Why PAD Remains Underdiagnosed, Undertreated, Screening, Diagnosis and Management

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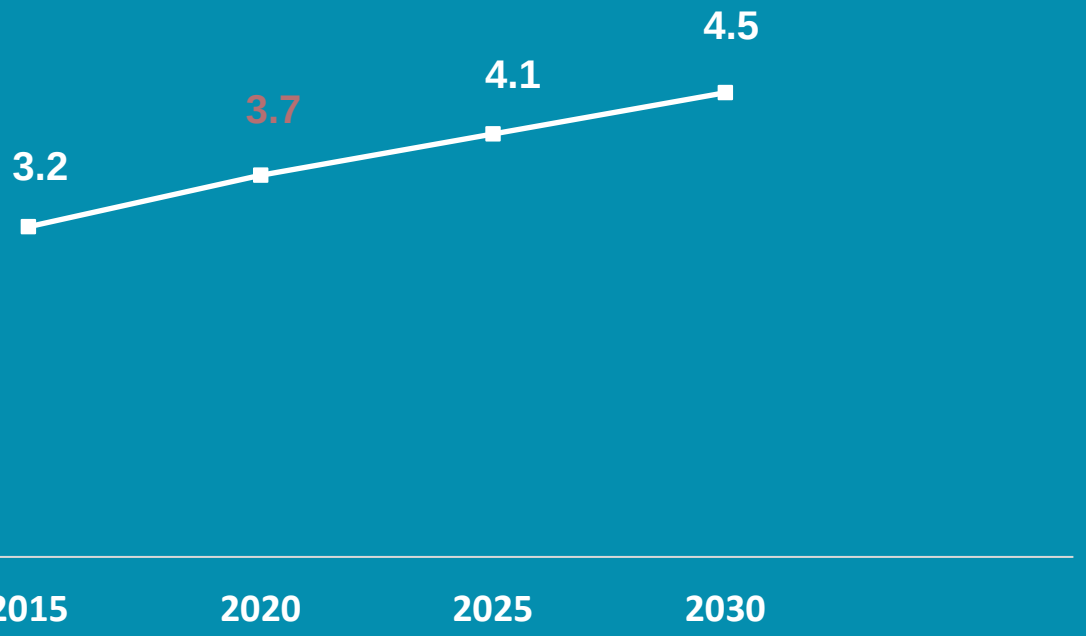
2023 Cors at the Shore

Disclosures

- CSI
- Boston Scientific
- Shockwave Medical
- Abbott
- Philips Medical
- Terumo Medical
- Cordis

U.S. CLI PREVALENCE 2015-2030

(Millions)



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Source: Yost ML. CLI US epidemiology supplement 2016. THE SAGE GROUP.

CLI ANNUAL ECONOMIC COST

Cost of Inpatient CLI Interventional Treatments: $4.2 Billion[1]

Cost of Incident CLI in Medicare: $12 Billion[2]

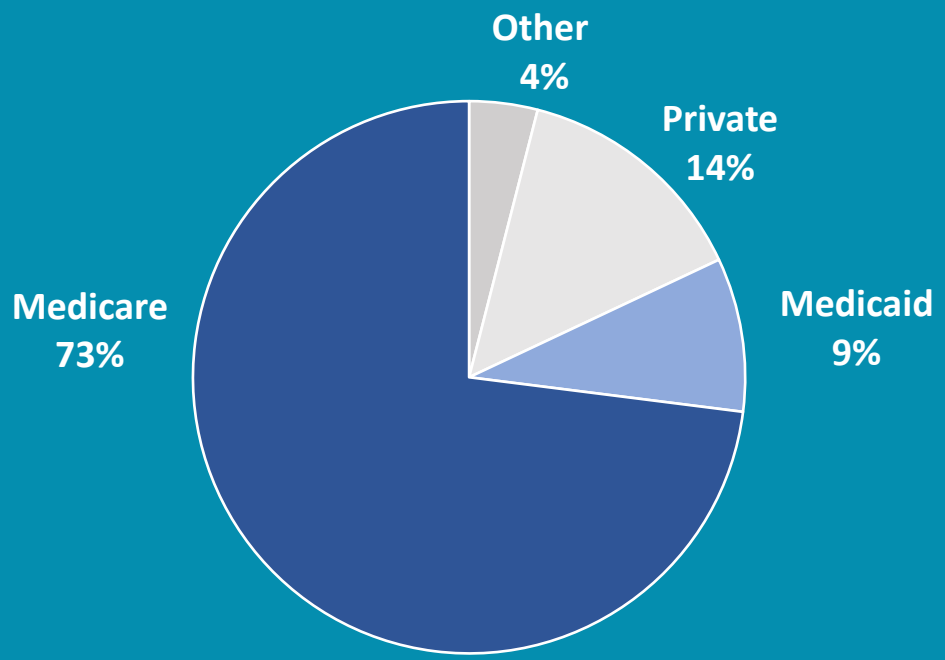
All-Cause Costs of Prevalent CLI: $220-$300 Billion[3]

