unspecified
 - T13.2 Dislocation, sprain and strain of unspecified joint and ligament of lower limb, level unspecified
 - T13.3 Injury of unspecified nerve of lower limb, level unspecified
 - T13.4 Injury of unspecified blood vessel of lower limb, level unspecified
 - T13.5 Injury of unspecified muscle and tendon of lower limb, level unspecified
 - T13.6 Traumatic amputation of lower limb, level unspecified
 - T13.8 Other specified injuries of lower limb, level unspecified
 - T13.9 Unspecified injury of lower limb, level unspecified
 - T24.0 Burn of unspecified degree of hip and lower limb, except ankle and foot
 - T24.1 Burn of first degree of hip and lower limb, except ankle and foot
 - T24.2 Burn of second degree of hip and lower limb, except ankle and foot
 - T24.3 Burn of third degree of hip and lower limb, except ankle and foot
 - T24.4 Corrosion of unspecified degree of hip and lower limb, except ankle and foot
 - T24.5 Corrosion of first degree of hip and lower limb, except ankle and foot
 - T24.6 Corrosion of second degree of hip and lower limb, except ankle and foot
 - T24.7 Corrosion of third degree of hip and lower limb, except ankle and foot
 - T25.0 Burn of unspecified degree of ankle and foot
 - T25.1 Burn of first degree of ankle and foot
 - T25.2 Burn of second degree of ankle and foot
 - T25.3 Burn of third degree of ankle and foot
 - T25.4 Corrosion of unspecified degree of ankle and foot
 - T25.6 Corrosion of second degree of ankle and foot
 - T25.7 Corrosion of third degree of ankle and foot
 - T33.^ Frostbite
 - T34.^ Frostbite with necrosis
 - T35.^ Frostbite unspecified
 - T79.6 Traumatic ischaemia of muscle
 - M12.55 Traumatic arthropathy, pelvic region and thigh
 - M12.56 Traumatic arthropathy, lower leg
 - M12.57 Traumatic arthropathy, ankle and foot
 - M12.58 Traumatic arthropathy, other site
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- M12.59 Traumatic arthropathy, unspecified site
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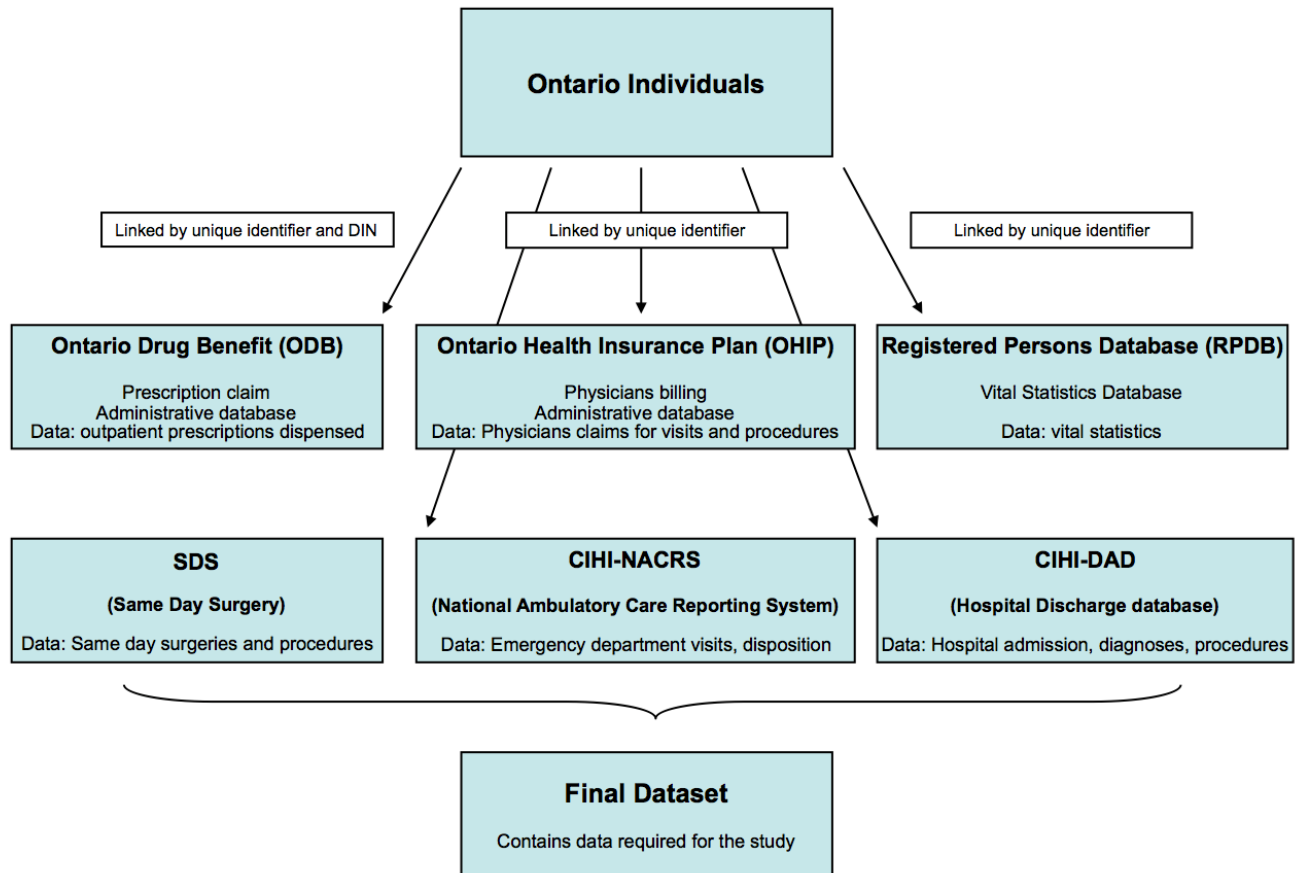
Other – ICD-10-CA Codes

