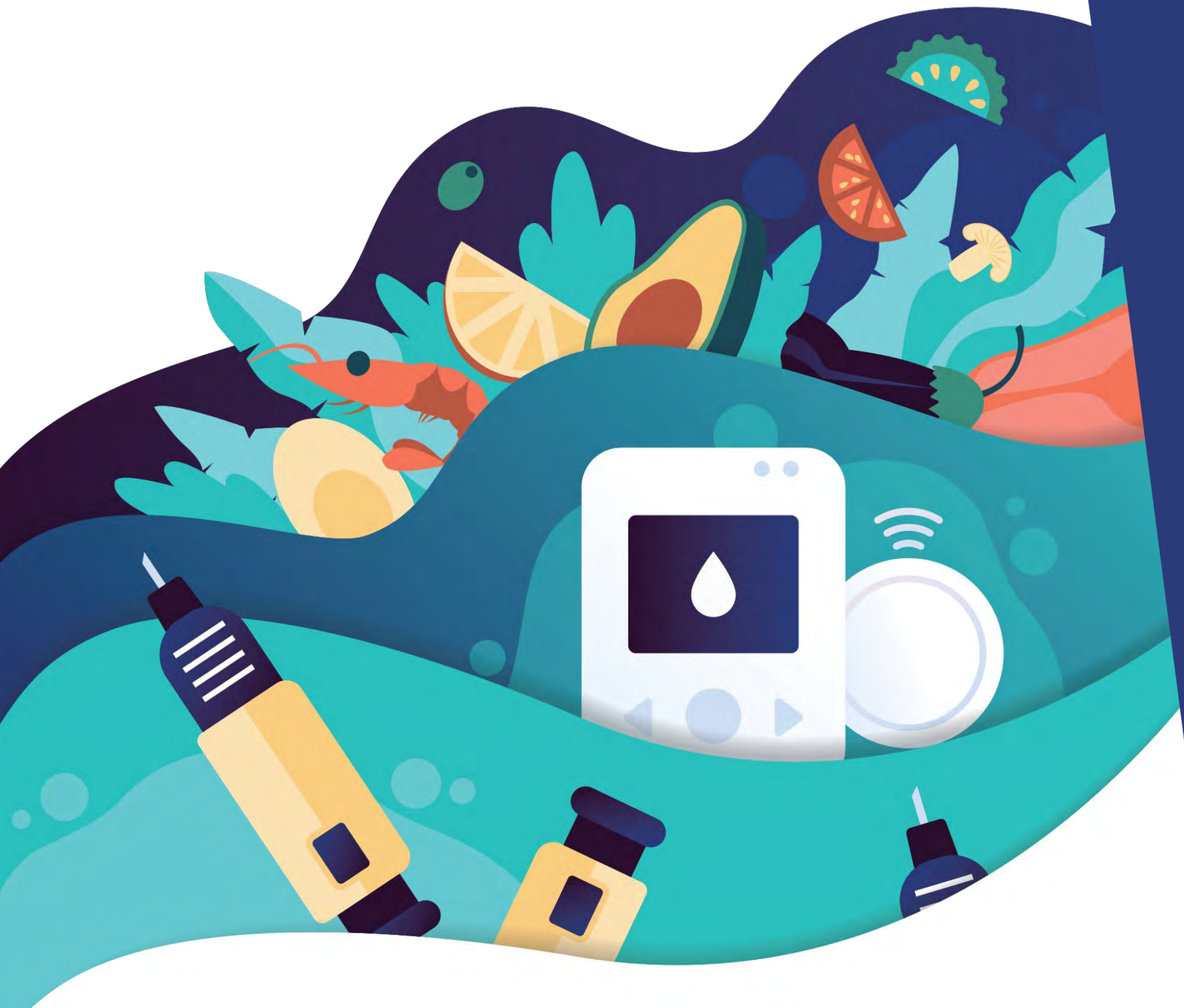


Michigan Collaborative for Type 2 Diabetes (MCT2D) Learning Community Event

Diabetes Complications: Foot Care

Brian M. Schmidt DPM
Associate Professor
Department of Internal Medicine
Metabolism, Endocrinology, and Diabetes – Podiatry

Disclosures

I have no conflicts of interest to declare

Objectives:

- Upon completion of this activity, participants will be able to describe the foot risk categories and use them to determine longitudinal care recommendations for a person with diabetes

- But first ….

Why should we care?

In 2017, estimated to be 425 million diabetics worldwide

IDF Diabetes Atlas, 8th ed

Lifetime risk of a diabetic to develop foot ulcer is: 34%

Amstrong, NEJM 2007

More than 50% of DFUs become infected Armstrong, NEJM 2007

20% of DFU result in amputation

Lipsky et al, Clin Infect Dis 2012

80% of 120,000 non-traumatic amputations are from diabetes

50% of people who suffer a proximal amputation, lose the other limb in ≤ 2 years

Why should we care?

The 5-year mortality rate after limb amputation is **68%**

Armstrong et al, IWJ 2007

Why else we should care?

$$$$

- **$850 billion** is worldwide expenditure of diabetes care in 2021
- Approximately $**20 billion** spent annually in U.S. on lower extremity complications

Driver et al, J Vasc Surg

What can we do?

Standardize your approach to diabetic foot and infections

Early identification is key to limb salvage

1. Understand Diabetic foot risk categories
2. Know a DFI classification system
3. Therapeutic Shoes and Inserts

What can we do?

Standardize your approach to diabetic foot and infections

Early identification is key to limb salvage

1. **Understand Diabetic foot risk categories**
2. Know a DFI classification system
3. Therapeutic Shoes and Inserts

Understand Diabetic Foot Risk Categories

Risk category 0	Risk category 1	Risk category 2	Risk category 3
Normal Plantar Sensation	Loss of Protective Sensation (LOPS)	LOPS with either High Pressure or Poor Circulation or Structural Foot Deformities or Onychomycosis	History of Ulceration, Amputation or Neuropathic Fracture
LOW RISK	MODERATE RISK	HIGH RISK	VERY HIGH RISK

Adapted from IDF Clinical Practice Recommendations on the Diabetic Foot 2017

Annual Diabetic Foot Exam

- American Diabetes Association recommends:
    - Perform complete foot exam at least once a year
        - Consists of:
            - History
            - General Inspection
            - Dermatological Assessment
            - Musculoskeletal Assessment
            - Neurological Assessment
            - Vascular Assessment
            - Risk classification and follow up

Understand Diabetic Foot Risk Categories

Risk category 0	Risk category 1	Risk category 2	Risk category 3
Normal Plantar Sensation	Loss of Protective Sensation (LOPS)	LOPS with either High Pressure or Poor Circulation or Structural Foot Deformities or Onychomycosis	History of Ulceration, Amputation or Neuropathic Fracture
LOW RISK	MODERATE RISK	HIGH RISK	VERY HIGH RISK

Patient education including advice on appropriate footwear; RTC annual

Understand Diabetic Foot Risk Categories

Risk category 0	Risk category 1	Risk category 2	Risk category 3
Normal Plantar Sensation	Loss of Protective Sensation (LOPS)	LOPS with either High Pressure or Poor Circulation or Structural Foot Deformities or Onychomycosis	History of Ulceration, Amputation or Neuropathic Fracture
LOW RISK	MODERATE RISK	HIGH RISK	VERY HIGH RISK

Consider accommodative footgear (“Diabetic Shoes”) and referral; RTC 3-6 months

Understand Diabetic Foot Risk Categories

Risk category 0	Risk category 1	Risk category 2	Risk category 3
Normal Plantar Sensation	Loss of Protective Sensation (LOPS)	LOPS with either High Pressure or Poor Circulation or Structural Foot Deformities or Onychomycosis	History of Ulceration, Amputation or Neuropathic Fracture
LOW RISK	MODERATE RISK	HIGH RISK	VERY HIGH RISK

Accommodative footgear and referral;
➡RTC 2-3 months

Blood Flow to the Feet – A Refresher

ABPI	Toe Brachial Index	Toe Pressure	Waveforms	$TcPO_2$* (indicating perfusion)
> 0.9 – 1.3	> 0.6	> 80 mmHg	triphasic	> 40 mmHg
> 0.6	> 0.4	>50 mmHg	biphasic/mono	30–39 mmHg
> 0.4	> 0.2	> 30 mmHg	biphasic/mono	20–29 mmHg
< 0.4	< 0.2	< 30 mmHg	monophasic	< 20 mmHg
> 0.9			An audible hand-held Doppler of the dorsalis pedis or posterior tibial artery that is triphasic/biphasic is equivalent to an ABPI > 0.9. **Beware** of falsely elevated ABPI levels that may be due to calcified vessels in persons with diabetes.[24]	

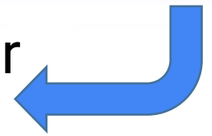
*Transcutaneous oxygen pressure

Canadian Association of Wound Care. Advances for the Management of Diabetic Foot Complications. Session workbook. 2016.

Understand Diabetic Foot Risk Categories

Risk category 0	Risk category 1	Risk category 2	Risk category 3
Normal Plantar Sensation	Loss of Protective Sensation (LOPS)	LOPS with either High Pressure or Poor Circulation or Structural Foot Deformities or Onychomycosis	History of Ulceration, Amputation or Neuropathic Fracture
LOW RISK	MODERATE RISK	HIGH RISK	VERY HIGH RISK

Accommodative footgear, referral, and consider multispecialty involvement



Understand Diabetic Foot Risk Categories

- How often would you recommend this person be seen by a podiatrist?

A.) Annual
B.) every 3 – 6 months
C.) every 1-2 months
D.) Once a week
E.) Every 2-3 months

Understand Diabetic Foot Risk Categories

- How often would you recommend this person be seen by a podiatrist?

A.) Annual
B.) every 3 – 6 months
C.) every 1-2 months
D.) Once a week
E.) Every 2-3 months

- Foot risk 2 = PVD = High Risk

What can we do?

Standardize your approach to diabetic foot and infections

Early identification is key to limb salvage

1. Understand Diabetic foot risk categories
2. **Know a DFI classification system**
3. Therapeutic Shoes and Inserts

Description	Severity grade	Score
a. No signs or symptoms of infection	Non infected	0
b. Erythema between 0.5 mm to 2 cm, induration, tenderness, warmth, and purulent discharge.	Mild	1
c. Erythema > 2 cm, muscle, tendon, orbone or joint infection.	Moderate	2
d. Any local infection with systemic inflammatory response (SIRS) manifested by at least 2 of following: • Temperature > 38 or < 36 • Heart rate > 90 beats/min, • Respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg, • White blood cell count > 12000 or < 4000 cells/μL or 10% immature (band) forms; or severe metabolic disturbances (hyperglycemia or hypoglycemia)	Severe	3

For severe infection and some moderate grade infection, hospitalization is needed for limb preservation.

→ No Abx, but wound care

Adapted from IDSA 2012

Description	Severity grade	Score
a. No signs or symptoms of infection	Non infected	0
b. Erythema between 0.5 mm to 2 cm, induration, tenderness, warmth, and purulent discharge.	Mild	1
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For severe infection and some moderate grade infection, hospitalization is needed for limb preservation.

→ PO Abx and wound care

Adapted from IDSA 2012

Description	Severity grade	Score
a. No signs or symptoms of infection	Non infected	0
b. Erythema between 0.5 mm to 2 cm, induration, tenderness, warmth, and purulent discharge.	Mild	1
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For severe infection and some moderate grade infection, hospitalization is needed for limb preservation.

Probe to bone testing

Adapted from IDSA 2012

Probe-to-Bone testing (PTB)

Use ‘blunt metal probe’

Can assist in diagnosis of diabetic foot osteomyelitis, but is largely <u>setting dependent</u>

Table 1. Descriptive characteristics of studies describing the probe-to-bone test.

