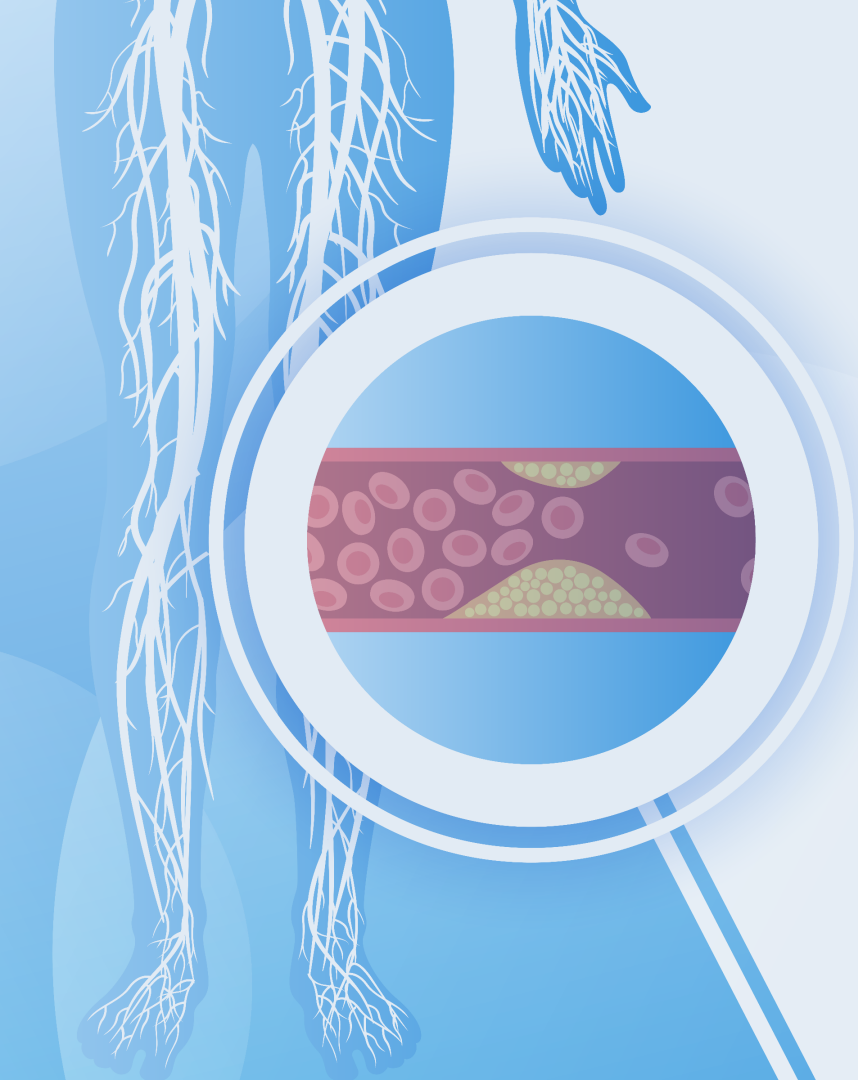
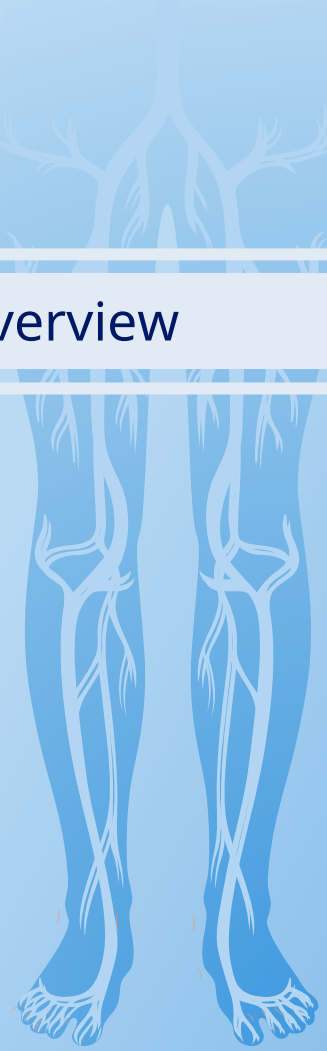


Peripheral Artery Disease (PAD) in T2D

Core Science Deck

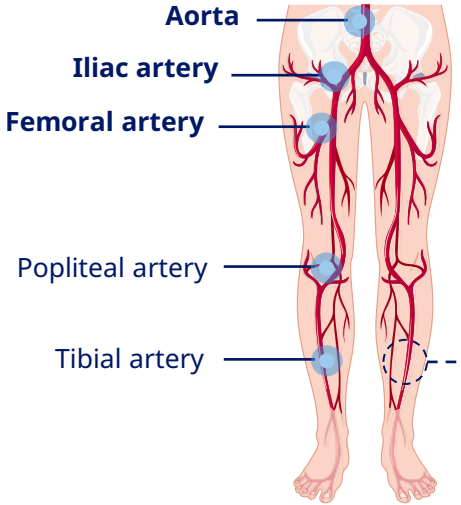
Overview



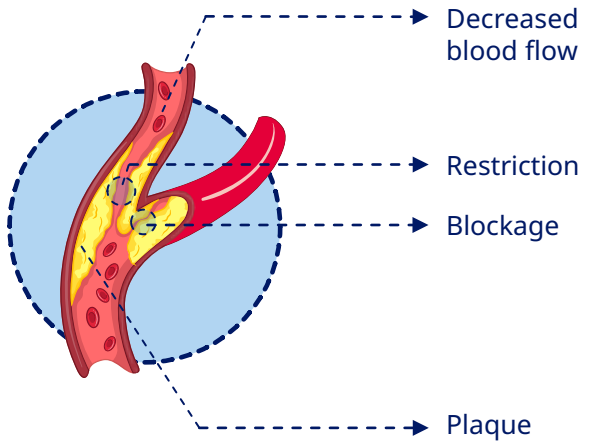
What is peripheral artery disease?

Peripheral artery disease is the **narrowing**
and/or **occlusion** of arteries outside of the heart and brain mainly attributed to atherosclerosis[1]

PAD affects lower extremities more commonly than upper extremities[2]



PAD is predominantly caused by
atherosclerosis (>90% of cases)[3]



PAD, peripheral artery disease. ASCVD- Atherosclerotic cardiovascular disease, a leading cause of mortality and morbidity globally, is caused by the build-up of plaque in the arterial walls and comprise conditions such as Coronory Heart disease, Cerebrovascular disease , PAD, aortic atherosclerotic disease [5]

1. Soyoye DO et al. World J Diabetes 2021;12:827–38; 2. Zemaitis M et al. StatPearls Publishing LLC. Available at: https://www.ncbi.nlm.nih.gov/books/NBK430745/ Accessed December 2023;3. Shu J, Santulli G. Atherosclerosis 2018;275:379–81.