1,2 Cost in 2016 $

3 Cost in 2018 $

Source: Kolte D, et al. Circulation. 2017;136(2):167-176. Mustapha JA. J Am Heart Assoc. 2018;7e009724. Yost ML. The cost of critical limb ischemia. THE SAGE GROUP. 2019.

WHO PAYS THE CLI BILL?



Source: AHRQ. Healthcare Cost and Utilization Project. HCUP Query. ICD-10 diagnosis codes primary CLI: 170.22, 170.24, 170.20. Available at: https://www.ahrq.gov/research/data/hcup/index.html. Accessed May 12, 2019.

CLI PATIENTS GETTING SICKER—HIGH NON-CLI ADMISSIONS ADD TO COSTS

SICKER CLI PATIENTS: INCREASING PREVALENCE OF HYPERTENSION, OBESITY, CKD AND DIABETES PLUS PATIENTS W/PRIOR AMPUTATION (2003-2011)

ONLY 54% ADMISSIONS DUE TO PRIMARY CLI—REST DUE TO DM, SEPTICEMIA, POST PROCEDURE COMPLICATIONS, CARDIOVASCULAR, ETC.

Source: Agarwal S. J Am Coll Cardiol 2016;67:1901-13.

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DIABETES SIGNIFICANTLY IMPACTS CRITICAL LIMB ISCHEMIA

- DM: More Severe Ischemia
- DM: More Likely to Present w/ Ulcers and Gangrene
- CLI Develops Suddenly in DM
- DM: More Amputations and Higher Risk (28X)
- Risk of Amputation ↑ w/ Severity of DM (Hba1c)
- DM: Increases CLI Costs

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Source: Yost ML. Diabetic foot ulcers. THE SAGE GROUP. 2010. Freisinger E. Cardiovasc Diabetol. 2017;16:41. Yost ML. The cost of critical limb ischemia. THE SAGE GROUP 2019.

CHRONIC KIDNEY DISEASE (CKD) INCREASES RISK OF AMPUTATION & MORTALITY

- 33%-44% of CLI Patients Have CKD
- 9%-12% Have Most Severe Form, ESRD
- Prevalence of CKD Increases with Severity of Ischemia
  - R4 16%, R6 42%
- CLI Patients w/ CKD Have Higher Risk of Mortality and Amputation

Source: Yost ML. The cost of critical limb ischemia. THE SAGE GROUP. 2019, Kolte D, et al. Circulation. 2017;136(2):167-176. Mustapha JA. J Am Heart Assoc. 2018;7e009724, O'Hare AMJ Am Soc Nephrol 2005;16:514-19 and Yost ML. CLI Global 2019, Dec. Available at: https://editions.mydigitalpublication.com/publication/?i=637766&p=1&pp=1&view=issueViewer .