Study (year)	N	Sens (%)	Spec (%)	PPV (%)	NPV (%)	LR(+)	LR(–)	Prev (%)	Method of diagnosis
Outpatient									
Shone et al (2006)	81	38	91	53	85	4.22	0.68	23.5	Clinical
Lavery et al (2007)	247[T] / 217[+]	87	91	57	98	9.4[T] / 6.5[+]	6.81[T] / 6.5[+]	20	Microbiology
Infected outpatient									
Morales Lozano et al (2010)	132	98	78	95	91	4.5	0.02	79.5	Clinical and microbiology
Inpatient									
Grayson et al (1995)	75	66	85	89	56	4.4	0.15	66	Histology
Mutluoglu et al (2012)	65	66	84	87	62	4.13	0.24	60	Imaging and clinical
Aragón-Sánchez et al (2011)	338	95	93	97	83	14.34	0.06	72.4	Histology and microbiology

Key: N – number of participants/ulcers; Sens – sensitivity; Spec – specificity; PPV – positive predictive value; NPV – negative predictive value; LR(+) – positive likelihood ratio; LR(–) – negative likelihood value; Prev – prevalence; [T] – total; [+] – infected

Wrobel J, Schmidt B (2016) Probe-to-bone testing for osteomyelitis in the diabetic foot: a literature review. The Diabetic Foot Journal

Description	Severity grade	Score
a. No signs or symptoms of infection	Non infected	0
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For severe infection and some moderate grade infection, hospitalization is needed for limb preservation.

→ Abx, urgent consult & hospitalization

Adapted from IDSA 2012

Description	Severity grade	Score
a. No signs or symptoms of infection	Non infected	0
b. Erythema between 0.5 mm to 2 cm, induration, tenderness, warmth, and purulent discharge.	Mild	1
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For severe infection and some moderate grade infection, hospitalization is needed for limb preservation.

→ IV Abx, hospitalization, and surgery

Adapted from IDSA 2012

Classification Practice

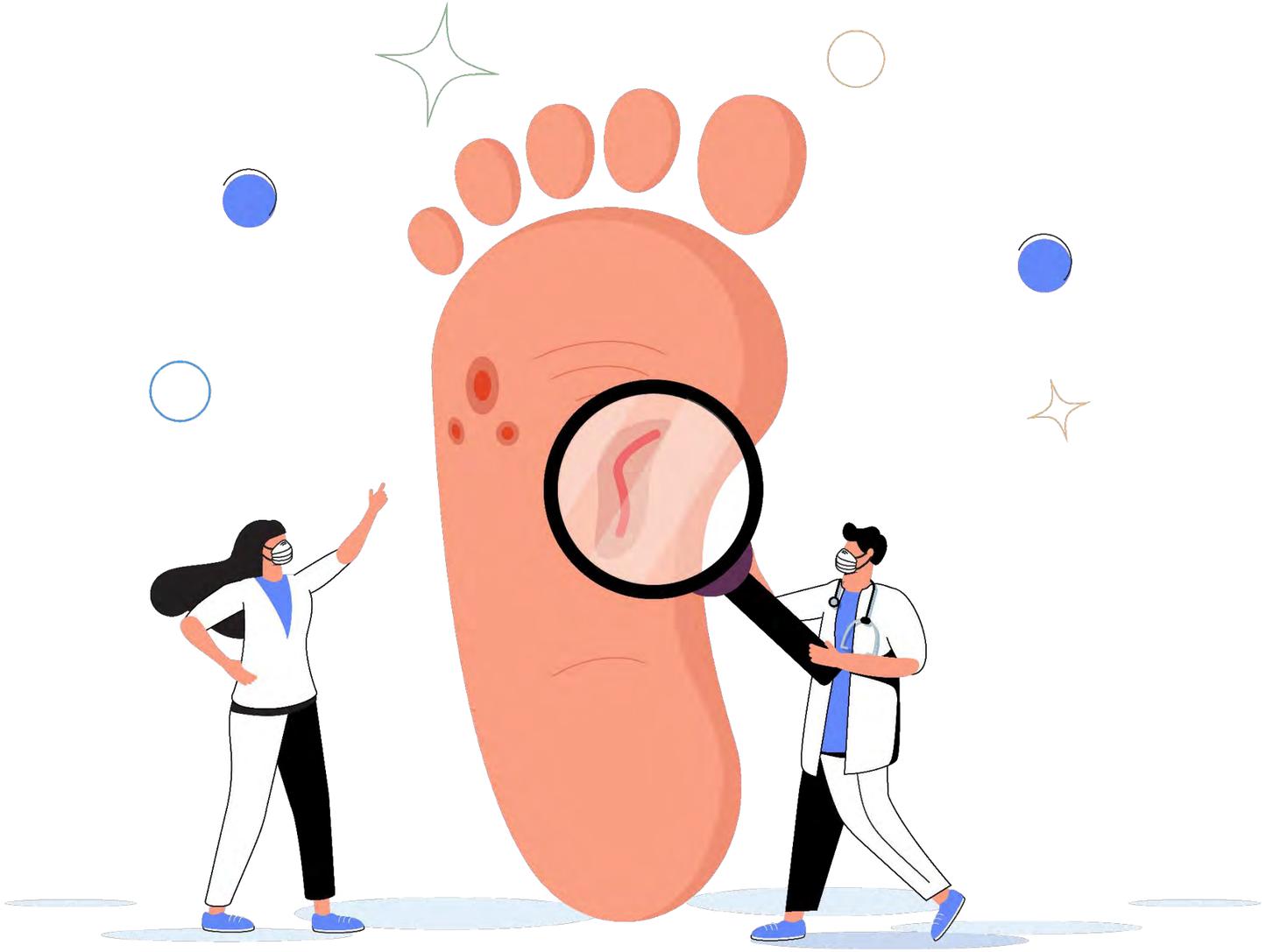
Classify wound based on clinical appearance

A.) 0 – No infection

B.) 1 – Mild

C.) 2 – Moderate

D.) 3 – Severe



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D.) 3 – Severe

What can we do?

Standardize your approach to diabetic foot infections

Early identification is key to limb salvage

1. Understand Diabetic foot risk categories
2. Know a DFI classification system
3. **Therapeutic Shoes and Inserts**

Therapeutic Shoes and Inserts

- Medicare Part B (Medical Insurance)
  - Covers the furnishing and fitting of either of these each calendar year, if you have diabetes and severe diabetes-related foot disease:
    - One pair of custom-molded shoes and inserts
    - One pair of extra-depth shoes
- Medicare also covers:
  - 2 additional pairs of inserts each calendar year for custom-molded shoes
  - 3 pairs of inserts each calendar year for extra-depth shoes
  - Medicare will cover shoe modifications instead of inserts.

Article ID
A52501

Article Title
Therapeutic Shoes for Persons with Diabetes - Policy Article

Therapeutic Shoes and Inserts

Therapeutic shoes, inserts and/or modifications to therapeutic shoes are covered if all of the following criteria are met:

- The beneficiary has diabetes mellitus; and
- The certifying physician has documented in the beneficiary's medical record one or more of the following conditions:
    1. Previous amputation of the other foot, or part of either foot, or
    2. History of previous foot ulceration of either foot, or
    3. History of pre-ulcerative calluses of either foot, or
    4. Peripheral neuropathy with evidence of callus formation of either foot, or
    5. Foot deformity of either foot, or
    6. Poor circulation in either foot; and

Article ID
A52501

Article Title
Therapeutic Shoes for Persons with Diabetes - Policy Article

Therapeutic Shoes and Inserts

Therapeutic shoes, inserts and/or modifications to therapeutic shoes are covered if all of the following criteria are met:

The certifying physician has certified that indications (1) and (2) are met and that he/she is treating the beneficiary under a comprehensive plan of care for his/her and that the beneficiary needs diabetic shoes. The certifying diabetesphysician must:

1. Have an in-person visit with the beneficiary during which diabetes management is addressed within 6 months prior to delivery of the shoes/inserts; and
2. Sign the certification statement (refer to the Policy Specific Documentation Requirements section below) on or after the date of the in-person visit and within 3 months prior to delivery of the shoes/inserts.

Article ID
A52501

Article Title
Therapeutic Shoes for Persons with Diabetes - Policy Article

Therapeutic Shoes and Inserts

Therapeutic shoes, inserts and/or modifications to therapeutic shoes are covered if all of the following criteria are met:

1. Prior to selecting the specific items that will be provided, the **supplier** must conduct and document an in-person evaluation of the beneficiary.
2. At the time of in-person delivery to the beneficiary of the items selected, the **supplier** must conduct an objective assessment of the fit of the shoe and inserts and document the results. A beneficiary's subjective statements regarding fit as the sole documentation of the in-person delivery does not meet this criterion.

Article ID
A52501

Article Title
Therapeutic Shoes for Persons with Diabetes - Policy Article

Therapeutic Shoes and Inserts

- If criteria 1-5 are not met, the therapeutic shoes, inserts and/or modifications will be denied as noncovered.
- Also need KX modifier or they will be non-covered.

Article ID
A52501

Article Title
Therapeutic Shoes for Persons with Diabetes - Policy Article

Therapeutic Shoes and Inserts

To meet criterion 2, the certifying physician must either:

1. Personally document one or more of criteria a – f in the medical record of an in-person visit within 6 months prior to delivery of the shoes/inserts and prior to or on the same day as signing the certification statement; or

2. Obtain, initial, date (prior to signing the certification statement), and indicate agreement with information from the medical records of an in-person visit with a podiatrist, other M.D or D.O., physician assistant, nurse practitioner, or clinical nurse specialist that is within 6 months prior to delivery of the shoes/inserts, and that documents criteria

Describe that wound (MEASURE - MIT)

- **M- Measure**
  - Dimensions
    - Length x Width
- **E – Exudate**
  - Malodor?
  - Color?
  - Consistency?
    - Thick, thin, viscous
- **A – Appearance**
  - Does it look ‘angry’

Describe that wound (MEASURE - MIT)

- **S-Suffering**
  - Painful to palpation?
  - Fluctuant / Soft tissue Crepitus
- **U - Undermining**
  - Are the edges of the wound contiguous?
  - Can you place an object under wound margins
- **R – Realm**
  - Location
- **E - Edge**

Describe that wound (MEASURE - MIT)

- **M – Moisture**
  - Color surrounding wound
  - Macerated
  - Dry, cracking, flaking
- **I - Infection**
  - Red
  - Hot
  - Swollen
- **T - Tissue**
  - Granular, Fibrotic, Necrotic, Slough, Punctate

Questions?