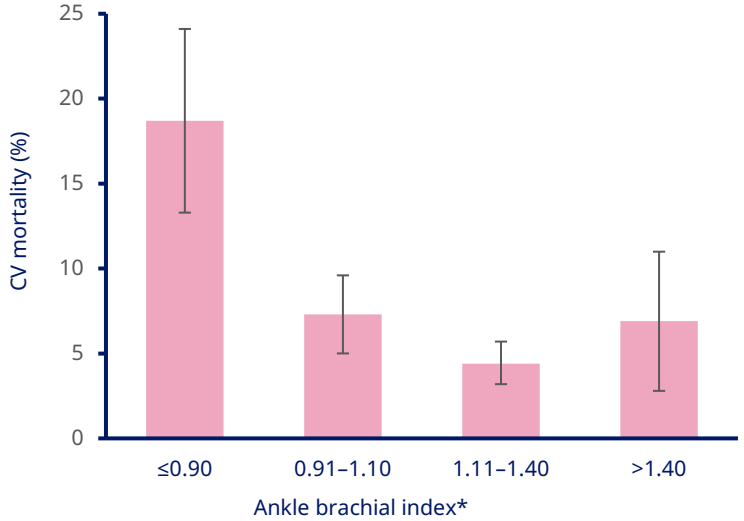
Global prevalence of PAD is high

- PAD affects **12–14%** of the general population[2]
  - However, PAD remains **underdiagnosed** compared with other CVD conditions,[3] making absolute numbers difficult to obtain
- Prevalence increases with age, affecting **up to 20%** of those **aged ≥60 years** and **nearly 50%** of those aged **≥85 years** in USA[4]
  - Incidence doubles with each advancing decade of life[3]
  - 72% increase in prevalence from 1990 to 2019[5]
- PAD affects women as often or more as men[3]
  - IC is more common in men than in women, who are more likely to present as asymptomatic or with atypical symptoms[3]

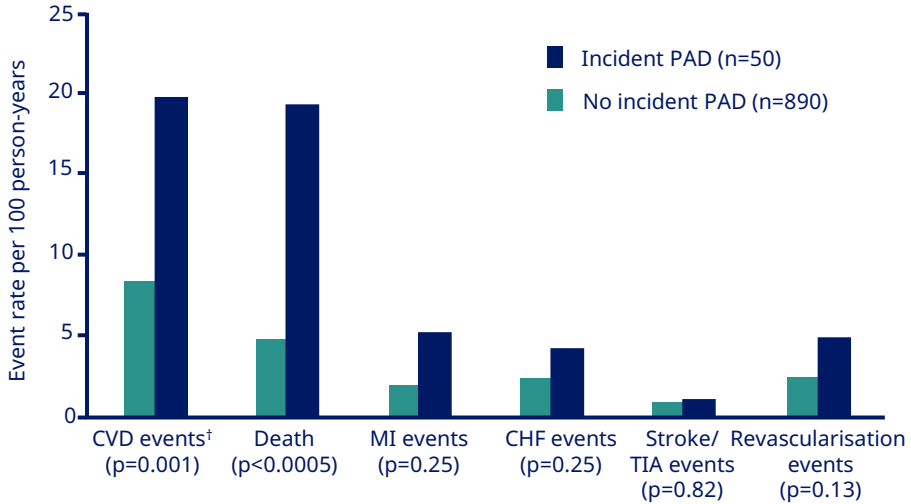
**Estimated global prevalence of PAD in people aged ≥25 years in 2015, according to a systematic review of 118 articles from 33 countries.*
CVD, cardiovascular disease; IC, intermittent claudication; PAD, peripheral artery disease.
1. Song P et al. Lancet Glob Health 2019;7:e1020–30; 2. Shammas NW. Vasc Health Risk Manag 2007;3:229–34; 3. Pabon M et al. Circ Res 2022;130:496–511;
4. Firnhaber JM, Powell CS. Am Fam Physician 2019;99:362–9; 5. Eid MA et al. J Vasc Surg 2023;77:1119–26.e1;

People with PAD have a higher risk of CV events vs those without PAD

Meta-analysis of male participants (N=24,955) from 16 studies showing CV mortality by PAD severity[1]



Prospective cohort study of people with stable CAD ± incident PAD over a 7.2-year follow-up period[2]



*PAD, peripheral artery disease ; CV, Cardiovascular; *Ankle brachial index is a diagnostic tool for PAD where a lower value indicates a more severe disease state. Error bars represent 95% confidence intervals.*
†The primary outcome (CVD events) included a composite of events: death, MI, CHF, stroke, TIA and coronary revascularisation. Secondary outcomes included those events assessed individually.
CAD, coronary artery disease; CHF, congestive heart failure; CV, cardiovascular; CVD, cardiovascular disease; MI, myocardial infarction; PAD, peripheral arterial disease; TIA, transient ischaemic attack.
1. Ankle Brachial Index Collaboration. JAMA 2008;300:197–208; 2. Grenon SM et al. Vasc Med 2013;18:176–84.

PAD is a major economic burden associated with substantial healthcare costs

The total US PAD-related annualised healthcare cost in the symptomatic PAD patient population was **$4,006** per patient[1]

PAD prevalence increased by 13.1% in high-income countries and **28.7% in low- and middle-income** countries between 2000 and 2010[2]

The number of **annual CV events are higher for people with PAD compared with CAD**, leading to greater hospitalisation rates and higher direct costs[1]

Total annual costs associated with vascular- related hospitalizations in PAD patients were estimated to be more than $21 billion between 2004 and 2010.[3]

CAD, coronary artery disease; CV, cardiovascular; PAD, peripheral artery disease.

1. . Bauersachs R et al. Cardiovasc Ther 2019;8295054. 2. Fowkes FG et al. Lancet 2013;382:1329–40; 3. Mahoney, Elizabeth M., et al. Circulation: Cardiovascular Quality and Outcomes 3.6 (2010): 642-651.

Symptoms and clinical manifestations

Spectrum of PAD symptoms

Increasing severity & risk of CV event or amputation

Asymptomatic PAD

No obvious symptoms[1]

PAD can be detected with blood pressure and imaging tests[1,2]

It has been estimated that 20–50% of people with PAD are asymptomatic[1]

Intermittent claudication and/or atypical leg pain symptoms

Exercise-induced pain in the legs and/or buttocks that goes away with rest[3]

Atypical leg symptoms occur in 40–50% of cases;[1] may be confused with lower extremity arthritis or degenerative spinal disease[4]

CLI*

Exhibits the following:[5]

1. Ischemic rest pain or ulcer necrosis
2. Limited to chronic ischemia
3. Limb-threatening ischemia usually requiring major amputation ≤6 months if blood flow does not improve
4. Objective ischemia (ankle pressure ≤50–70 mmHg,† toe pressure ≤30–50 mmHg† and transcutaneous oxygen pressure ≤30–50 Torr)

ALI*

Sudden onset (<2 weeks), claudication deteriorates; severe hypoperfusion characterized by '6 Ps':[5]

1. Pain at rest
2. Pallor
3. Pulseless
4. 'Perishingly' cold
5. Paresthesia
6. Paralysis

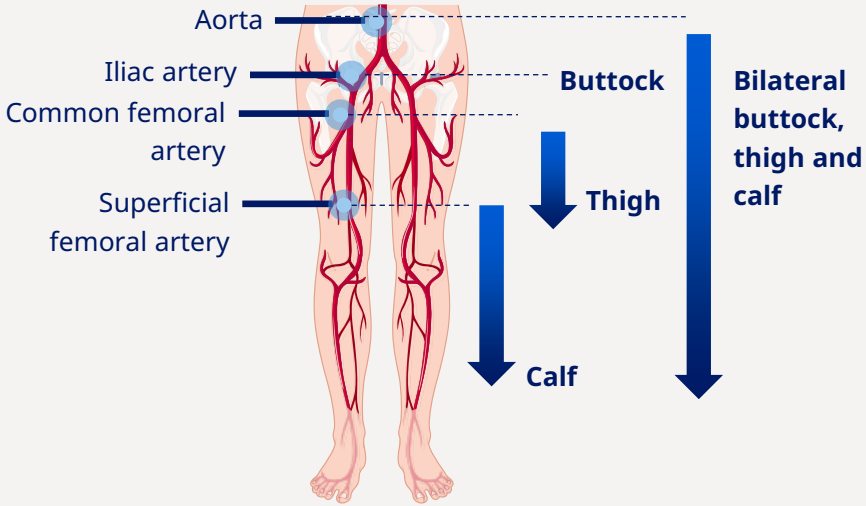
*PAD, peripheral artery disease, CV- Cardiovascular *Critical limb ischaemia is also known as chronic limb-threatening ischaemia.[4,] †Ankle pressure and toe pressure intervals measured at either signs of tissue loss or symptoms at rest pain. ALI, acute limb ischaemia; CLI/CLTI, critical limb ischaemia/chronic limb-threatening ischaemia; CV, cardiovascular; PAD, peripheral arterial disease.*