CLI PATIENTS HAVE POLYVASCULAR DISEASE

- 60%-80% CLI Patients Have Coronary or Cerebrovascular Disease
- Cardiovascular Hospitalizations, Revascularizations, and Deaths Add to CLI Costs
- MACE Increases with the Number of Vascular Beds Involved
- MACE Increases per Patient cost by $45,527

MACE = MI, Stroke, and CV Death

Source: Yost MJ. The cost of critical limb ischemia. THE SAGE GROUP. 2019. Sigvant B, et al. J Vasc Surg. 2016;64(4):1009-1017.e3. Norgren L, et al. Eur J Vasc Endovasc Surg. 2018;55(1):109-117, Berger A, et al. Am J Cardiol. 2019;123(12):1893-1899 and Gutierrez JA. JAMA Netw Open. 2018 Nov 2;1(7):e185239.

CV RISK FACTORS UNDERTREATED IN CLI PATIENTS

RISK FACTORS UNDERTREATED EVEN COMPARED WITH IC PATIENTS!

CV RISK FACTOR MODIFICATION THEAPIES UNDERUTILIZED

Statins prescribed in 50%-62%,
Antiplatelets in 60%-90%
Anti-hypertensives in only 53%-71%

GLUCOSE INADEQUATELY CONTROLLED IN 63%-92%

SMOKING PERSISTS IN 27%-52% OF CLI PATIENTS

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Source: Armstrong EJ. J Am Heart Assoc 2014;3:e000697, Howard DPJ. Circulation 2015; 132: 1805-15, Chung J. J Vasc Surg 2013; 58:972-80 and Arya S. J Vasc Surg. 2018 Jan;67(1):217-228.e1.

POOR GLUCOSE MANAGEMENT IN DIABETIC CLI PATIENTS—INCREASES MORBIDITY & COSTS

Elevated Glucose (Hba1c) Increases the Risk of

- Amputation
- Reamputation
- Revascularization

Risk of Amputation & Reamputation Increases In Dose-Response Manner as Glucose Levels Rise Above Normal (Hba1c ≥ 6%)

Source: Arya S. J Vasc Surg. 2018 Jan;67(1):217-228.e1 and Yost ML. The cost of critical limb ischemia. THE SAGE GROUP 2019.

INADEQUATE MEDICAL MANAGEMENT INCREASES MAJOR ADVERSE EVENTS & DEATH

RESULT: MAJOR ADVERSE CARDIAC (MACE) AND LEG EVENTS (MALE) AND HIGHER COSTS

SUBOPTIMAL MEDICAL MANAGEMENT INCREASES RISK OF AMPUTATION AND/OR DEATH 8.5X

OPTIMAL CV RISK MANAGEMENT COULD SAVE >$14 BILLION

Source: Armstrong EJ. J Am Heart Assoc 2014;3:e000697, Howard DPJ. Circulation 2015; 132: 1805-15, Chung J. J Vasc Surg 2013; 58:972-80 and Yost PAD real cost THE SAGE GROUP 2011.

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PHARMACEUTICAL THERAPIES THAT REDUCE THE RISK OF AMPUTATION

Statins (EUCLID Trial)

Xa Inhibitor Rivaroxaban + Aspirin

Reduced Total Amputations by 58% (COMPASS Trial)

Reduced Amputations After Revascularization (VOYAGER Trial)

PCSK9 Inhibitor Evolocumab + Statins

Reduced MA (FOURIER Trial)

Long CA. Circ Cardiovasc Qual Outcomes. 2020;13:e006399., Anand SS. J Am Coll Cardiol 2018;71:2306–15, Anand SS. Lancet 2018; 391: 219–29, Bonaca MP. N Engl J Med 2020;382:1994-2004 and Bonaca MP. Circulation. 2018;137:338–350.