References

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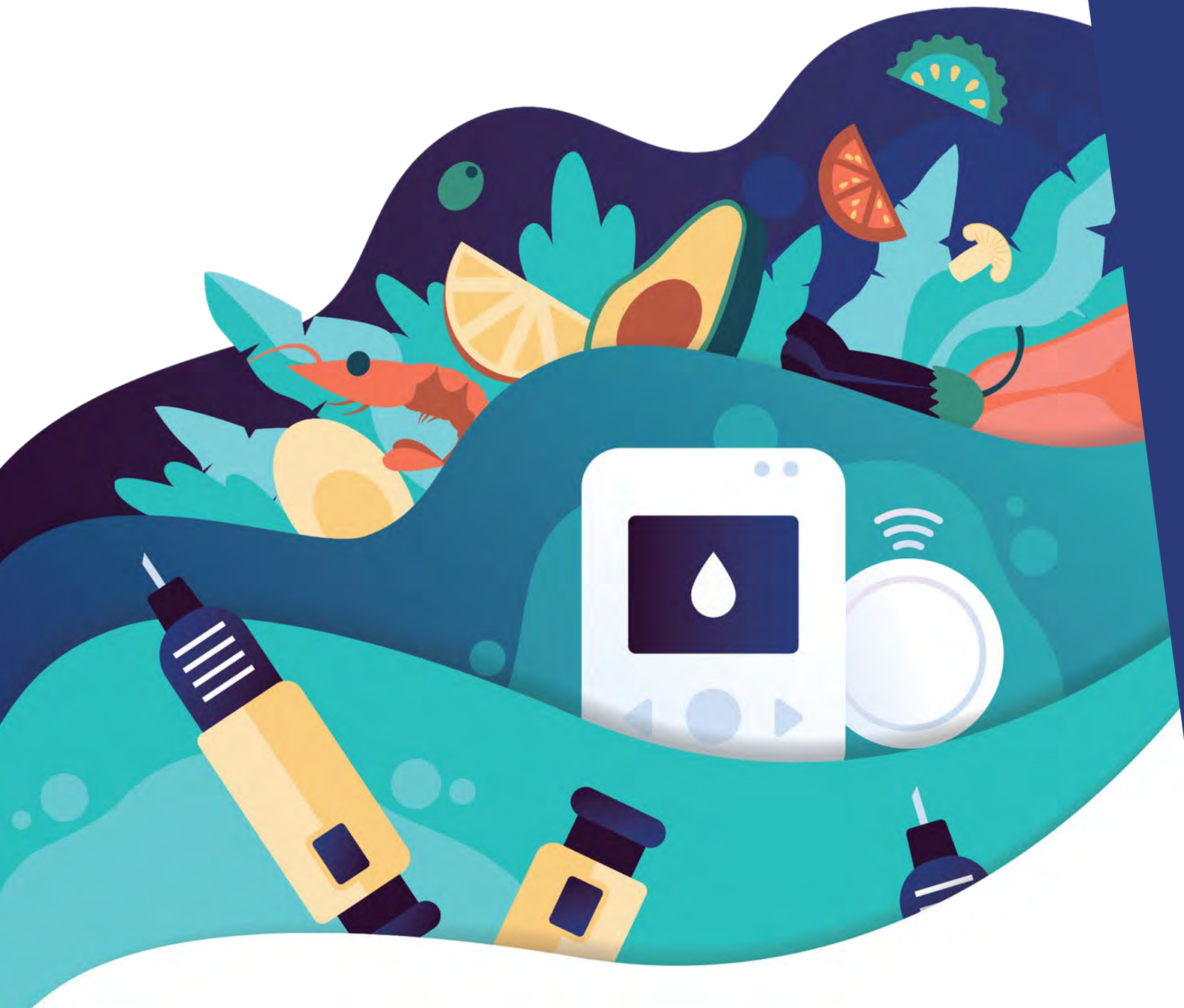
- Aragon-Sanchez J, Lipsky BA, Lazaro-Martinez JL. Diagnosing diabetic foot osteomyelitis: is the combination of probe-to-bone test and plain radiography sufficient for high-risk inpatients? Diabet Med 2011; 28: 191_4.



Michigan Collaborative for Type 2 Diabetes (MCT2D) Learning Community Event

Understanding and Treating Painful Diabetic Neuropathy

Lynn Ang, MD
Clinical Associate Professor
Metabolism, Endocrinology and Diabetes (MEND)
University of Michigan

Disclosure

- **No disclosure or conflict of interest**

Objectives

- To discuss the various forms of diabetic peripheral neuropathy (DPN)
- To summarize simple, sensitive, and cost-effective diagnostic steps for people with DPN
- To provide new evidence-based recommendations for the prevention and management of painful DPN

Case

- 60 year old man with 12 years of type 2 diabetes (HbA1c 8-9%), hypertension, dyslipidemia, CAD and chronic low back pain presenting for a clinic visit with burning pain in both feet, worse at night.
- Medications: Metformin 2000 mg/day, lisinopril 40 mg/day, metoprolol 100 mg/day, atorvastatin 80 mg/day, aspirin 81 mg/day, amitriptyline 75 mg/day (recently added by PCP), oxycodone 15 mg q6 hours prn (for back pain)

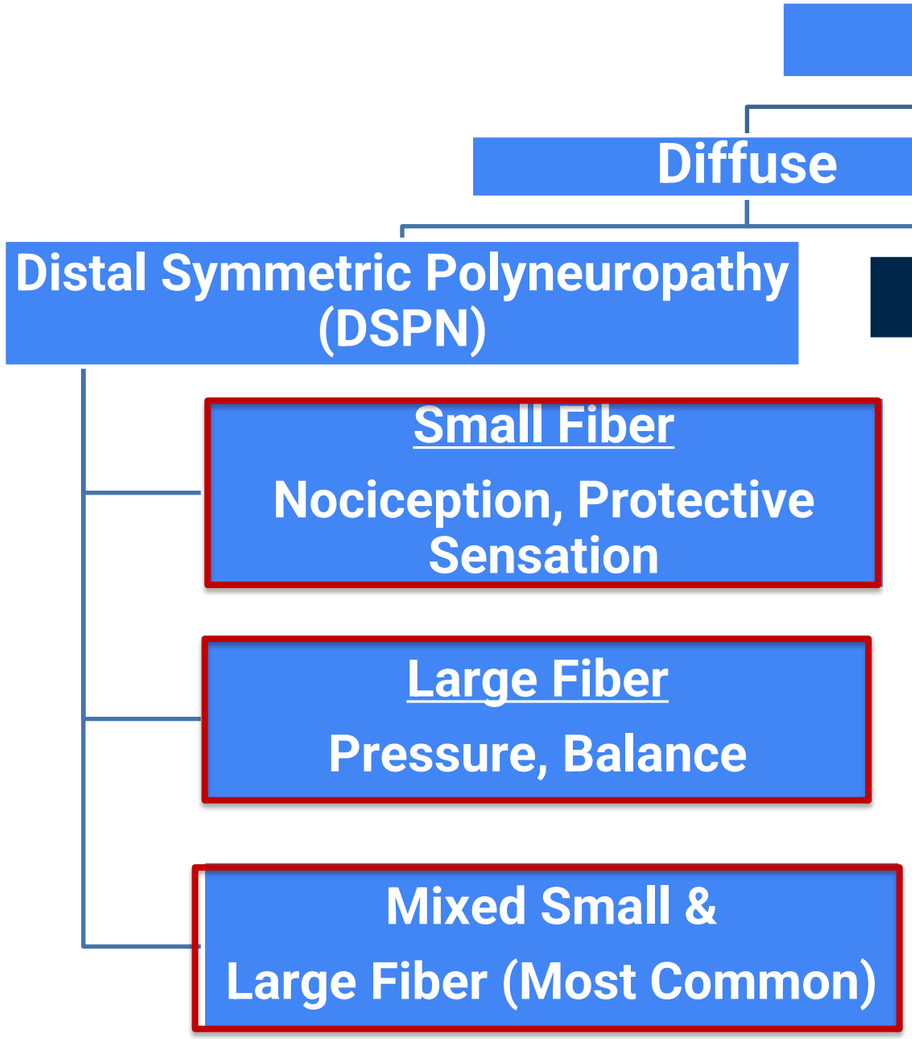
Examination
BP: 140/85 mmHg
BMI: 35
Central adiposity

Laboratory:
POC HbA1c 8.2%
Total cholesterol 190 mg/dL
LDLc 70 mg/dL
Triglycerides 256 mg/dL
HDLc 38 mg/dL.

Objectives

- To discuss the various forms of diabetic peripheral neuropathy (DPN)
- To summarize simple, sensitive, and cost-effective diagnostic steps for people with DPN
- To provide new evidence-based recommendations for the prevention and management of painful DPN

Classification of Diabetic Neuropathy

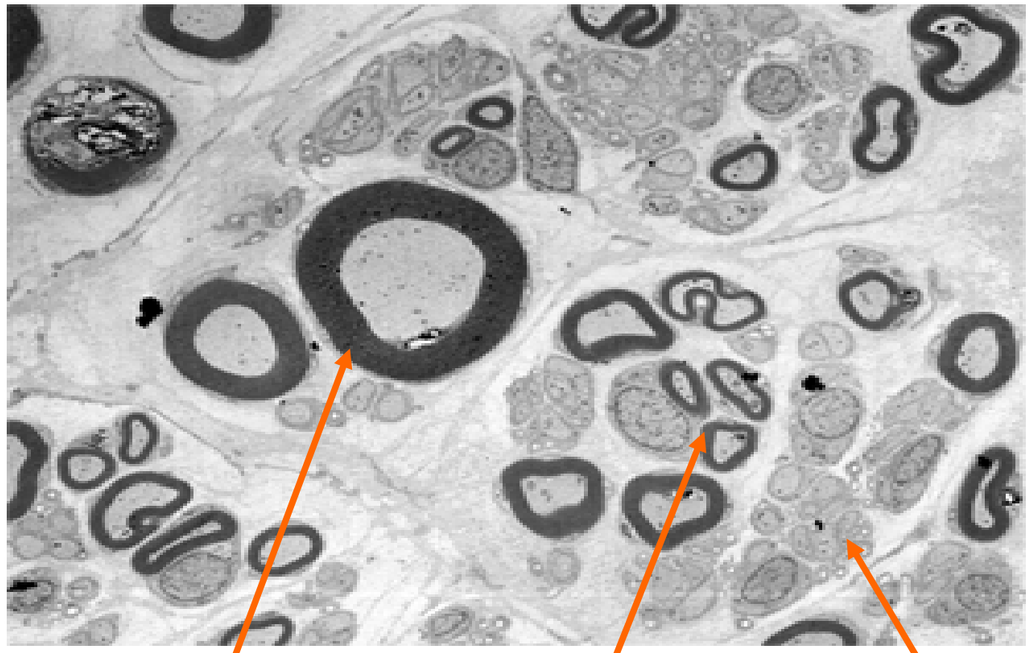


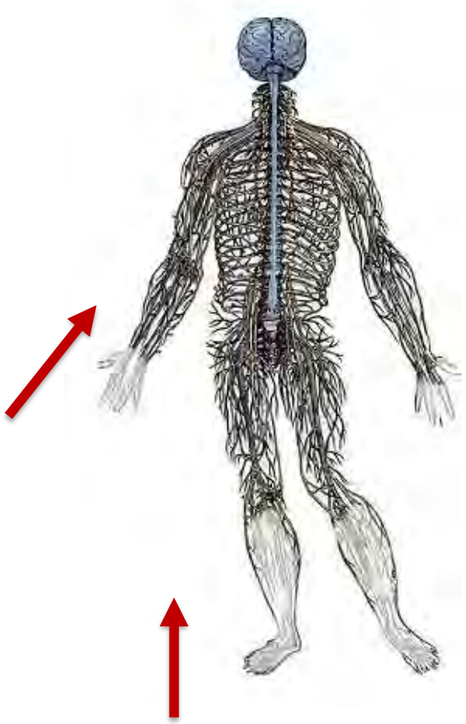
Nondiabetic Neuropathies common in Diabetes

- Pressure palsies
- Chronic inflammatory demyelinating polyneuropathy
- Radiculoplexus neuropathy
- Acute painful small-fiber neuropathies (treatment induced)

Adapted from Pop-Busui, Boulton, et al, Diabetes Care 2017;40:136-154

DPN: Involved Nerve Fibers and Pattern of Loss





Large myelinated fiber
Pressure, Balance

Small myelinated fiber

Unmyelinated fibers

Nociception, Protective Sensations

Objectives

- To discuss the various forms of diabetic peripheral neuropathy (DPN)
- To summarize simple, sensitive, and cost-effective diagnostic steps for people with DPN
- To provide new evidence-based recommendations for the prevention and management of painful DPN

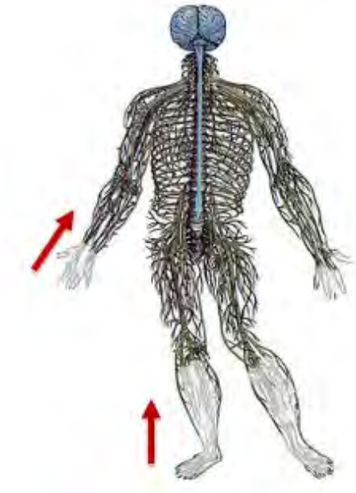
Evaluation of Small Myelinated Fibers in Clinical Care

Nerve Function

- Nociception (pain and temperature)
- Protective sensations

History

- Burning
- Lancinating
- Electric shocks
- Stabbing
- Hyperalgesia
- Allodynia



Exam

- Thermal discrimination (hot/cold)
- Pinprick sensation

Pop-Busui, Boulton, et al, Diabetes Care 2017;40:136-154

Shillo P, et al. Curr Diabetes Reports 2019; 19:32.
Iqbal Z et al. Clinical Therapeutics 2018; 40(6):828-49.