1. Olin JW, Sealove BA. Mayo Clin Proc 2010;85:678–92; 2. Aboyans V et al. Eur J Vasc Endovasc Surg 2018;55:305–68; .3. Criqui MH et al. Circulation 2021;144:e171–91; 4. Gerhard-Herman MD et al. Circulation 2017;135:e686–725; .5 Norgren L et al. Eur J Vasc Endovasc Surg 2007;33(Suppl 1):S1–75

Intermittent claudication is the most common symptom of PAD[1]

- Early symptom experienced by 10–35% of people with PAD[3]
  - Characterized by pain in lower extremities (e.g. calf) that develops with walking or other exertion[1,2,4]
  - Resolves within 10 minutes of rest[4]
- Prevalence of PAD is similar between men and women;1 however, incidence of IC is higher in men than women at all ages[5]

The site of pain can indicate the site of PAD[5]



PAD, peripheral artery disease. IC- intermittent claudication

1. Boyko EJ et al. Peripheral Arterial Disease, Foot Ulcers, Lower Extremity Amputations, and Diabetes. In: Cowie CC et al., editors. Diabetes in America. 3rd edition. 2018. Available at: https://www.ncbi.nlm.nih.gov/books/NBK567977/ Accessed January 2024; 2. Criqui MH et al. Circulation 2021;144:e171–91 3. Olin JW, Sealove BA. Mayo Clin Proc 2010;85:678–92; 4. Criqui MH, Aboyans V. Circ Res 2015;116:1509–26;
5. Kannel et al., 1970 available at https://www.ahajournals.org/doi/pdf/10.1161/01.CIR.41.5.875

Risk factors for PAD

Modifiable risk factors

- **Diabetes**[1,2,4]
  Can double the risk of PAD
- **Obesity/ overweight**[2,4]
- **Hypertension**[1,2,4]
  Association more evident for SBP than DBP[1]
- **High homocysteine levels**[3]
- **Smoking**[2,4]
  Risk is higher in current vs former smokers
- **Dyslipidemia**[2,4]
  Including high LDL-C and triglycerides
- **Physical inactivity**[1]
  Inversely related to physical activity
- **Inflammation**[3,4]
  As assessed by hs-CRP

Non-modifiable risk factors

- **Age**[2,4]
  Risk increases with age
- **Race and ethnicity**[1,4]
  Black individuals have greater risk for PAD vs White, Hispanic or Asian
- **Family history/genetic factors**[3]
  Greatest risk in those with family history of PAD, CVD or stroke

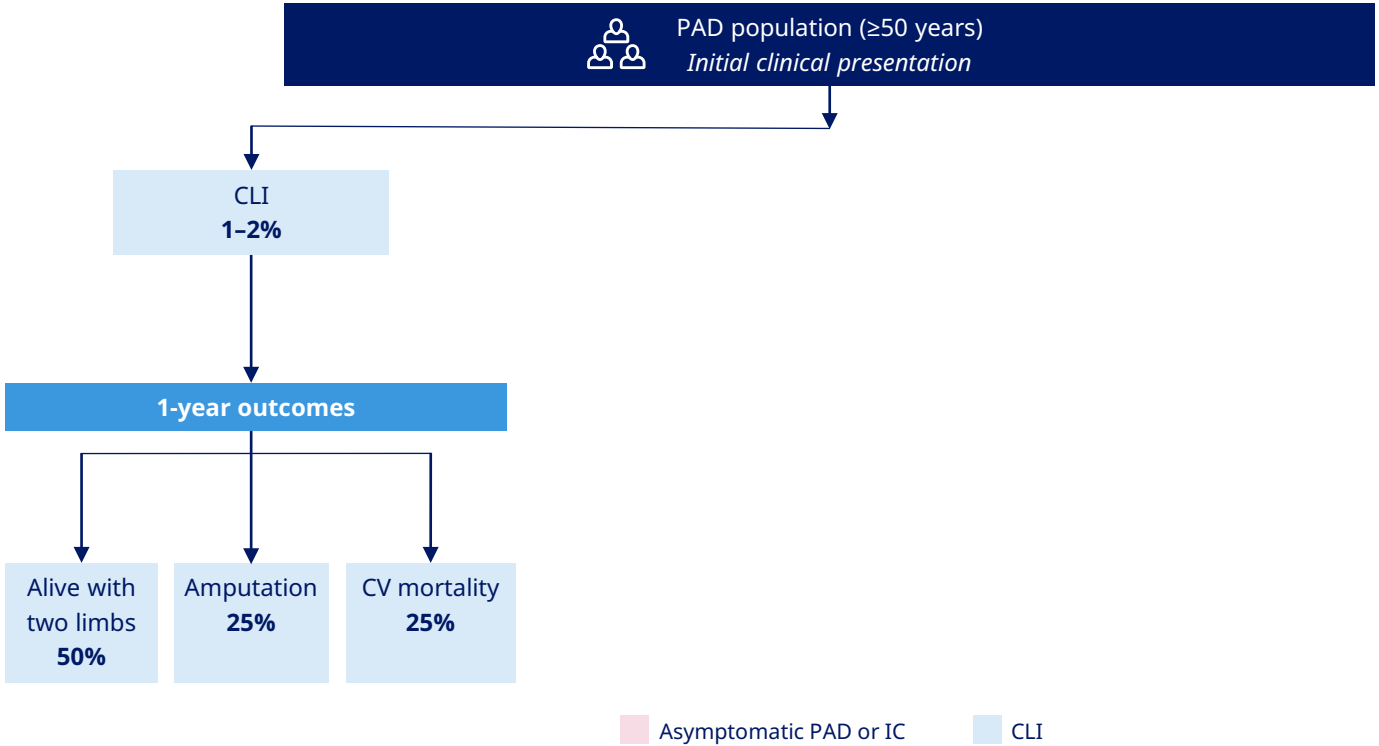
Other risk factors

- Socioeconomic and/or psychosocial factors[3]
- CKD and renal impairment[2,3]
- Heavy metals/ radiation/injury[1]

PAD, peripheral artery disease CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; hs-CRP, high sensitivity-C-reactive protein; LDL-C, low-density lipoprotein-cholesterol; PAD, peripheral arterial disease; SBP, systolic blood pressure