- T84.54 Infection and inflammatory reaction due to knee prosthesis
 - T84.^ Complications of internal orthopaedic prosthetic devices, implants and grafts
 - T84.^ Complications of internal orthopaedic prosthetic devices, implants and grafts (hip prosthesis, knee prosthesis, internal fixation device of bones of limb, Infection and inflammatory reaction due to internal joint prosthesis, Infection and inflammatory reaction due to internal fixation device [any site])
 - L08.0 Pyoderma
 - L51.2 Toxic epidermal necrolysis
 - L88.^ Pyoderma gangrenosum
 - L89.^ 'decubitus ulcer'
 - L97.^ Lower limb ulcer not otherwise classified
 - M00.^ Pyogenic arthritis
 - M01.^ Direct infections of joint in infectious and parasitic diseases classified elsewhere
 - M84.^ Disorders of continuity of bone (malunion, nonunion, delayed union) of fracture
 - M89.0^ - Complex regional pain syndrome
 - M96.6^ Fracture of bone following insertion of orthopaedic implant, joint prosthesis, or bone plate
 - Q27.31 Peripheral arteriovenous malformation of lower limb
 - Q27.38 Peripheral arteriovenous malformation of other site
 - Q27.8 Other specified congenital malformations of peripheral vascular system
 - Q27.9 Congenital malformation of peripheral vascular system, unspecified - Anomaly of artery or vein not otherwise specified
 - Q65.^ Congenital deformities of hip
 - Q66.^ Congenital deformities of feet
 - Q68.2 Congenital deformity of knee
 - Q68.3 Congenital bowing of femur
 - Q68.4 Congenital bowing of tibia and fibula
 - Q68.5 Congenital bowing of long bones of leg, unspecified
 - I80.^ Phlebitis and thrombophlebitis
 - I83.^ Venous ulcer
 - I87.0^ Postthrombotic syndrome
 - I87.1 Compression of vein
 - I87.2 Venous insufficiency (chronic)(peripheral)
 - I89.0 Lymphoedema, not elsewhere classified
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Abbreviations: ICD-10-CA, International Statistical Classification of Diseases, Tenth Revision, Canadian Version.

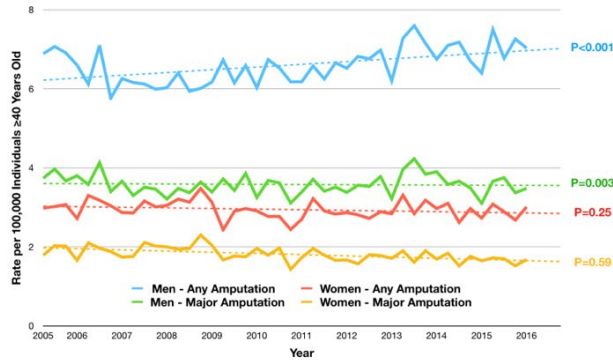
Supplemental Figures

Supplemental Figure 1. Overview of Ontario healthcare administrative databases.

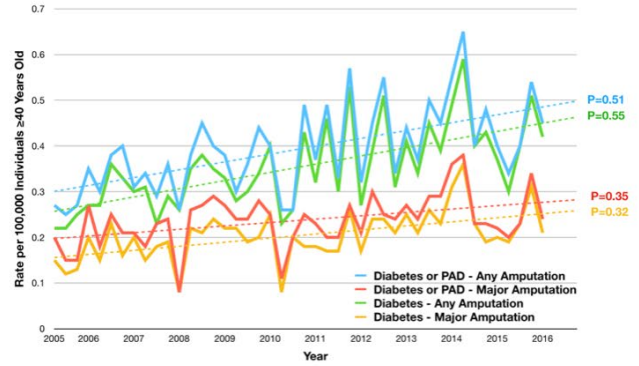


Supplemental Figure 2. Diabetes and/or PAD-related any lower extremity amputations by sex (A), among immigrants (B), lowest income quintile (C), and those residing in long-term care (D).