Evaluation of Large Myelinated Fibers in Clinical Care

History

- Numbness
- Tingling
- Poor balance

Nerve Function

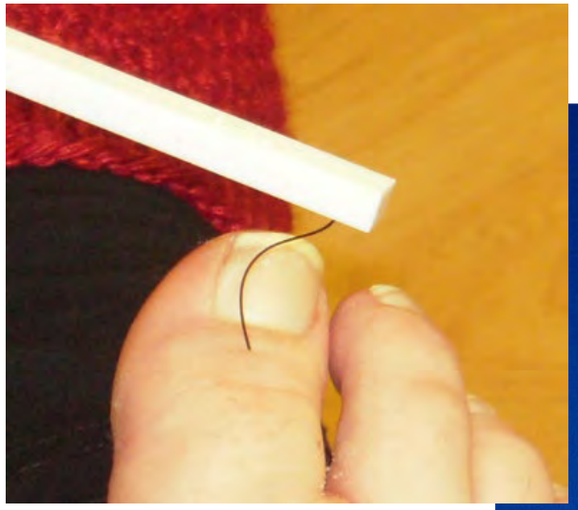
- Pressure
- Balance

Exam

- Vibration perception
- Proprioception
- Ankle reflexes
- 10 gm monofilament

Pop-Busui, Boulton, et al, Diabetes Care 2017;40:136-154
Iqbal Z et al. Clinical Therapeutics 2018; 40(6):828-49.

Diagnosis of DPN



Screening Instruments

	Michigan Neuropathy Screening Instrument (MNSI) Index	Toronto Clinical Neuropathy Score (TCNS)	Neuropathy Disability Score (NDS)
Symptoms	15 items Self-administered	6 item symptom score	None
Exam	Inspection Vibration testing Ankle Reflexes	Reflex score (knee, ankle) Sensory test score (pinprick, temperature, light touch, vibration and position sense)	Sensation (vibration, temperature, pin-prick) Ankle Reflexes
DPN +	≥4 points for questionnaire ≥2 for exam	6-8: Mild neuropathy 9-11: Mod neuropathy ≥12: Severe neuropathy	0-2: Mild neuropathy 6-8: Mod neuropathy 9-10: Severe

Feldman EL et al, Diabetes Care 1994; 17(11):1281-89.
Herman WH, Pop-Busui R, Feldman EL et al. Diabet Med 2012; 29(7):937-44.
Bril V and Perkins BA, Diabetes Care 2002; 25(11):2048-52.
Young MJ, Boulton AJM et al, Diabetologia 1993;36:150-4.

DPN Screening

Type 1 diabetes

Begin

After 5 years of diagnosis

Frequency

Annually

Type 2 diabetes

Begin

At the time of diagnosis

Frequency

Annually

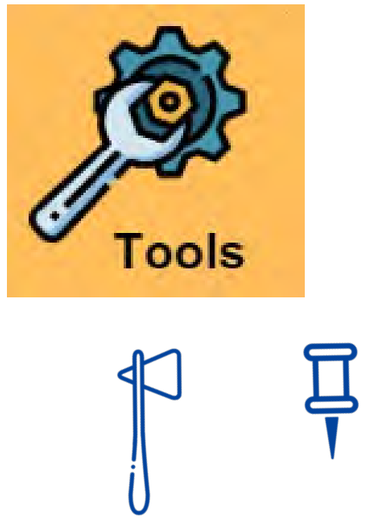
***Feet at high risk for ulceration should be inspected at every visit – includes known neuropathy, prior ulceration or amputation**

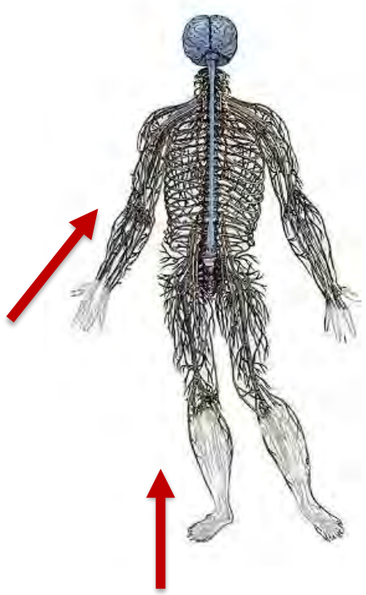
ADA Standards of Care: 2025
Pop-Busui, Boulton, et al, Diabetes Care 2017;40:136-154

DPN Screening

Screening: 2 or more of the following

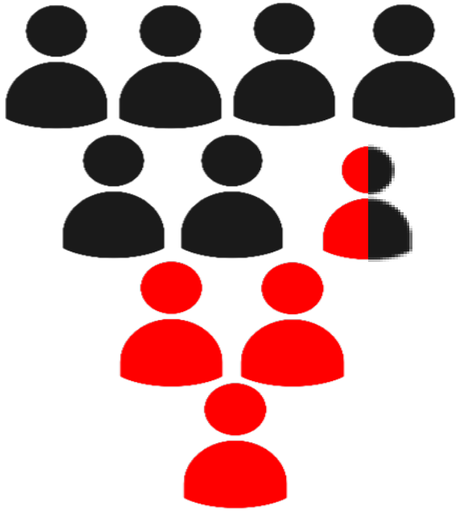
- Temperature, Vibration, Pinprick, light touch or reflexes
- Distal to Proximal
- Symmetric





Prevalence of DPN in Diabetes Mellitus

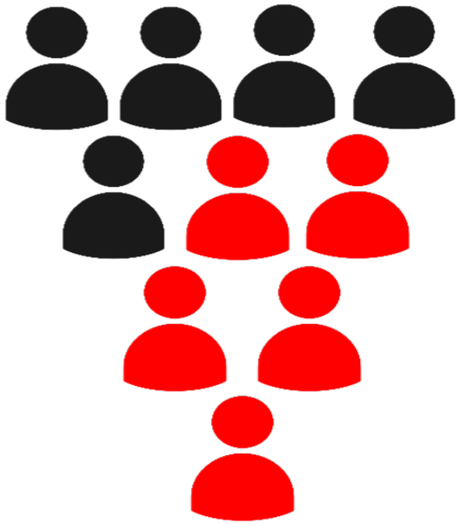
Up to 35% after >25 years of diabetes



Type 1 Diabetes

Martin CL et al, Diabetes Care 2014; 37(1):31-38.
Tesfaye S et al, Diabetologia 1996; 39:1377-84.
Jaiswal M et al, Diabetes Care 2017; 42(6):1-7.

Up to 50% after 10 years of diabetes



Type 2 Diabetes

Pop-Busui, Boulton, et al, Diabetes Care 2017;40:136-154
Ang L, Pop-Busui R, et al, Curr Diab Rep 2014;14(9):528.
Ziegler D, et al, Diabetes Care 2008; 31(3):464-9.

DPN prevalence in youth

Diabetes in Youth Cohort (SEARCH) study
~2,000 youth with T1D and T2D

Type 1 Diabetes

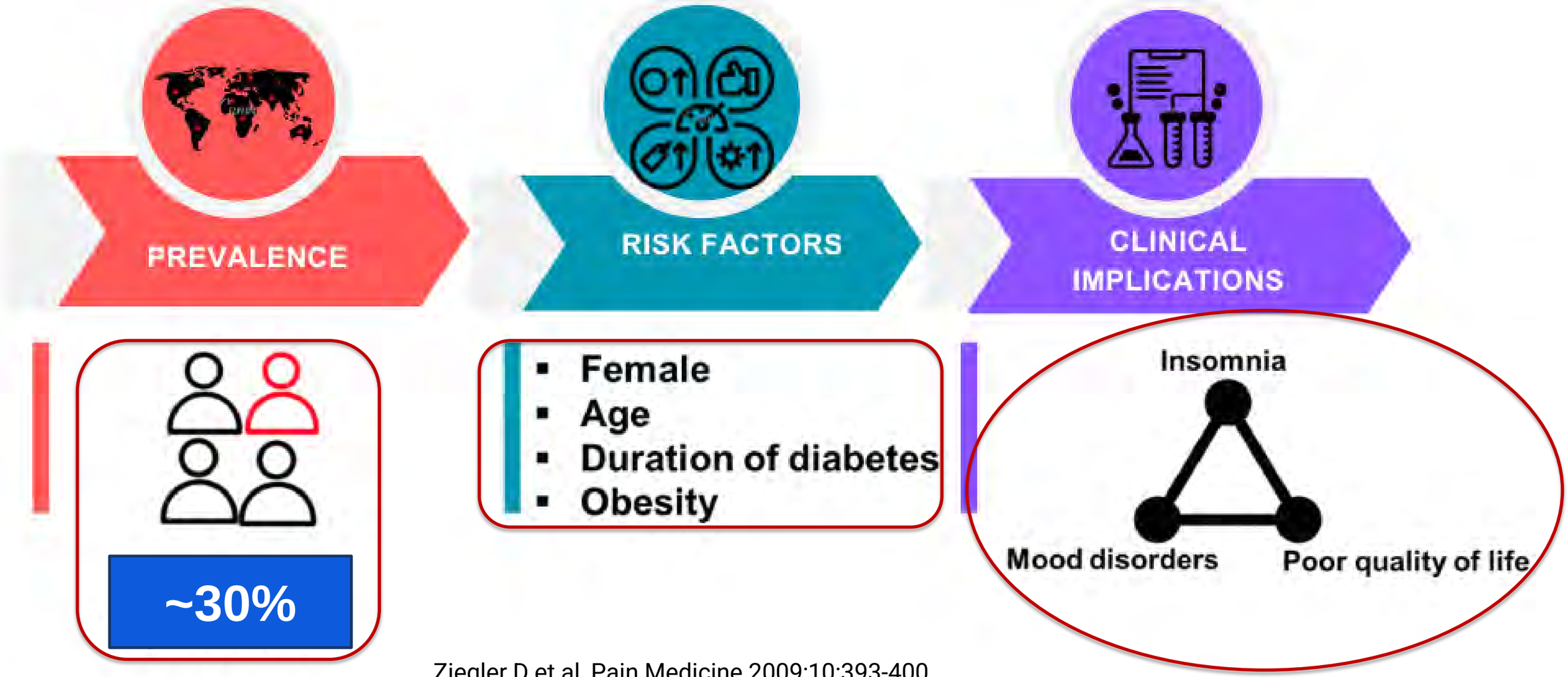
- SEARCH: Prevalence of 7% after ~9 years of diabetes

Type 2 Diabetes

- SEARCH: 22% prevalence after ~9 years of diabetes.