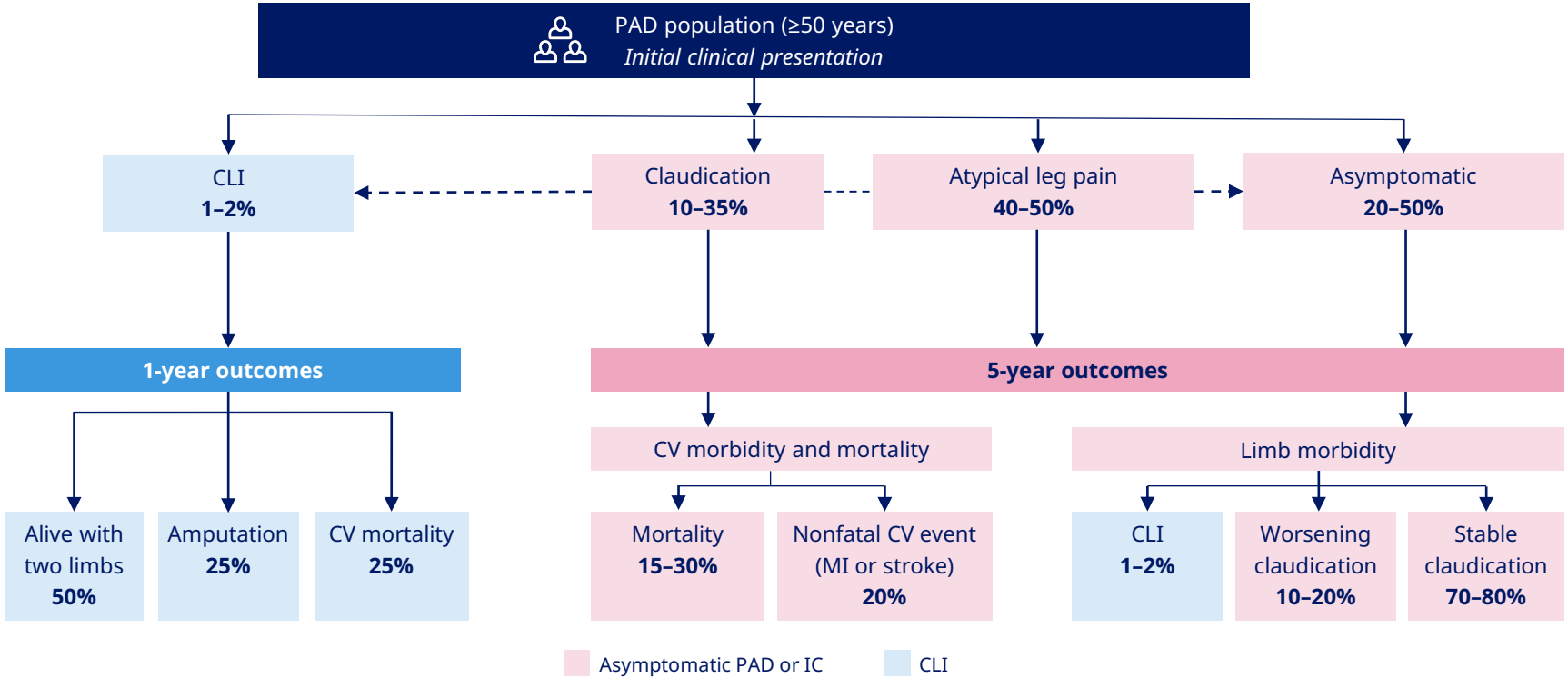
1. Criqui MH et al. Circulation 2021;144:e171–91; 2. Song P et al. Lancet Glob Health 2019;7:e1020–30; 3. Criqui MH, Aboyans V. Circ Res 2015;116:1509–26. 4 . Olin JW, Sealove BA. Mayo Clin Proc 2010;85:678–92

Natural history of PAD: typical disease progression



PAD, peripheral arterial disease ; CV, Cardiovascular; CLI/CLTI, critical limb ischaemia/chronic limb-threatening ischaemia; CV, cardiovascular; IC, intermittent claudication; MI, myocardial infarction; PAD, peripheral arterial disease. Olin JW, Sealove BA. Mayo Clin Proc 2010;85:678–92.

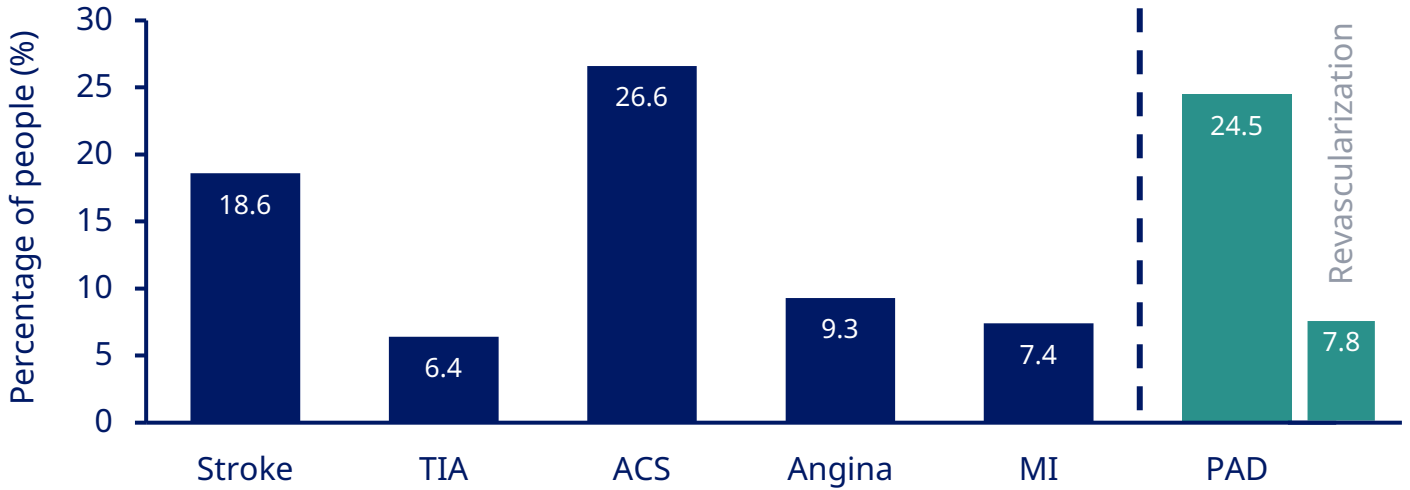
Natural history of PAD: typical disease progression



PAD, peripheral artery disease ; CV, Cardiovascular; CLI/CLTI, critical limb ischaemia/chronic limb-threatening ischaemia; CV, cardiovascular; IC, intermittent claudication; MI, myocardial infarction; PAD, peripheral arterial disease. Olin JW, Sealove BA. Mayo Clin Proc 2010;85:678–92.

People with diabetes have an increased risk of ASCVD, including PAD

RWE database study of people with T2D in the USA (N=1,202,596), of which 45.2% had established ASCVD