NEW PHARMACEUTICAL THERAPIES THAT REDUCE MA RISK UNDERUTILIZED

Data on Percent of PAD Patients Prescribed 2 New Therapies in PAD/CLI Unavailable (Xa Inhibitor Rivaroxaban & PCSK9 Inhibitor Evolocumab)

Statins, Particularly High-Intensity Statins, are Underutilized in PAD/CLI Patients

Women & AA Even Less Likely to Be Treated with Statins-Especially High- Intensity

Since Classic CV Risk Factor Reduction Therapies are Underutilized, Highly Likely the New Protective Therapies are Underutilized

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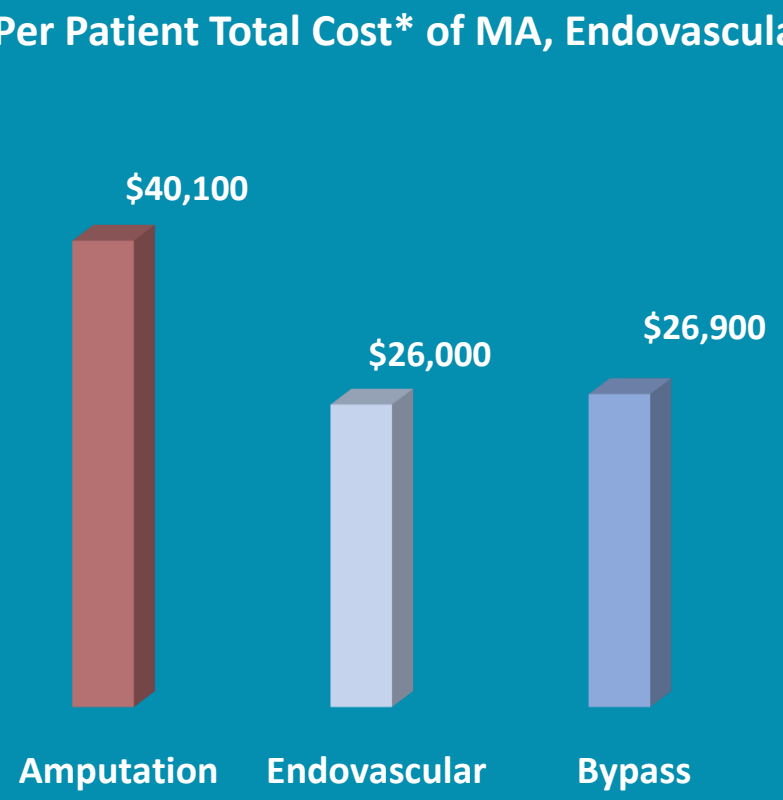
Source: Chung J. J Vasc Surg 2013; 58: 972-80, Arya S. Circulation. 2018 April 03; 137(14): 1435–1446, Soden PA. J Vasc Surg. 2018 Feb;67(2):e56.e3, Pabon M. Circulation Research. 2022;130:496–511 and Yost ML. Opinion.

AMPUTATION COSTS MORE THAN REVASCULARIZATION



*Total cost = procedure cost + morbidity, mortality, & revisions

Source: Yost ML. Cost-benefit analysis of critical limb ischemia in the era of the Affordable Care Act. Endovasc Today. 2014 May. Yost ML. The cost of critical limb ischemia. THE SAGE GROUP. 2019.

AMPUTATION ANNUAL ECONOMIC COST*

$33 Billion in Direct Medical Costs (MA & Minor)

(Inpatient & Outpatient)

$11 Billion Lifetime Costs (MA)

(Medical, Non-Medical & Unreimbursed Patient Costs)

$44 Billion Total Costs

*2018 $

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Source: Yost ML. The cost of critical limb ischemia. THE SAGE GROUP 2019.

CLI TREATMENT A ”PATHWAY TO AMPUTATION”

Major Amputation Frequently the First and Only Therapy for CLI

Diagnostic Testing Underutilized

No Angiogram in 61%-84% Prior to Major Amputation (MA)

Revascularization Underutilized

No Revascularization in 51%-71% Prior to MA

Low Referrals to Vascular Specialists* Prior to Amputation

Only 31% Medicare Patients Referred to Vascular Specialist Prior to Major or Minor Amputation

*Vascular Specialist = Cardiologist, Interventional Radiologist or Vascular Surgeon

Source: Allie DE. Eurointervention, 2005;1:60-69, Goodney PP. Circ Cardiovasc Qual Outcomes. 2012;5:94-102, Vemulapalli S. Circ Cardiovasc Qual Outcomes. 2014 Jan;7(1):142-50 and Mustapha JÁ. J Am Heart Assoc. 2018 Aug 21;7(16):e009724.