Jaiswal, Busui et al; Diabetes Care Volume 40, September 2017

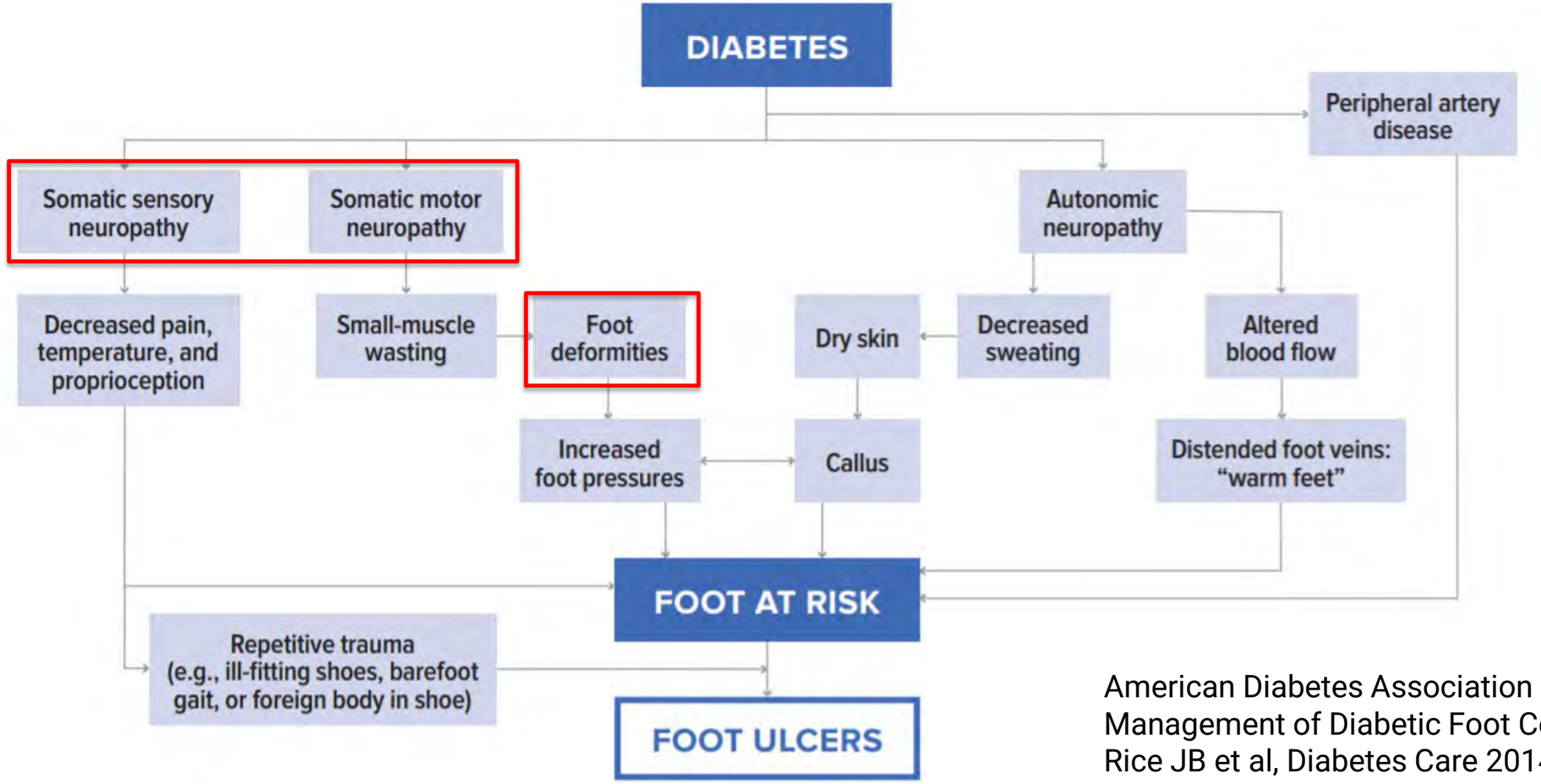
Painful DPN



Ziegler D et al, Pain Medicine 2009;10:393-400.
Kallinikou D, et al, Diabetes Metab Res Rev 2019;13:e3178.

DPN and Diabetic Foot Ulcers

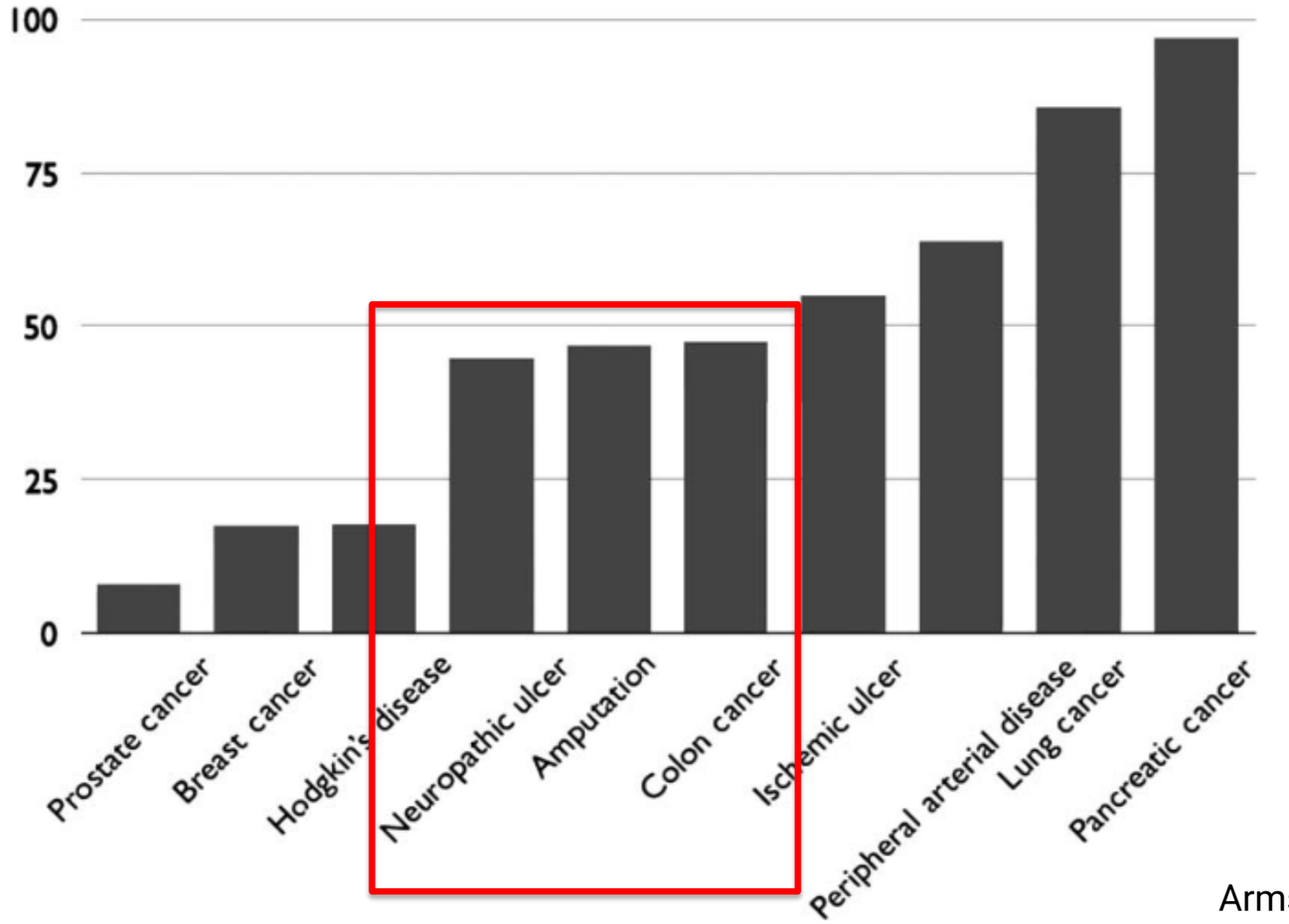
Annual incidence of foot ulcers is 2-6%
Lifetime risk of foot ulcers is 15-34%



American Diabetes Association "Diagnosis and Management of Diabetic Foot Complications" 2018
Rice JB et al, Diabetes Care 2014; 37(3):651-58.

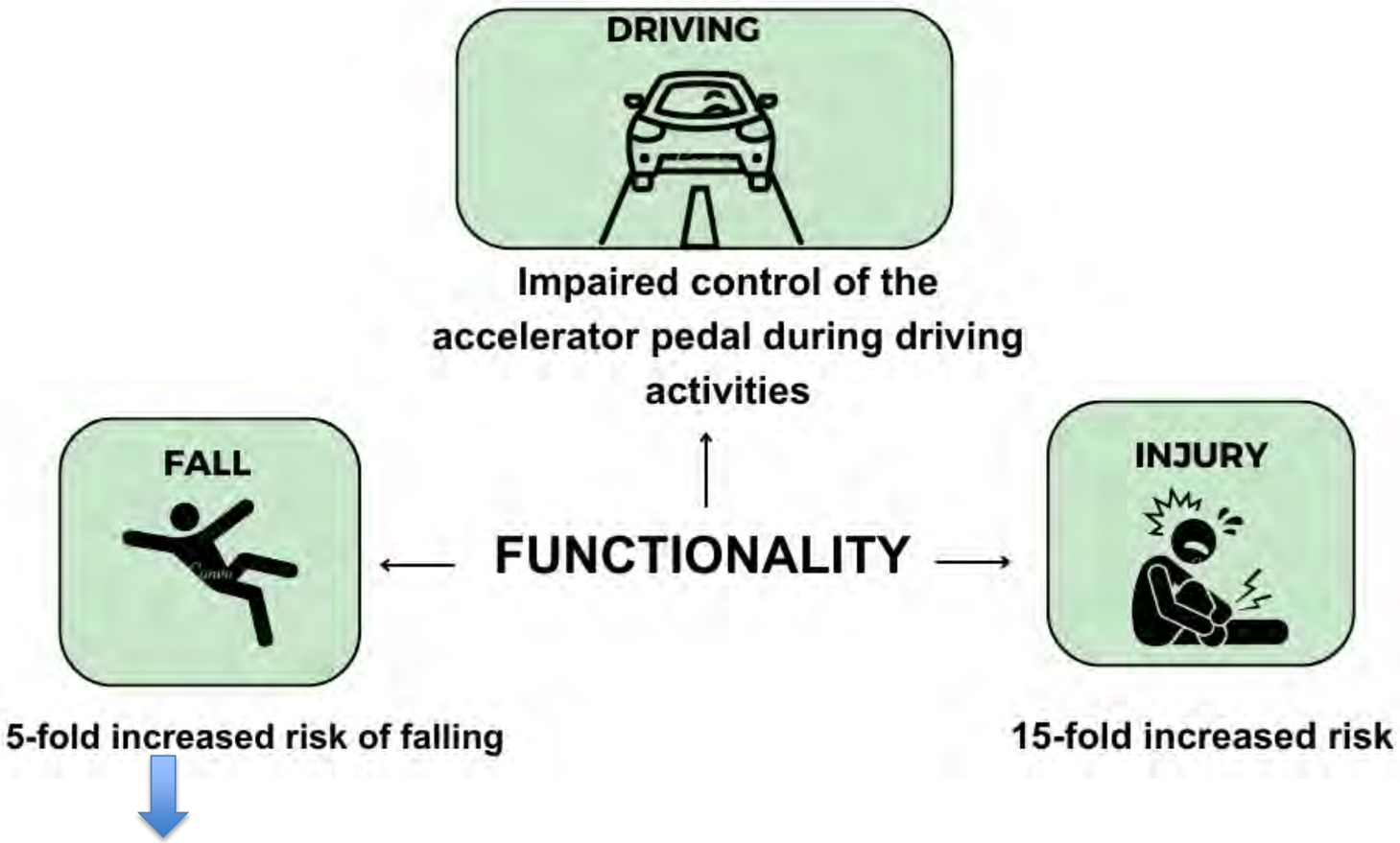
DPN and Terminal Diabetes

5 year mortality % rivals that of cancer



Armstrong DG et al, IWJ 2007;4(4):286-7.

DPN and Impaired Functionality



Increased mortality and decreased quality-of-life

Brown SJ, Boulton AJM et al; Diabetes Care 2014;38:1116-22.
Timar B et al, PLOS One 2016; 11(4):e0154654.
Wallace C et al, Diabetes Care 2002;25(11):1983-86.
Perazzolo D, Boulton AJM et al; Diabetic Medicine 2019; 00:1-8.