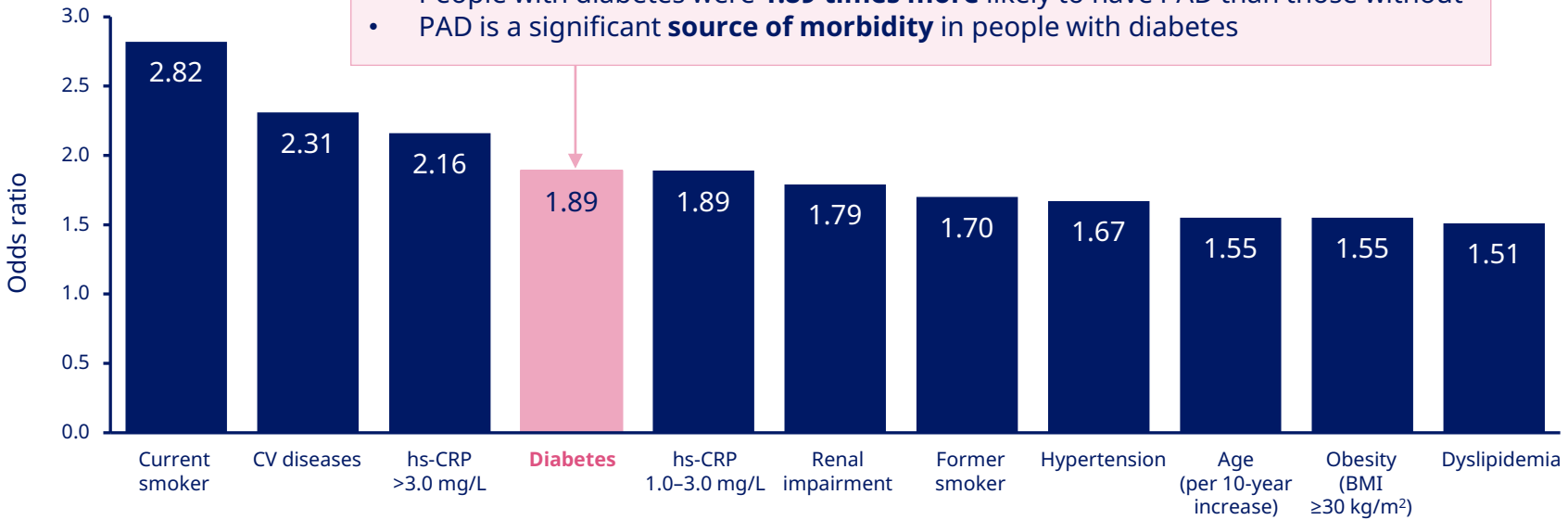


*Revascularisation not included in any vascular bed category for this analysis. PAD presumed to be of atherosclerotic origin. *ASCVD as defined by 2017 American Diabetes Association guidelines.*
PAD, peripheral artery disease ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; MI, myocardial infarction; PAD, peripheral arterial disease; RWE, real-world evidence; TIA, transient ischaemic attack.
1. Weng W et al. Clin Diabetes Endocrinol 2020;6:5;

Diabetes is one of the main risk factors of PAD

Worldwide estimates from a meta-analysis of **118 studies from low- and high-income countries**

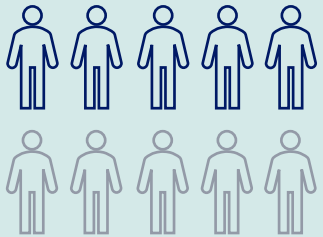
- People with diabetes were **1.89 times more** likely to have PAD than those without
- PAD is a significant **source of morbidity** in people with diabetes



BMI, body mass index; CV, cardiovascular; hs-CRP, high-sensitivity C-reactive protein; PAD, peripheral artery disease.
Song P et al. Lancet Glob Health 2019;7:e1020–30.

Prevalence of PAD is higher in people with T2D than in those without

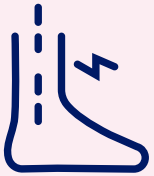
The prevalence of PAD is up to twice as high in people with diabetes as in the general population, and the prevalence of concomitant PAD in people with diabetes is over **50%** [1,2]



Glucose intolerance is associated with a >20% prevalence of an abnormal ankle brachial index* relative to 7% in those with normal glucose tolerance[2]

>20%

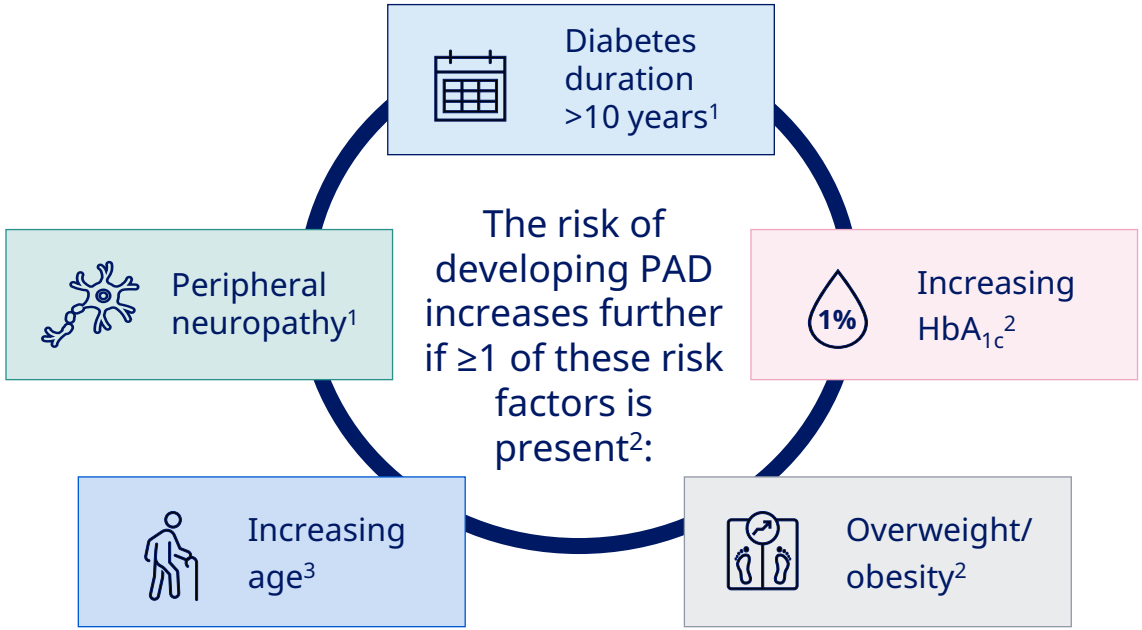
Approximately 50–70% of people with chronic limb-threatening ischemia have diabetes[3]



50–70%

**Ankle brachial index is a diagnostic tool for PAD where a lower value indicates a more severe disease state.*
CV, cardiovascular; PAD, peripheral artery disease.
1. Soyoye DO et al. World J Diabetes 2021;12:827–38; 2. Thiruvoipati T et al. World J Diabetes 2015;6:961–69; 3. Marx N et al. Eur Heart J 2023:44:4043–140.

PAD Risk Factors within the T2D Population



Each 1% increase in HbA_{1c} is associated with a **nearly 30% increase** in the risk of developing PAD[4]

PAD, peripheral artery disease.

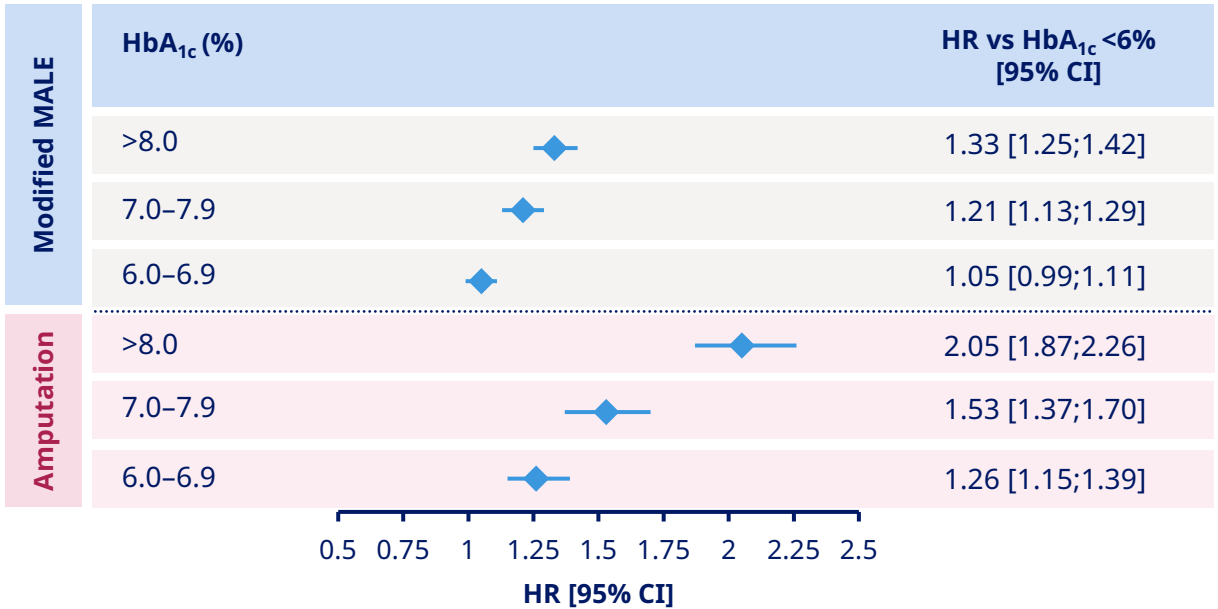
1. Piliponienė L et al. Medicina 2021;57:1380; 2. American Heart Association. Peripheral Artery Disease and Diabetes, 2021. Available at: https://www.heart.org/en/health-topics/diabetes/diabetes-complications-and-risks/peripheral-artery-disease--diabetes Accessed January 2024; 3. Thiruvoipati T et al. World J Diabetes 2015;6:961–9. 4. Heikkinen et al. "Diabetes care for patients with peripheral arterial disease." European Journal of Vascular and Endovascular Surgery 33.5 (2007): 583-591.