FACTORS THAT REDUCE THE RISK OF AMPUTATION & MORTALITY

An Angiogram Reduces the Odds of Major Amputation by 90%

Evaluation by Vascular Specialist* Increases the Odds of Diagnostic Testing

Revascularization Significantly Reduces the Risk of MA or Death Versus No Revascularization

Unrevascularized CLI Patients ≈ 2x-3x More Likely to Die or Undergo MA

Treatment at Centers with High Revascularization Volumes Significantly Increases Odds of Revascularization & Reduces Odds of MA

*Vascular Specialist = Cardiologist, Interventional Radiologist or Vascular Surgeon

Source: Henry AJ. J Vasc Surg. 2011 Feb;53(2):330-9, Vemulapalli S. Circ Cardiovasc Qual Outcomes. 2014 Jan;7(1):142-50, Armstrong EJ. J Med Econ. 2017 Nov; 20(11):1148-1154, Chung J. J Vasc Surg. 2013 Oct;58(4):972-80, Goodney PP. Circ Cardiovasc Qual Outcomes. 2012;5:94-102 and Medhekar AN. J Vasc Surg. 2017 Aug;66(2):476-487.

LACK OF KNOWLEDGE & AWARENESS DELAYS REFERRALS TO SPECIALISTS

Survey of Internists, Nephrologists & Endocrinologists:

74% Use Watchful Waiting as ‘Treatment’ for PAD

63% Do Not Consider Chronic Non-Healing Wounds a Reason for Specialist Referral

* Specialist = Cardiologist, Interventional Radiologist or Vascular Surgeon

Source: Chopra P. Vasc Dis Mgmt. 2017;14:E137-42.

NON-SPECIALIST PHYSICIANS AND TRAINEES LACK AWARENESS

Systematic Literature Review Found Lack of Knowledge & Understanding of PAD Among

- Non-specialist Healthcare Professionals
- Medical Students and Doctor Trainees-
  - Knowledge Modest to Poor
  - Low Awareness of ABI & Few Able to Perform ABI

Medical Student Survey Found Low Awareness of Vascular Surgery Specialty--Procedures Performed and Types of Disease Treated

Source: Bridgwood BM. Vasc Med 2020, Vol. 25(3) 263–273, Farber A. J Vasc Surg 2010;51:771-5.

PUBLIC LACK OF KNOWLEDGE & AWARENESS

- 2006 National Survey Only 26% Familiar w/PAD
  - Low Knowledge of Risk Factors, Leg Symptoms and Possibility of Amputation

- 2018 AHA Survey: < 50% Familiar with PAD, Its Leg Symptoms & Risk of Amputation
  - Blacks and Hispanics Lowest PAD Awareness and Greatest Knowledge Gaps. Only 6% Aware of Symptoms & Risk of Amputation!

Source: Hirsch AT. Circulation. 2007; 116:2086–2094 and AHA PAD roundtable report. 2019. Available at: https://www.heart.org/-/media/files/health-topics/peripheral-artery-disease/pad-roundtable-report--final.pdf?la=en.

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AMPUTATIONS INCREASED BY DELAYED REFERRALS

Delayed Diagnosis & Treatment Increases MA Risk

CLI Versus No CLI Increases MA Risk 3.5X

In Patients with ABI < 0.80, MA Risk Increases by 1.4X for Every 0.10 Decrease in ABI