Painful DPN is Associated with Increased Mood Symptoms

Table 4

Scores on QOL and Related Measures by BPI-DPN Average Pain Severity

Subject Scores	BPI-DPN Average Pain Severity			
	Mild	Moderate	Severe	ANOVA *F*, *P*-value[a]
Norm-based SF-12v2 scale scores, mean (SD)				
Physical functioning	36.1 (11.9)	31.4 (10.0)	28.4 (8.7)	9.8928, 0.0001
Role physical	39.1 (10.9)	34.6 (8.7)	31.6 (9.7)	10.3730, 0.0000
Bodily pain	43.4 (10.6)	34.5 (10.9)	26.9 (11.3)	37.5740, 0.0000
General health	38.7 (11.8)	34.8 (10.4)	28.9 (10.6)	14.0057, 0.0000
Vitality	43.9 (11.1)	41.9 (9.8)	38.3 (9.9)	5.1251, 0.0066
Social functioning	44.1 (12.1)	36.6 (11.8)	32.5 (10.9)	16.8391, 0.0000
Role emotional	43.0 (12.8)	37.3 (12.9)	31.2 (14.4)	12.7136, 0.0000
Mental health	46.7 (12.2)	43.7 (10.3)	39.7 (10.0)	7.0033, 0.0011
Physical component summary	37.5 (9.8)	31.7 (9.1)	27.6 (8.0)	20.0572, 0.0000
Mental component summary	47.8 (12.7)	43.7 (11.4)	39.1 (9.6)	9.4991, 0.0001
HADS, mean (SD)				
Anxiety score	6.7 (4.5)	8.9 (4.1)	11.0 (4.4)	16.8033, 0.0000
Depression score	6.1 (4.2)	7.9 (3.9)	10.3 (4.3)	17.4129, 0.0000
EQ-5D, mean (SD)				
EQ-5D utility scores	0.7 (0.2)	0.5 (0.3)	0.2 (0.3)	44.7734, 0.0000
Current health, mean (SD)	63.8 (19.5)	55.5 (21.4)	49.3 (29.2)	6.2107, 0.0024

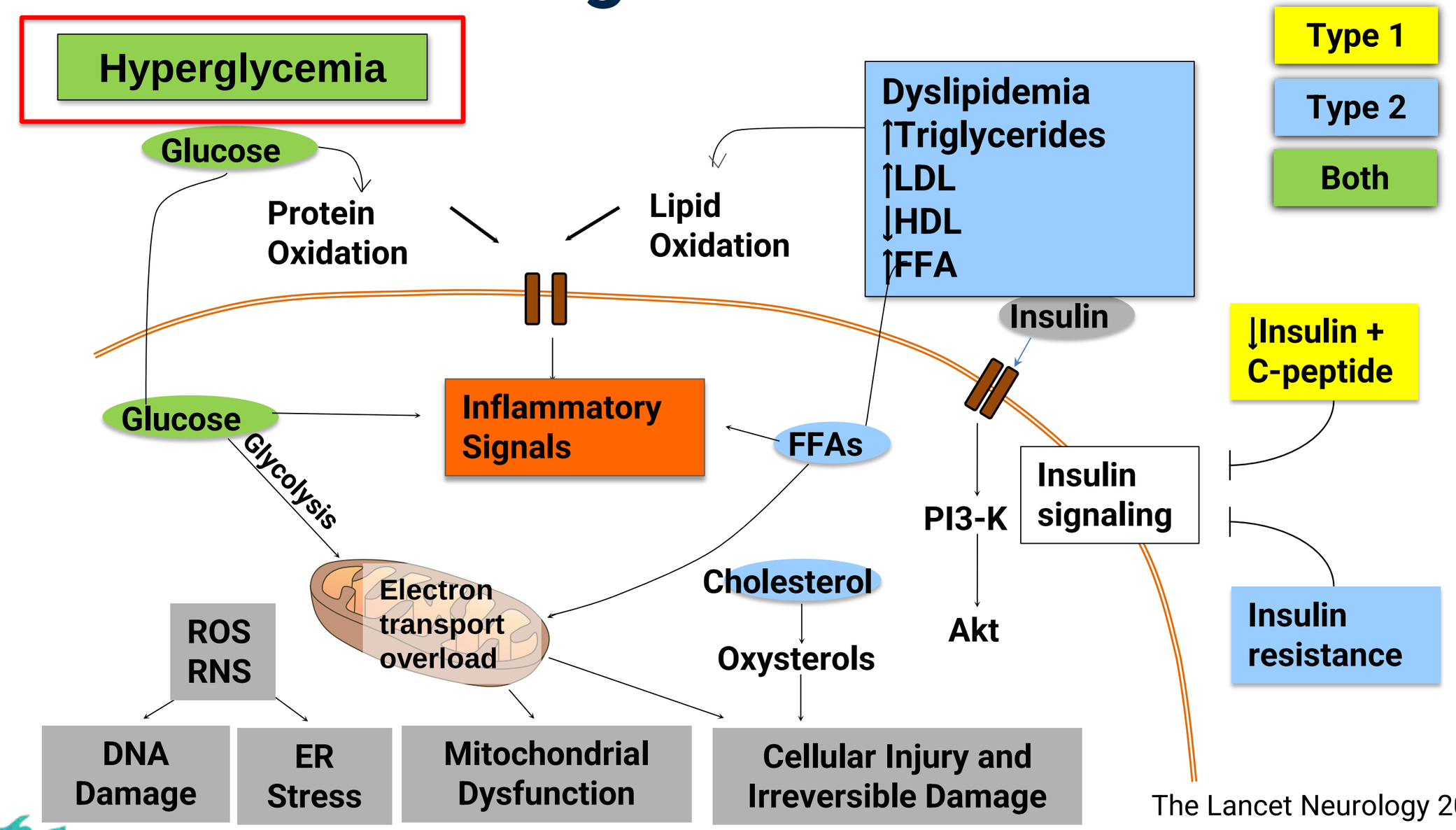
Total *n*'s for individual rows range from 238–254 due to missing values.
[a] $P < 0.01$ for all pair-wise comparisons, except $P < 0.05$ for the comparisons of current health scores for the mild vs. moderate and severe pain groups; and $P = 0.09$ for the comparison of current health scores for the moderate vs. severe pain group.

Gore et al. J Pain Symptom Manage, 2005;30(4):374-85.

Objectives

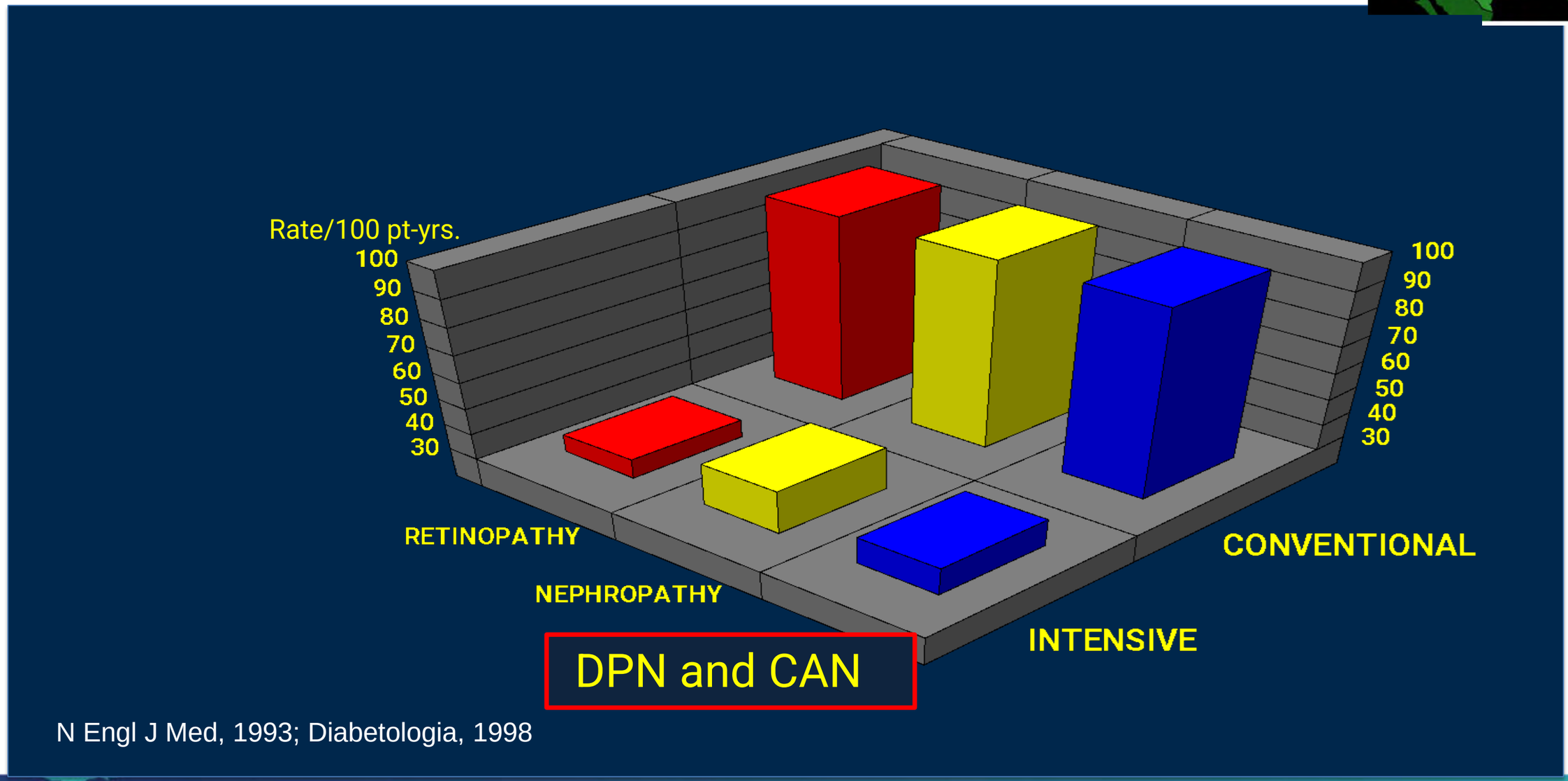
- To discuss the various forms of diabetic peripheral neuropathy (DPN)
- To summarize simple, sensitive, and cost-effective diagnostic steps for people with DPN
- To provide new evidence-based recommendations for the prevention and management of painful DPN