Poor glycemic control associated with worse outcomes in PAD patients

Database study of people undergoing revascularization for PAD (N=26,799)

59.9%
had preop-diabetes

33.2%
had high HbA_{1c} levels (>7%)



Modified MALE was a composite incident amputation (mid/hind-foot, below and above knee)/repeat revascularisation.
CI, confidence interval; HR, hazard ratio; MALE, major adverse limb events; PAD, peripheral artery disease.
Arya S et al. J Vasc Surg 2018;67:217–28.

There are several unmet needs for people with PAD and T2D

Under-diagnosis	People may be **asymptomatic** due to **altered pain perception** from comorbidities of diabetes, such as peripheral neuropathy[1–3]	Screening tools may be underutilized[1]	**50%** of people >50 years old were not aware that **diabetes is a risk factor** for PAD[4]	People with diabetes **lack awareness** of PAD symptoms[1]
Poor prognosis	People with diabetes have **worse PAD outcomes** than those without (mortality and amputation rates)[5]	PAD+T2D patients are **~5x likely** to have limb amputations vs PAD patients without T2D[5] and have **~3-4x** higher mortality and **higher risk of stroke and heart failure** compared to either condition alone[5]	**Diabetes negatively affects neovascularization** of the limb in PAD[6]	
Limited treatment options	**Data on efficacy** of glucose-lowering treatments in PAD and T2D **are limited** and there is **need** for disease-modifying glucose-lowering **treatment options** for people with PAD and T2D[7,8]	T2D is associated with **greater severity** and more diffuse PAD relative to nondiabetics. It also correlates **to greater risk of mortality** and **impaired quality of life**.[3]		

PAD, peripheral artery disease.

1. Akalu Y, Birhan A. J Diabetes Res 2020:9419413; 2. Sunner SS et al. CJC Open 2021;3:936–49; 3. Thiruvoipati T et al. World J Diabetes 2015;6:961–9; 4. Hirsch AT et al. Circulation 2007;116:2086–94;
5. Abramson BL et al. Can J Cardiol 2022;38:560–87; 6. Singh MV, Dokun AO. Front Cardiovasc Med 2023;10:1148040; 7. Rannelli L et al. Can J Gen Intern Med 2019;14:13–7; 8. Chatterjee S et al. Curr Probl Cardiol 2019;44:207–22.

Recommended diagnostic testing for people with suspected PAD

2016 AHA/ACC,[1] 2023 ESC[2] and 2024 ESVS[3] guidelines

ABI for diagnosing PAD

- Resting ABI is recommended to establish a PAD diagnosis in people where PAD is suspected[1]

Physiological testing

- TBI should be measured to diagnose people when ABI is considered high or in people with clinical suspicion of PAD, despite a normal ABI*[1,3]
- People with exertional non-joint-related leg symptoms[2] and a normal ABI (>0.90 and ≤1.40)[1,3] or a normal ABI at rest,[3] should undergo exercise treadmill ABI testing to evaluate PAD[1–3]

Imaging for anatomic assessment

- Duplex ultrasound, CTA or MRA of the lower extremities is useful to diagnose anatomic location and severity of stenosis when revascularization is considered[1,2]
- Invasive angiography is useful for people with CLI when revascularization is considered[1]

**Defined as >1.3 or 1.4 across the literature. Information taken from the strongest class of recommendation and levels of evidence. ABI, ankle brachial index; ACC, American College of Cardiology; AHA, American Heart Association; CLI/CLTI, critical limb ischaemia/chronic limb-threatening ischaemia; CTA, computed tomography angiography; ESC, European Society of Cardiology; ESVS, European Society for Vascular Surgery; MRA, magnetic resonance angiography; PAD, peripheral artery disease. TBI, Toe-brachial index1. Gerhard-Herman MD et al. Circulation 2017;135:e686–725; 2. Marx N et al. Eur Heart J 2023:44:4043–140; 3. Nordanstig J et al. Eur J Vasc Endovasc Surg 2024:67:9–96.*

ADA STANDARDS OF MEDICAL CARE IN DIABETES – 2024

Peripheral Artery Disease (PAD)

ADA recommends screening for asymptomatic PAD using ankle brachial index in people with diabetes at high risk for PAD, including any of the following:

age ≥ 50 years

diabetes with duration ≥ 10 years

comorbid microvascular disease

clinical evidence of foot complications

or any end-organ damage from diabetes.

Initial screening for PAD should include:

- Assessment of lower-extremity pulses, capillary refill time
- Rubor on dependency
- Pallor on elevation, and venous filling time
- Individuals with a history of leg fatigue, claudication, and rest pain relieved with dependency or decreased or absent pedal pulses should be referred for ankle-brachial index with toe pressures and for further vascular assessment as appropriate

American Diabetes Association (ADA). Diabetes Care 2024;47(Supplement_1)

Early-stage PAD Management

Non-pharmacological measures for CV risk factor management in all people with PAD[1,2]

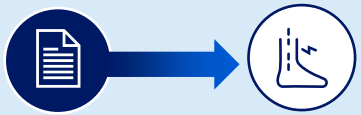
Pharmacotherapy targeting individual risk factors	
Therapy	**Options**
Diabetes management for glycemic control that also reduce CV risk[2,3]	SGLT2i[3] and GLP-1RAs[3]
Lipid-lowering drugs to improve CV outcomes[4]	Statin therapy[5], ezetimibe[5] and PCSK9 inhibitors[5]
Antiplatelet therapy to manage aggregation of platelets and increased adhesions[4]. Antiplatelet and statin agents are customized to additional risk factors, such as whether the patient also has diabetes mellitus or hypertension[1].	Aspirin[5], clopidogrel[5] and ticagrelor[5]
Anticoagulants to reduce risk of thrombi-dependant complications[4] should be considered for individuals with stable coronary and/or peripheral artery disease (PAD) and low bleeding risk to prevent major adverse limb and cardiovascular events[1].	Heparin[3] and rivaroxaban[5]
Peripheral vasodilators/viscosity reductors to reduce symptoms of peripheral ischaemia and claudication[4]	Cilostazol (although infrequently used owing to heart failure contraindications and subtle benefits)[4]
Blood pressure management to reduce CV risk while maintaining limb perfusion[4]	ACE inhibitors and angiotensin receptor blockers[4]

ACE, angiotensin-converting enzyme; CV, cardiovascular; GLP-1RA, glucagon-like peptide-1 receptor agonist; PAD, peripheral artery disease; PCSK9, proprotein convertase subtilisin/kexin type 9; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

1. American Heart Association. Peripheral Artery Disease and Diabetes, 2021. Available at https://www.heart.org/en/health-topics/peripheral-artery-disease/prevention-and-treatment-of-pad; 2.Aboyans V et al. Eur Heart J 2018;39:763–816; 3. Nordanstig J et al. Eur J Vasc Endovasc Surg 2024;67:9–96.; 4. Abramson BL et al. Can J Cardiol 2022;38:56087; 5. Bevan GH, White Solaru KT. Arterioscler Thromb Vasc Biol 2020;40:541–53.