Delayed Diagnosis & Treatment Increases Minor Amputation Risk

CLI Versus No CLI Increases Minor Amp Risk 2.8X

Data from the EUCLID Trial

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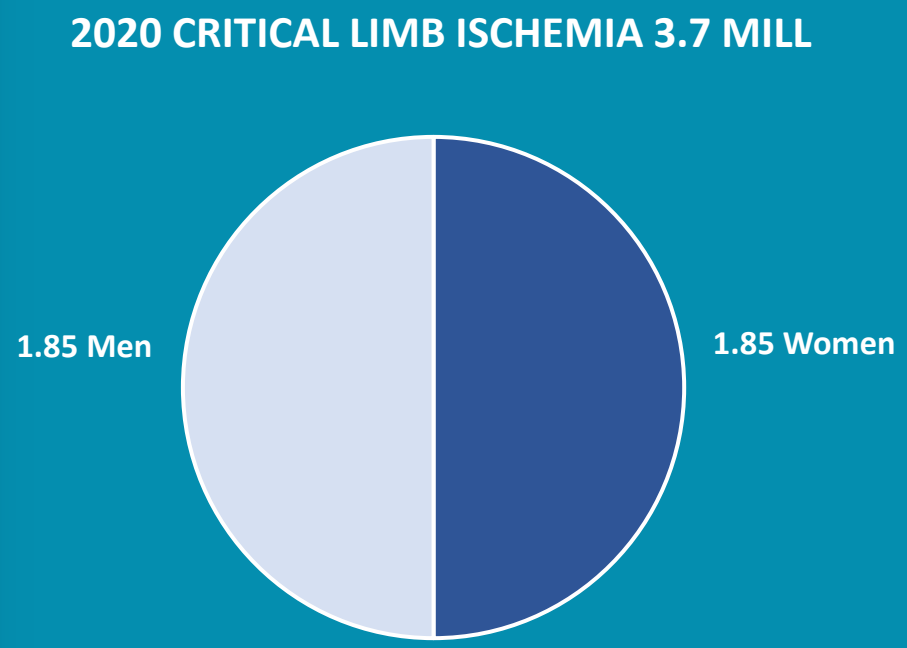
Source: Long CA. Circ Cardiovasc Qual Outcomes. 2020 Jul;13(7):e006399 and Govsyeyev N. J Vasc Surg. 2022 Feb;75(2):660-670.e3.

AMPUTATION LOTTERY

- Probability of Major Amputation Depends on Who You Are and Where You Live
- Amputation Varies by Race, Sex, Age, Socioeconomic Status, Hospital Volume, Geographic Location
- Medicare & Medicaid-More Likely Than Private, Medicaid Most Likely!

Source: Henry. J Vasc Surg 2011; 53(2): 330-9el , Baser. Vasc Dis Mgmt 2013; 10: E25-36, Goodney. Cardiovasc Qual Outcomes 2013; 5:94-102, Jones. J Am Coll Cardiol 2012; 59(13s1):E1670, Margolis, DJ. Diabetes Care. 2011; 34(11):2363-7 and Eslami. J Vasc Surg 2007; 45: 55-9.

WOMEN AND CRITICAL LIMB ISCHEMIA



- More Women than Men Present with CLI Initially
  - Reflects Higher Prevalence of AS/AT, Underdiagnosis & Lower Rates of Intervention at Earlier Stages
- Female Gender Significantly Increases Odds of AKA

Source: Yost ML. Cut Suppl US 2016 THE SAGE GROUP, Teodorescu VJ. J Vasc Surg 2013;57:18S-26S, Lefebvre KM. Vasc Med 2015 Feb;20(1):51-9. and Yost ML. CLI Global 2020, Mar. Available at: https://www.cliglobalsociety.org/resources/Compendium/2020/CLIG_0320.pdf.

CONCLUSIONS

- MULTIPLE FACTORS CONTRIBUTE TO HIGH CLI COSTS AND AMPUTATIONS
- DELAYED DIAGNOSIS & TREATMENT
- UNDERUTILIZATION OF DIAGNOSTIC TESING PRIOR TO AMPUTATION
- UNDERUTILIZATION OF REVASCULARIZATION PRIOR TO AMPUTATION
- LOW REFERRALS TO VASCULAR SPECIALISTS (IC, VS & IR)