Pathogenesis of DPN



The Lancet Neurology 2012, 11(6): 521

Glucose Control and Neuropathy



N Engl J Med, 1993; Diabetologia, 1998

Challenge in EDIC Study: Glucose Control is Difficult to Maintain

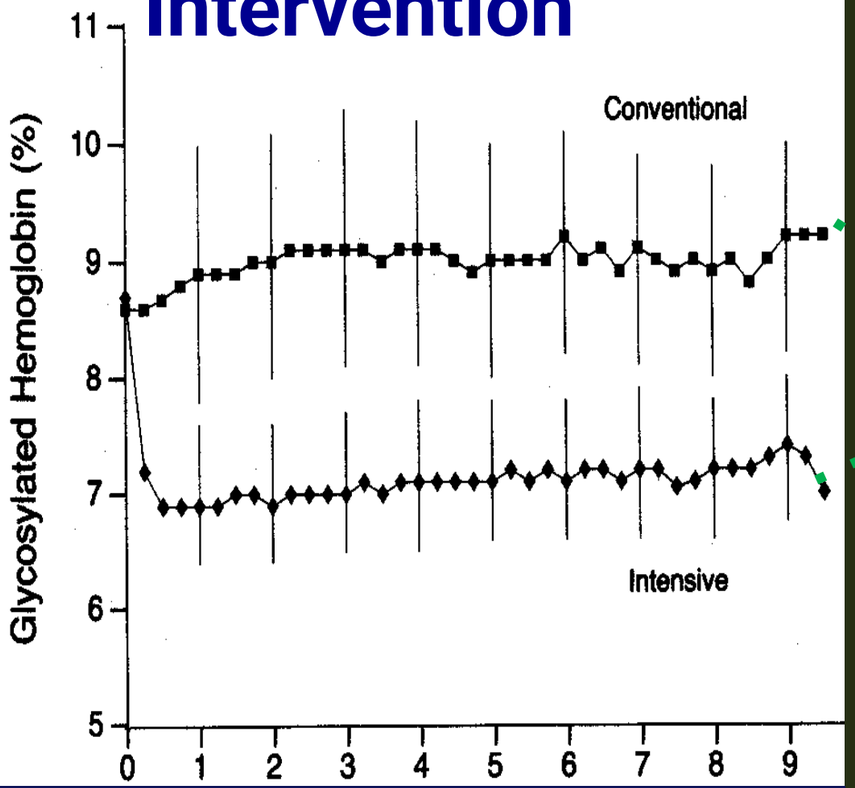
DCCT

Intervention

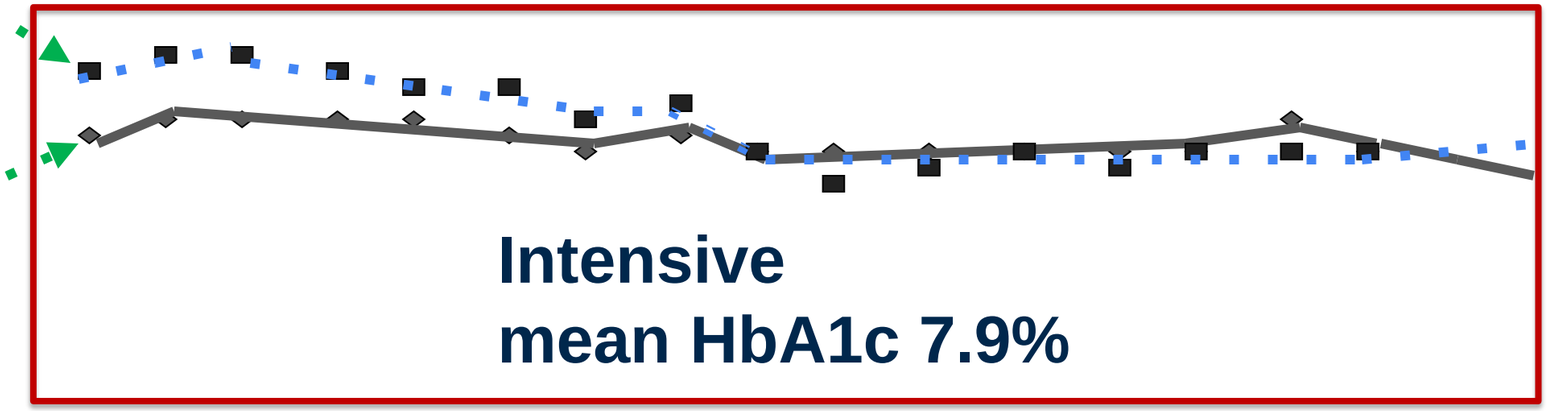
Training

EDIC

Observation



Conventional
mean HbA1c 8.0%



Intensive
mean HbA1c 7.9%

DCCT
1983-93

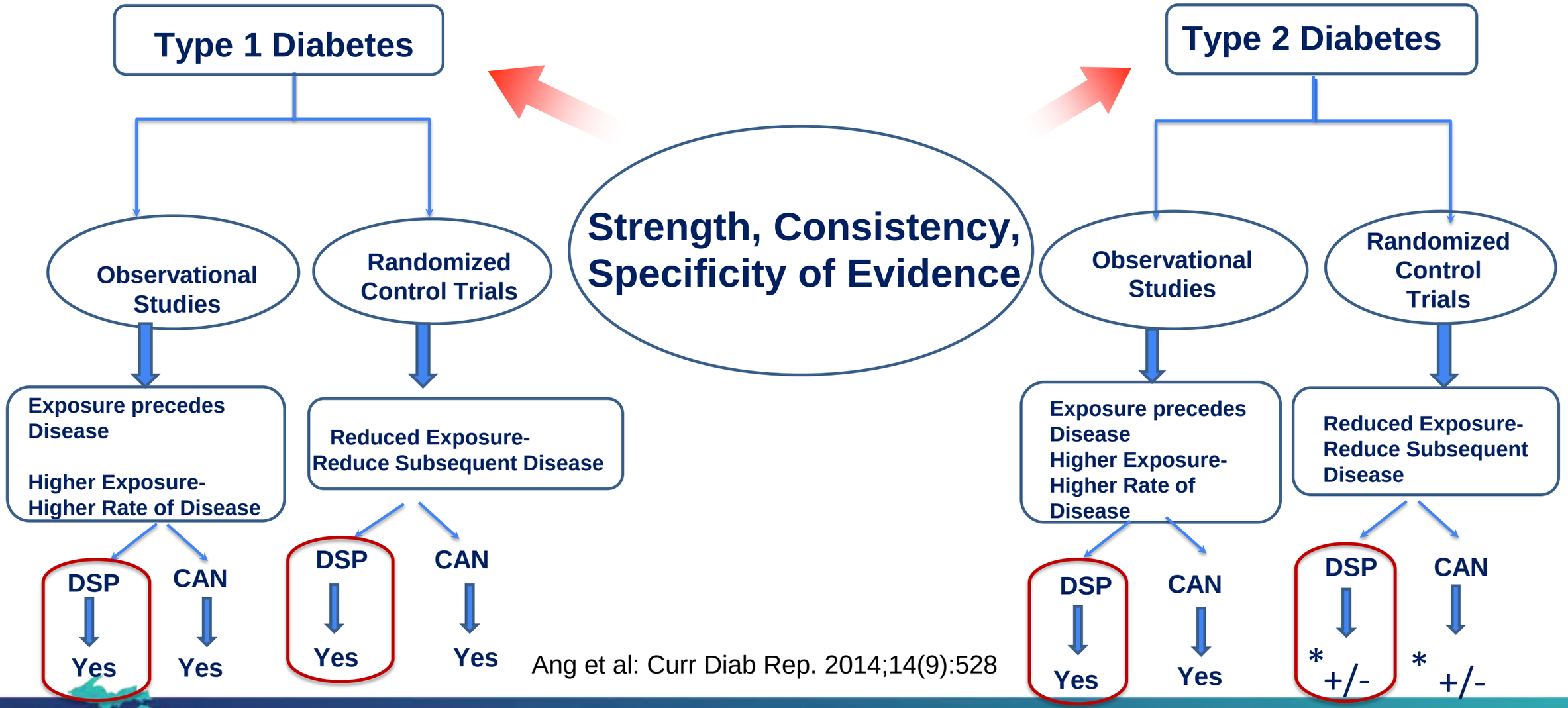
EDIC
1994-present

Glycemic Control:
Lessons learned from DCCT/EDIC for Type 1 Diabetes

Variable	Group	DCCT Baseline %	DCCT Closeout %	EDIC Year 13/14 %
Clinical neuropathy	INT	10	15 **	34 *
	CONV	8	22	41
Abnormal NCS	INT	31	30% Reduction	55 **
	CONV	34		68
Confirmed clinical neuropathy	INT	7	9 **	26 *
	CONV	5	16	34

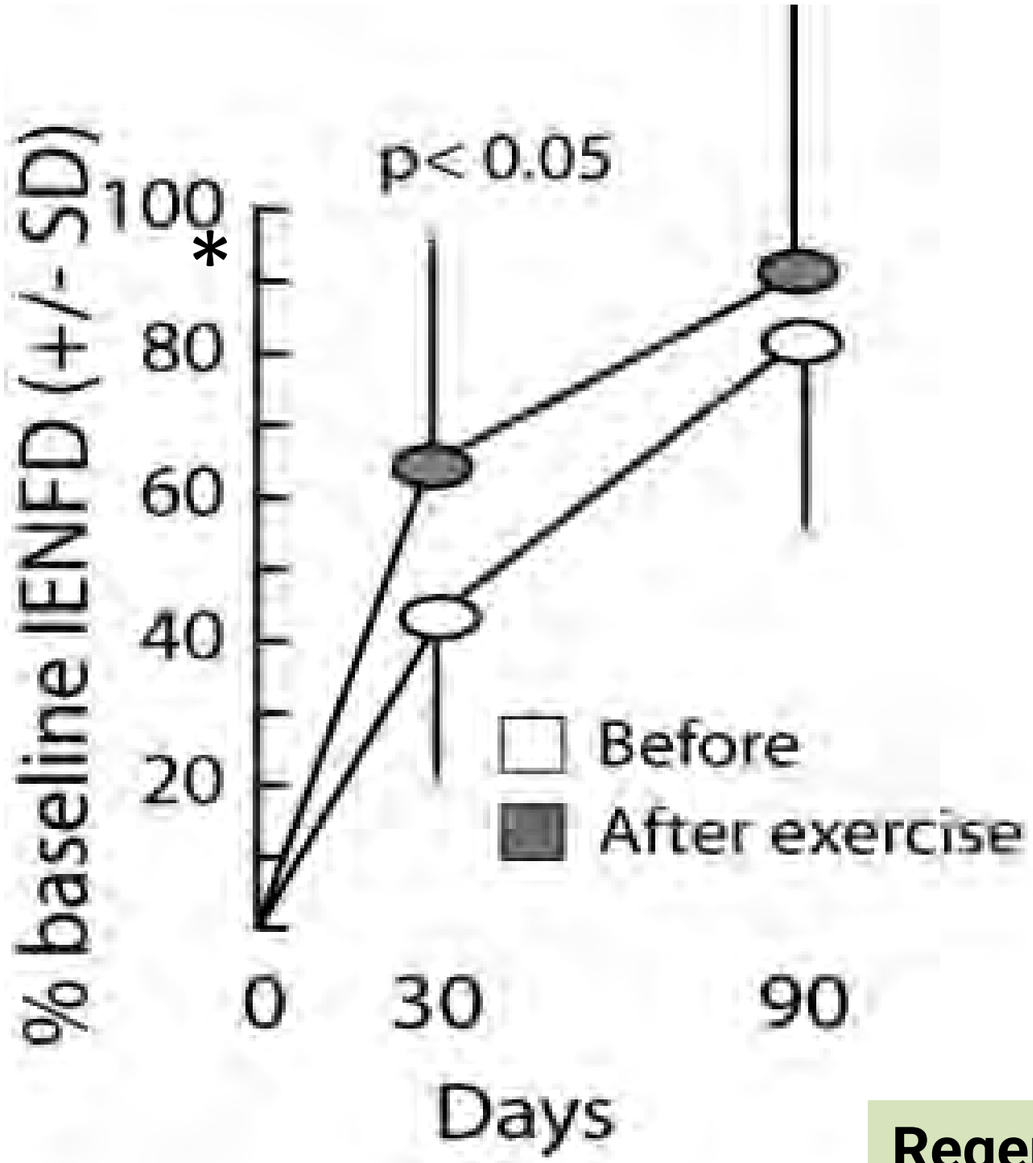
Glucose Control and Neuropathy

*



Ang et al: Curr Diab Rep. 2014;14(9):528

Exercise and DPN



*IENFD = intraepidermal nerve fiber density

Regeneration of nerves

Singleton JR, et al. Annals of Neurology, 2016; 77(1):146-53.