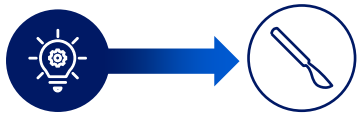
Undertreatment and poor outcomes are unmet needs in people with PAD and T2D

A 2021 Scientific Statement from the American Heart Association



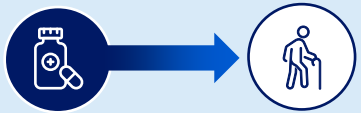
Underutilization of evidence-based prevention measures

Despite guidelines recommending antiplatelet therapy, statins, antihypertensive agents, glycaemic control, smoking cessation and supervised exercise therapy, people with PAD remain **undertreated** and **better adherence** is needed



Improvement in diagnosis is needed to improve outcomes

Increasing awareness of PAD, including the diagnosis, clinical manifestation, and complications, is **critical to improving overall outcomes** among this population



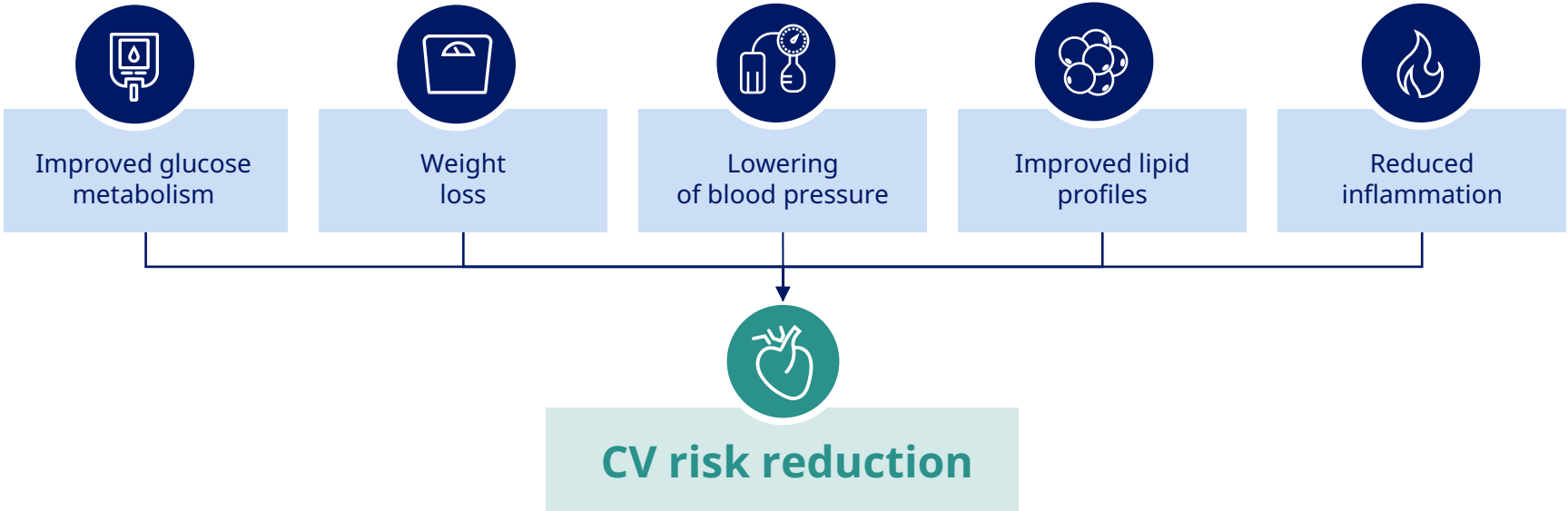
Need for better control of symptoms

RCTs investigating the effects of medical therapies (in particular, glucose-lowering) on **functional capacity and walking distance**, in people with PAD and T2D are needed

AHA, American Heart Association; PAD, peripheral artery disease; RCT, randomised controlled trial.
Criqui MH et al. Circulation 2021;144:e171–91.

GLP-1RAs have several effects that support the rationale for use in people with PAD and T2D

Potential benefits



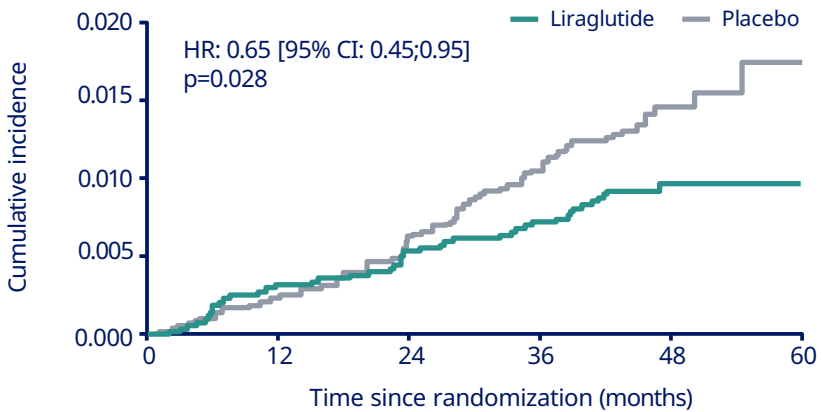
CV, cardiovascular; GLP-1RA, glucagon-like peptide-1 receptor against; PAD, peripheral artery disease.
Drucker DJ. Cell Metab 2016;24:15–30.

Liraglutide (1.8 mg) significantly reduced the risk of amputations vs placebo

Post hoc analyses of LEADER

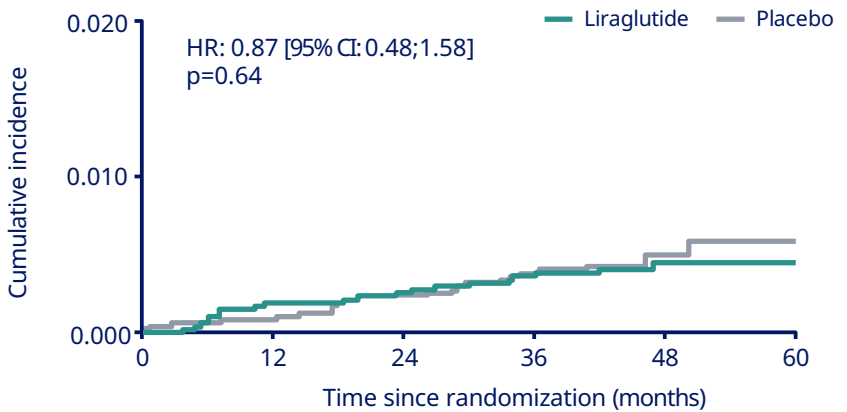
Proportion of people with T2D and high CV risk experiencing amputation or peripheral revascularization

Amputations



Liraglutide	4,668	4,585	4,482	4,353	1,713	10
Placebo	4,672	4,590	4,451	4,299	1,691	15

Peripheral revascularization



	4,668	4,591	4,496	4,369	1,719	10
	4,672	4,597	4,468	4,323	1,699	15

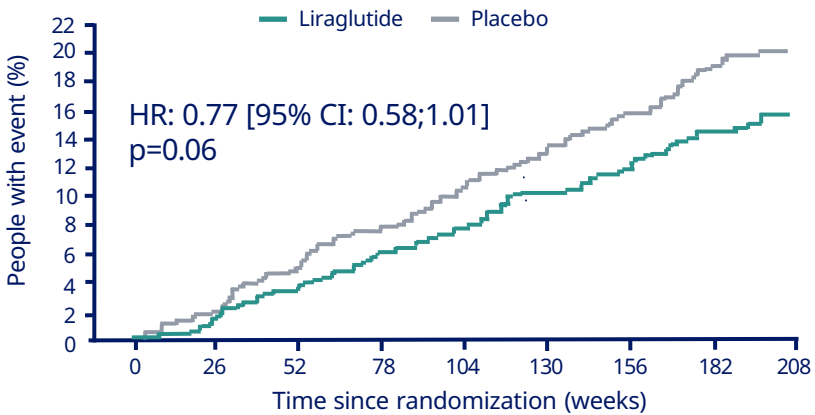
CI, confidence interval; CV, cardiovascular; HR, hazard ratio; PAD, peripheral artery disease.