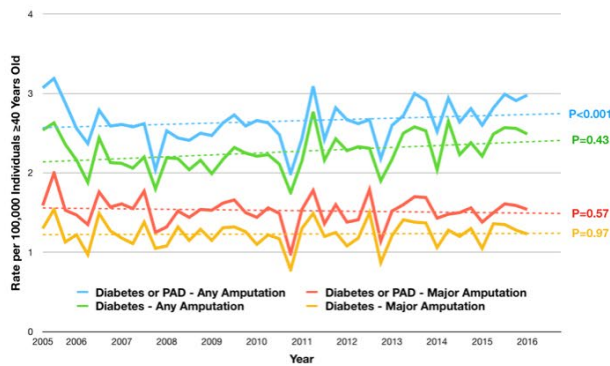
A) Sex



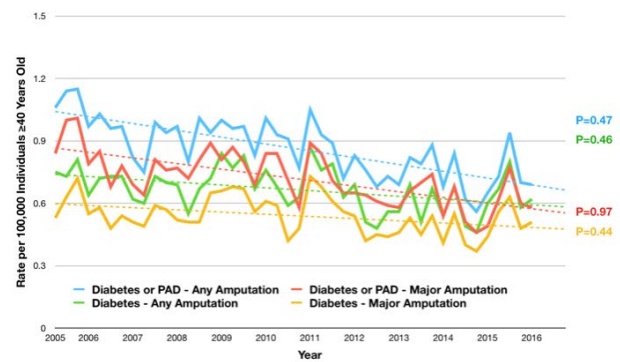
B) Immigrants



C) Lowest Income Quintile

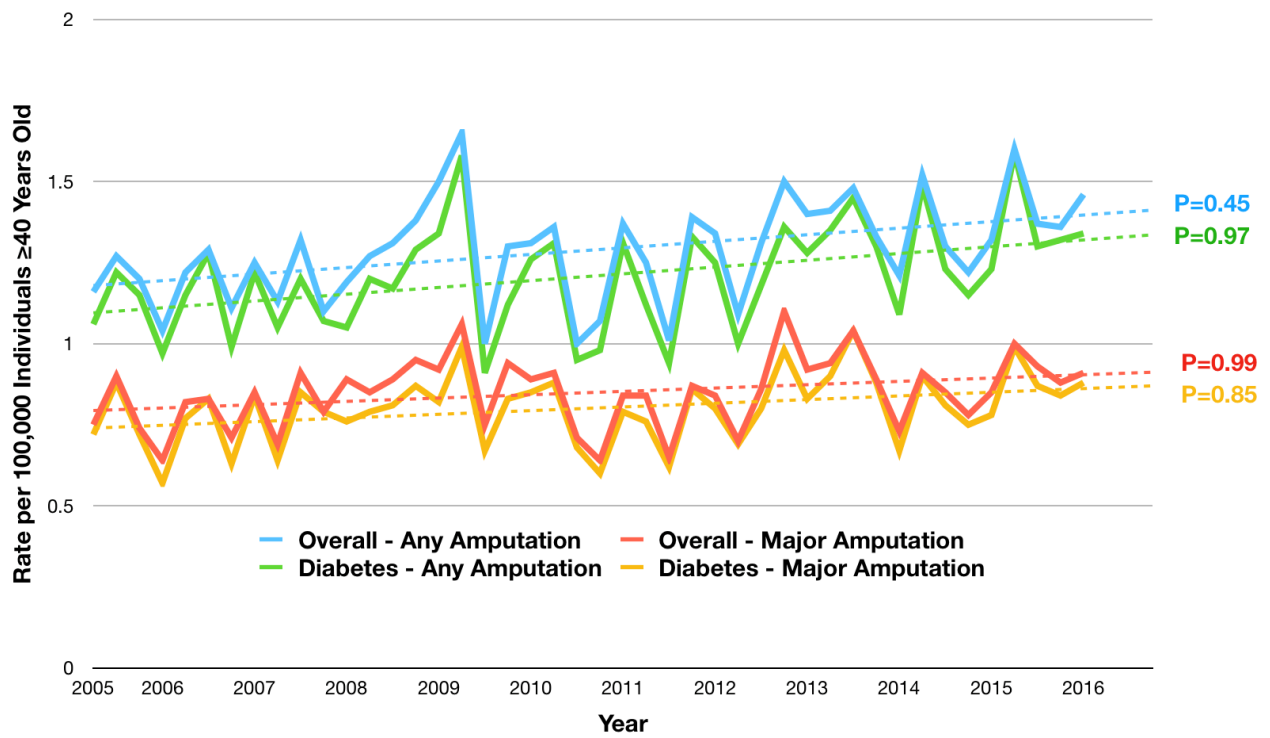


D) Long-Term Care



Abbreviations: PAD = peripheral artery disease.

Supplemental Figure 3. Diabetes and/or PAD-related any lower extremity amputations among those on dialysis.



Abbreviations: PAD = peripheral artery disease.

Supplemental Results

SGLT-2 Inhibitor Use. Among individuals 66 years or older in the study, ≤ 6 had filled a prescription for a SGLT-2 inhibitor within 150 days prior to the index amputation.

Supplemental References

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