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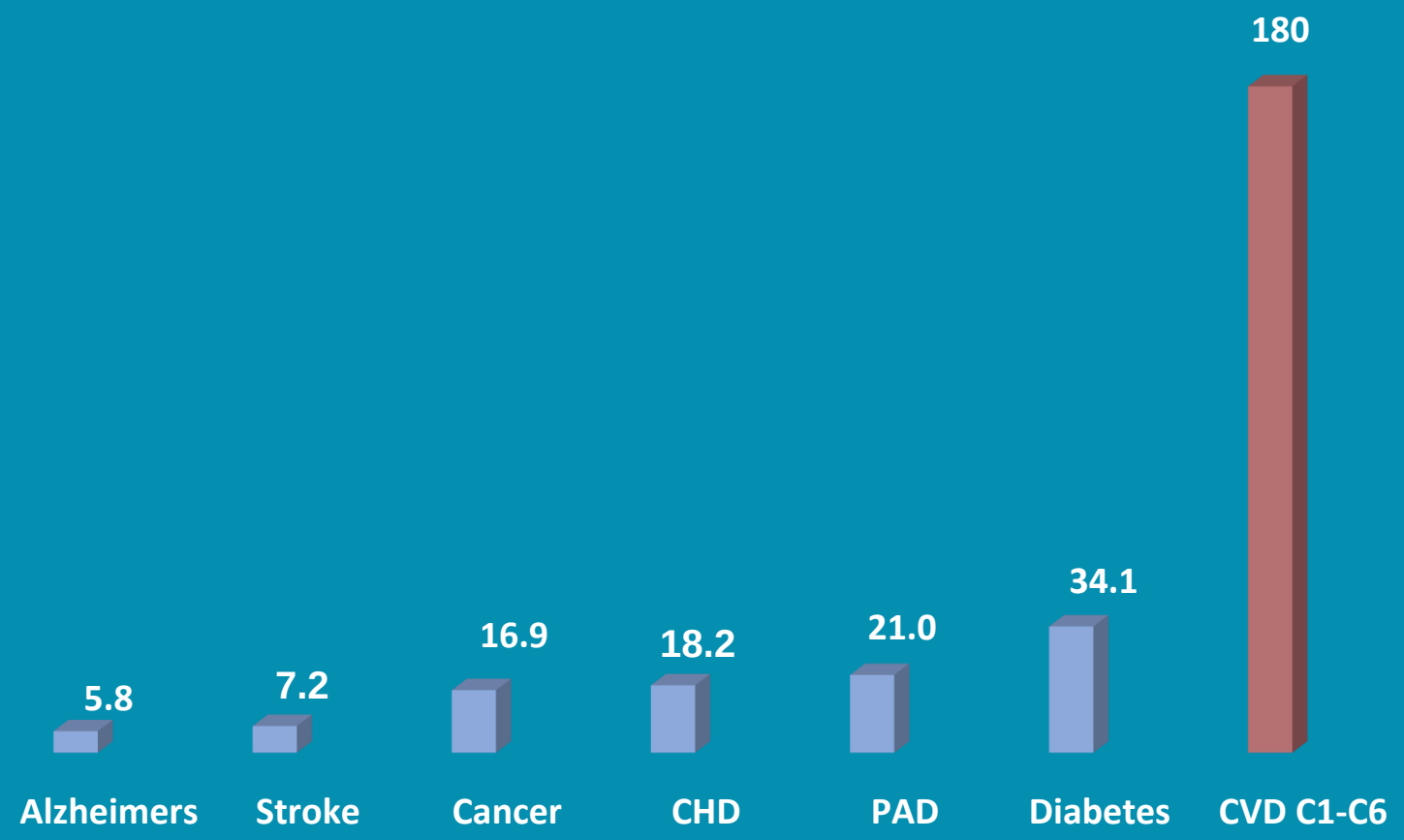
CONCLUSIONS/SOLUTIONS

- WE NEED TO SCREEN HIGH-RISK POPULATIONS TO IDENTIFY PAD/CLI AT EARLIER STAGES
- Early Referral to CLI specialists

2020 U.S. PREVALENCE OF SELECTED CHRONIC DISEASES

(Millions)



Source: Alzheimer's Association 2020, ACS Cancer facts and figures 2020, Virani SS. Circulation 2020;141:e139–e596, CDC National Diabetes Statistics report 2020, Yost ML. Vasc Dis Mgmt 2023 and Yost ML Chronic Venous Disease THE SAGE GROUP 2016.