Exercise and DPN

Flow mediated dilation (FMD) response in SFA using Color Doppler Ultrasonography

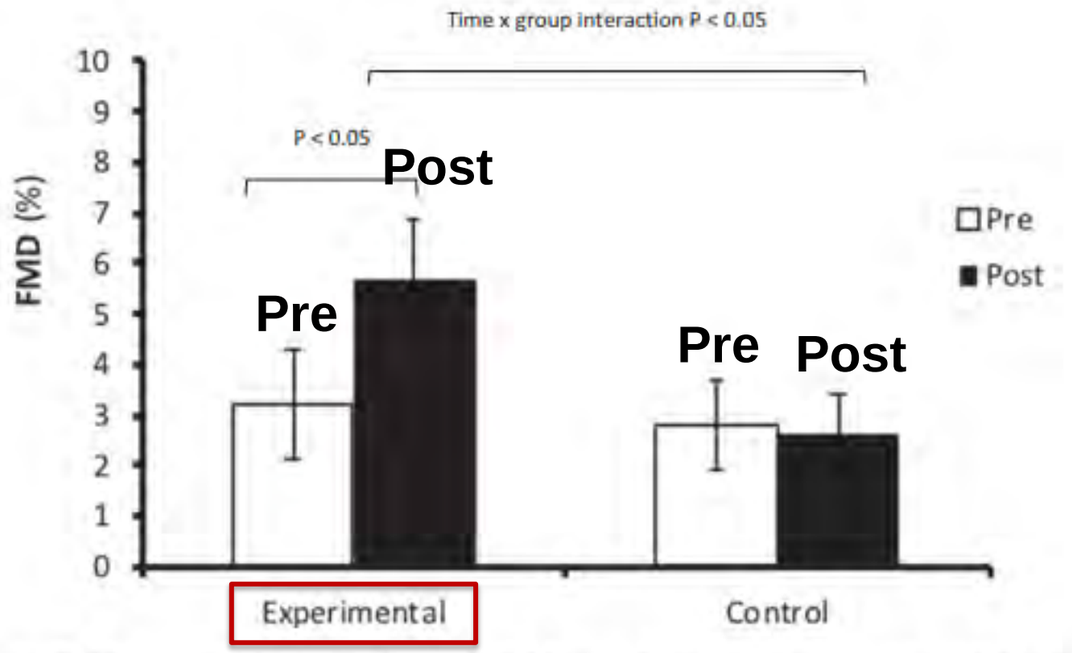
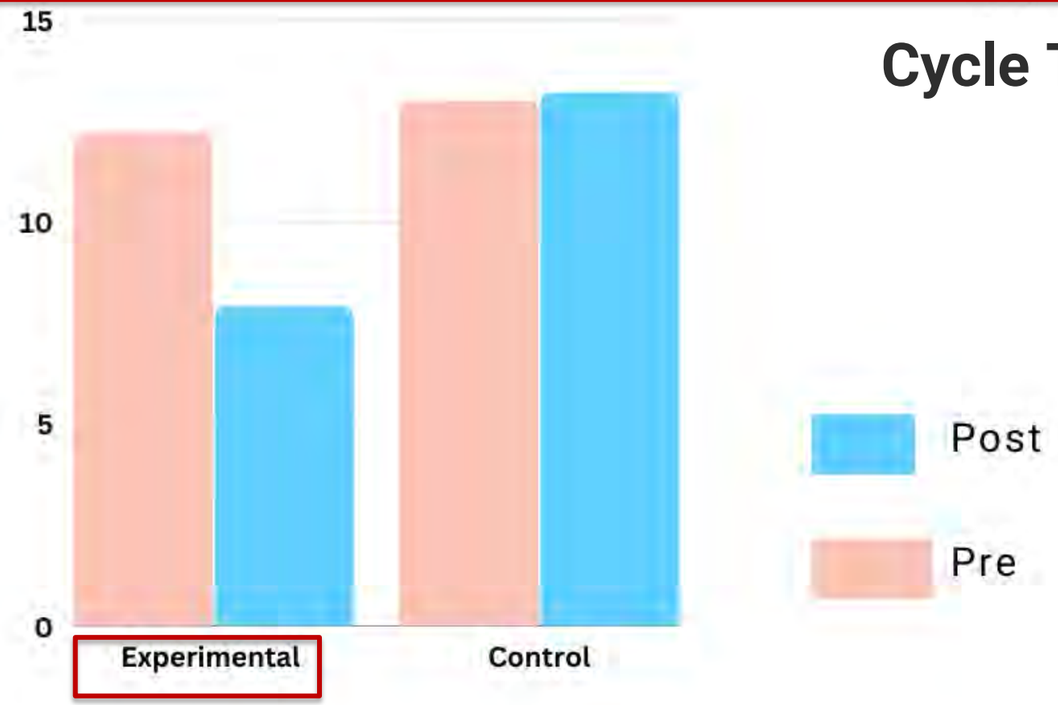


Fig. 2. Hyperemic dilation of superficial femoral artery in the experimental and control groups at baseline and following 12-week.

F. Gholami, et al. Experimental Gerontology 131 (2020) 1

Cycle Training



Michigan Diabetic Neuropathy Score (MDNS)

Vascular function and neuropathic symptoms

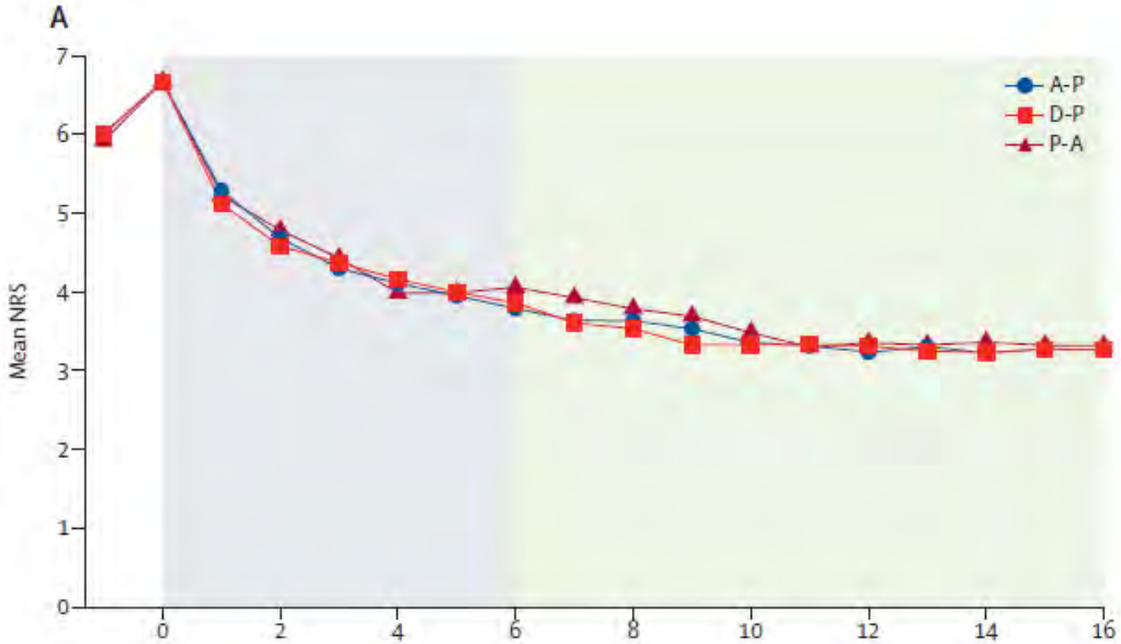
Management of Painful DPN

Drug	Drug Class	Dose		Number Needed to Treat*
		Initial	Effective	
Pregabalin**	Anticonvulsant	25-75 mg, 1-3x daily	300-600 mg/day	3.3-7.7
Duloxetine**	Antidepressant	20-30 mg/day	60-120 mg/day	3.8-11
Gabapentin	Anticonvulsant	100-300 mg, 1-3x daily	1800-3600 mg/day	3.3-7.2
Amitryptyline/ Tricyclics	Antidepressant	10-25 mg daily	25-100 mg/day	2.1-4.2
Capsaicin 8%** Patch	Topical	Apply on mapped painful areas of the feet, up to a total combined surface area of 1,120 cm^2 for both feet for 30 minutes		Not available

*Based on 30-50% improvement in symptoms
**FDA approved for painful DPN treatment

Combination Therapy: OPTION-DM

Multicenter, randomized, crossover trial
N=130 started a first pathway (amitriptyline supplemented with pregabalin; A-P)
N= 97 started a second pathway (pregabalin supplemented with amitriptyline; P-A)
N= 84 started a third pathway (duloxetine supplemented with pregabalin; D-P)



Mean daily pain intensity of the treatment pathways

Tesfaye et al: Lancet Vol 400 August 27, 2022

Opioids for Painful DPN?

American Journal of Case Reports

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Cardiac Arrest Following Drug Abuse with Intravenous Tapentadol: Case Report and Literature Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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2 Division of Critical Care Medicine, New York Presbyterian-Lawrence Hospital Center Affiliated with Columbia University College of Physician and Surgeons, Bronxville, NY, U.S.A.

Patil PR et al, Clin J Pain 2015; 31(5):414-24.
Hoffman EM et al, JAMA Neurology 2017; 74(7):773-79.
Khaja M et al, American Journal of Case Reports 2017; 18:817-21.

ADA Position Statement Algorithm for Treatment of DPN

Is pain due to DPN confirmed?

No/Not sure

Refer to Neurology/Pain Clinic

Yes

Assess comorbidities, potential for AEs,, drug interactions, costs to select initial therapy from the 3 choices below

NO OPIOIDS!

*** Voltage gated ligand (pregab gabapentin**

venlafaxine)

Desipramine)

saicin 8% patch

No clinically meaningful effect

Switch to another agent from above

Try combining agents from above

No clinically meaningful effect/ Not tolerated

Refer to Pain Clinic

Adapted from Pop-Busui, Boulton, et al, Diabetes Care 2017, 40: 136-54

Case

- 60 year old man with 12 years of type 2 diabetes (HbA1c 8-9%), hypertension, dyslipidemia, CAD and chronic low back pain presenting for a clinic visit with burning pain in both feet, worse at night.
- Medications: Metformin 2000 mg/day, lisinopril 40 mg/day, metoprolol 100 mg/day, atorvastatin 80 mg/day, aspirin 81 mg/day, amitriptyline 75 mg/day, oxycodone 15 mg q6 hours prn (for back pain)

Examination

BP: 140/85 mmHg

BMI: 35

Central adiposity

Laboratory:

POC HbA1c 8.2%

Total cholesterol 190 mg/dL

LDLc 70 mg/dL

Triglycerides 256 mg/dL

HDLc 38 mg/dL

Case (continued)

Q.1) What should be the next diagnostic steps?

A. Refer to neurology and EMG testing.
B. Perform a focused neurological exam in the office and test for vibration and pinprick touch sensation in the office.
C. Assess light touch sensation in the office.
D. Check Vitamin B12 and serum immunoelectrophoresis.

Correct Answers: B, D

DPN Mimics

METABOLIC DISEASE
Thyroid
Renal

SYSTEMIC DISEASE
Vasculitis
Paraproteinemia
Amyloidosis

INFECTIOUS
HIV
Hepatitis B
Lyme disease

INFLAMMATORY
Chronic inflammatory demyelinating polyradiculoneuropathy

NUTRITIONAL
Vitamin B12 deficiency
Pyridoxine
Thiamine
Tocopherol

INDUSTRIAL AGENTS
Acrylamide
Organophosphorous agents

DRUGS
Alcohol
Amiodarone
Chemotherapy

HEAVY METALS
Arsenic
Mercury

HEREDITARY

Pop-Busui, Boulton, et al, Diabetes Care 2017;40:136-154

Case (continued)

Q.2) How would you manage pain in this patient?

A. Start amitriptyline 50 mg at night
B. Prescribe pregabalin 75 mg twice/day and titrate dose to 300 mg/day
C. Recommend tapentadol extended release 50 mg twice a day
D. Stop oxycodone

Correct Answer: B and D

Take Home Messages

- DPN is a prevalent complication of both type 1 and type 2 diabetes.
- Has important clinical consequences: severe pain, impaired function, low quality of life, depression and anxiety, increased mortality, and amputation risk.
- It can be easily diagnosed using history, targeted physical examination and simple, readily available instruments.
  - Sophisticated techniques and referrals to neurology are rarely needed, unless symptoms and signs are atypical.
- Pain management should follow evidence and avoid narcotics.

Questions?

Thank you