Dhatariya K et al. Diabetes Care 2018;41:2229–35.

Liraglutide (1.8 mg) and OW s.c. semaglutide (0.5 mg,1.0 mg) numerically reduced the risk of MACE in people with PAD and T2D vs placebo

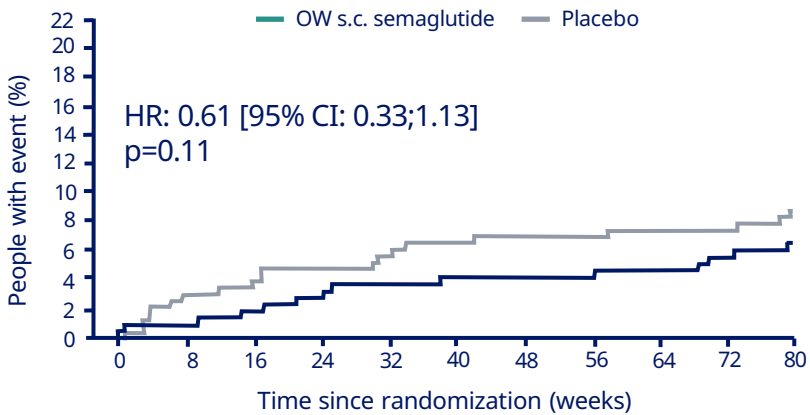
Proportion of people with T2D and PAD at baseline experiencing MACE over time

LEADER



Liraglutide	573	562	551	533	519	500	491	473	166
Placebo	611	599	574	555	535	518	499	480	167

SUSTAIN 6



Semaglutide	230	224	219	218	216	212
Placebo	230	222	216	213	211	207

Analysis from time to randomisation to first EAC-confirmed MACE. Data are without adjustment for baseline variables. All randomised people were included in the analyses from the time of randomisation until death or end of follow-up. CI, confidence interval; EAC, event adjudication committee; HR, hazard ratio; MACE, major adverse cardiovascular events; OW, once-weekly; PAD, peripheral artery disease; s.c., subcutaneous.

Verma S et al. Diabetes Obes Metab 2022;24:1288–99.

STRIDE: Effects of OW s.c semaglutide (1.0 mg) on Functional Capacity in Patients With T2D and Peripheral Artery Disease: Trial design

792 people with T2D

- Age ≥18 years
- T2D diagnosis ≥180 days prior to screening
- HbA_{1c} ≤10%
- PAD with intermittent claudication (Fontaine stage IIa) ≥3 months and:
  - Pain-free walking distance >200 m
  - Maximum walking distance ≤600 m on a graded treadmill test
  - ABI ≤0.90 or TBI ≤0.70

Trial information

- **Trial objective:** to compare the effect of OW s.c. semaglutide on functional capacity in terms of maximum walking distance in people with PAD and T2D, vs placebo
- Randomized, phase 3b, double-blind, parallel-group trial

Primary endpoint

- Change from baseline in maximum walking distance on a constant load treadmill test† at week 52

**OW s.c. semaglutide dose escalation from starting dose of 0.25 mg; doubled every 4 weeks until trial maintenance dose achieved. †Treadmill at constant speed and incline (3.2 km/h, 12%).*
ABI, ankle brachial index; OW, once-weekly; PAD, peripheral artery disease; s.c., subcutaneous; SoC, standard of care; TBI, toe brachial index; VascuQol-6, Vascular Quality of Life Questionnaire-6.
ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT04560998. Accessed May 2023; Data on file.

Summary

- PAD is the occlusion of arteries outside of the heart and brain, often in the lower extremities, predominantly caused by atherosclerosis
- PAD, may be asymptomatic (especially early-stage PAD), or manifest as intermittent claudication, or acute or CLI
- PAD is associated with an increased risk of CV events and mortality, poor QoL, and is a major economic burden
- Low awareness, underdiagnosis and undertreatment are major unmet needs for people with PAD
- People with T2D have a higher risk of developing PAD and often have worse outcomes than people without T2D
- There are currently no disease-modifying glucose-lowering treatment options for people with PAD and T2D

CLI/CLTI, critical limb ischaemia/chronic limb-threatening ischaemia; CV, cardiovascular; GLP-1RA, glucagon-like peptide-1 receptor agonist; OW, once-weekly; PAD, peripheral artery disease; QoL, quality of life, s.c., subcutaneous.

Different tests can be used to diagnose PAD[1–4]

Physiological testing

- **Ankle brachial index (ABI)**
- **Toe brachial index (TBI)**
- **Segmental pressure measurements**
- **Pulse volume recording**

Functional capacity testing

Walking tests

- 6-minute walking test
- Constant load test
- Graded exercise test

Short physical performance battery

- Sit & stand test
- Balance
- Gait speed

Questionnaires

- Walking Impairment Questionnaire
- Edinburgh Claudication Questionnaire

Imaging tests

- **Duplex ultrasound**
- **Digital subtraction angiography**
- **Computed tomography angiography**
- **Magnetic resonance angiography**

ABI, ankle brachial index; PAD, peripheral artery disease; TBI, toe brachial index.

1. Gerhard-Herman MD et al. Circulation 2017;135:e686–725; 2. Aboyans V et al. Eur J Vasc Endovasc Surg 2018;55:305–68; 3. Criqui MH et al. Circulation 2021;144:e171–91. 4. American Heart Association. Peripheral Artery Disease and Diabetes, 2021. Available at https://www.heart.org/en/health-topics/peripheral-artery-disease/diagnosing-pad . 5. Yasuda, Tomohiro, et al. Scientific reports 7.1 (2017): 17425.

PATIENT PROFILE

Novo Nordisk®

WALTER

Summary

- Male, 50
- Architect
- Enjoys walks in the park and reading
- Additionally, gained some weight in the past years and developed lower leg pain when walking.
- Comes to see a specialist to discuss HbA_{1c} that has increased over the past months
- Is very scared of disease progression and wants to do what he can for a healthy retirement
- Wants to feel control over the disease and ensure no further increase in CV risk

Patient characteristics

HbA_{1c}-8.9	Blood pressure (mmHg)- 145/95	Skin exam – WNL
BMI- 34	Cholesterol panel HDL- 28; LDL- 120; TG, 230 TC, 225	NT-proBNP –WNL
K+ 3.7		eGFR- WNL
ABI- 0.72 TBI- 0.64	AST- 120 ALT-62	UACR- WNL CV risk score 19.8% (ACC calculator)

Medical history

- Metabolic syndrome >10 years
- T2D duration 4 years
- Metformin 1000mg BID
- Sitagliptin 100mg QD
- Simvastatin 40mg QHS
- Ramipril 5mg
- Dilated Eye Exam -4 yrs ago
- Foot Exam – 4 yrs ago
- No family history of CVD disease
- Non-smoker

BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease; HbA_{1c}, glycated hemoglobin; HDL, high density lipoprotein; T2D, type 2 diabetes