VARICOSE VEINS (VV) C2

U.S. PREVALENCE 59 Million (≈70% Women)

SYMPTOMS: HEAVINESS, TIREDNESS, TENDERNESS, ITCHING, ACHING, PAIN AND SWELLING, BUT MAY BE ASYMPTOMATIC

NOT “JUST A COSMETIC PROBLEM” A MANIFESTATION OF CVI (C3-C6)

VV PROGRESS TO MORE SEVERE DISEASE (C3-C6) INCLUDING ULCERS

AT 2%-4% ANNUAL RATE (LOW RISK PTS)

5%-8% RATE (HIGH RISK PTS)

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Source: Yost ML, Chronic venous disease (CVD). THE SAGE GROUP; 2016, Mallick R. AM Health and Drug Benefits 2016;9(8):455-64, Lee AJ. J Vasc Surg Venous Lymphat Disord. 2015;3(1):18-26 and Pannier F. Phlebology 2012;27 Suppl1:23-26 Shepard AC. Phlebolymphology 2012;19(3):138-47.

VARICOSE VEINS AND DVT

VV INCREASE THE RISK OF DVT
BY 5X-7X IN 2 STUDIES

VV INCREASE THE RISK OF ULCERS IN PTS PATIENTS
BY 3.2X (RIETE Registry)

Source: Chang SL. JAMA 2018;319(8):807-17, Müller-Bühl U. Vasa. 2012;41:360–365 and Galanaud JP. Thromb Haemost 2018 Feb;118(2):320-328..

VENOUS ULCERS

ANNUAL INCIDENCE

1-2+ MILLION

Rate 0.4%-1.7% in Population Ages 18+

INCIDENCE INCREASES W/ AGE

Rate 1.2%-2.2% Age ≥ 65

Vs 0.5% Age 18-64

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Source: Fowkes FGR. Angiology 2001;52(Suppl 1):S5-S15, Rice JB. J Med Econ 2014; 17(5):347-56, Margolis DJ. J AM Acad Dermatol 2002;46(3):381-6 and Yost ML, Chronic venous disease (CVD). THE SAGE GROUP; 2016.

VENOUS ULCERS - POOR HEALING RATES

6 MO	35%-50% UNHEALED
2 YEARS	20% UNHEALED

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Source: Hankin CS. J Manag Care Pharm 2012;18(5):375-84 and Ma H. J Vasc Surg 2014;2:355-61.

VENOUS ULCERS—HIGHLY RECURRENT

1-YEAR RECURRENCE

20%-40%

5-YEAR RECURRENCE

50%

RISK FACTORS FOR RECURRENCE

Type of Therapy— Compression Alone w/o Surgical Correction of Venous Insufficiency

Longer Ulcer Healing Time

Location of Reflux—DVI* Present Increases Risk 2.4X

Presence of PAD or RA**

*DVI = Deep Venous Insufficiency **PAD = Peripheral Artery Disease, RA =Rheumatoid Arthritis

Yost ML. Chronic venous disease (CVD). Beaufort, SC. THE SAGE GROUP; 2016

VENOUS ULCERS REDUCE QUALITY OF LIFE

- Ulcer Treatment Burdensome & Time Consuming
- Chronic Pain: Sleep Loss
- Reduced Mobility 81%-93%: Problems Daily Living, Self Care, Inability to Work & Inability to Exercise
- Odor, Swelling, Discharge
- Negative Emotional Impact: Fear, Depression, Social Isolation
- Physical Impairment Ranked Similar to CHF and Chronic Lung Disease

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Source: Phillips T. J Am Acad Dermatol 1994;31(1):49-53, Sen CK. Wound Repair Regen 2009;17(6):763-71, Heber OR. Health Qual Life Outcomes 2007;5:44, Maddox J. Nursing Stand 2012;26(38): 42-49 and Carradice D. Br J Surg. 2011Aug;98(8):1089-98.