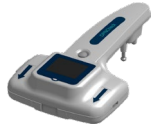
NeuroMetrix DPNCheck

DPNCheck 2.0 Device Training

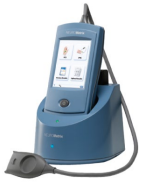
Commercial stage neurotechnology company

- Based in Woburn, MA
- Trade on Nasdaq (NURO)
- Over 5M patients served
- Trusted by largest VBC providers and MA payors
- Three commercial products
- Extensive IP portfolio
- Fully integrated operations

DPNCheck®



ADVANCE®



Quell®

Our mission is to improve patient outcomes and population health by detecting, quantifying, and helping providers to reduce the impact of neurological disorders

Polyneuropathy Background

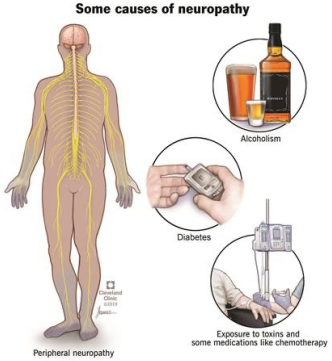
Polyneuropathy is common and leads to substantial morbidity and mortality

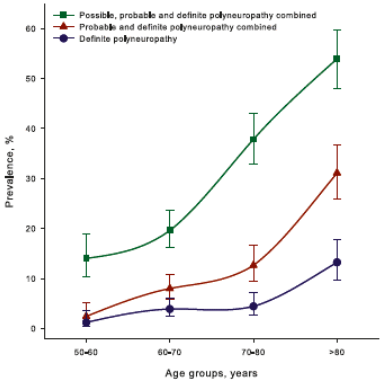
- Clinical testing has low sensitivity for early-stage disease
- Laboratory testing is expensive, only appropriate for confirmation
- Unmet need for accurate, widely available, screening test for polyneuropathy

Prevalence*

10% in overall population

Up to 30%+ in Medicare Population





foot ulcers / amputation

falls

neuropathic pain

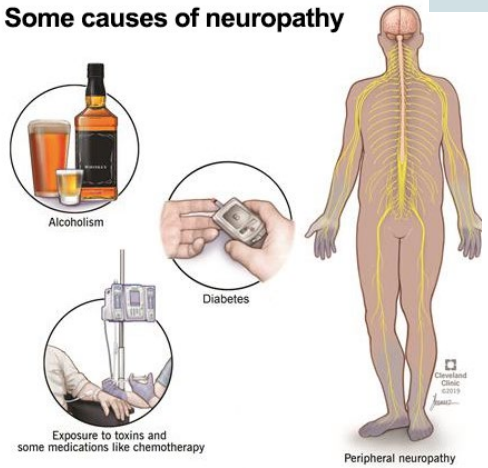
Multiple Causes → High Prevalence → Serious Complications

*Mold et al. 2004. Hanewinckel et al. 2016. Singer et al. 2012. Dyck et al. 1993.

Etiology of Peripheral Neuropathies

- **Metabolic**
  - Diabetes (30% of patients)
  - Metabolic syndrome
    (IGT, hypertension, dyslipidemia, obesity)
  - B12 deficiency
  - Thyroid disease
- **Chronic Hypoxia**
  - Obstructive sleep apnea
  - COPD
- **Toxic**
  - Chemotherapy Induced Peripheral Neuropathy (CIPN)
  - Alcoholic neuropathy, uremic neuropathy
- **Inflammatory**
  - Rheumatoid arthritis
  - Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
  - Guillain-Barré syndrome (GBS)
- **Infectious**
  - HIV, Lyme disease
- **Hereditary**
  - Charcot-Marie-Tooth (CMT)

"Current evidence supports the association of the metabolic syndrome and its individual components with neuropathy."

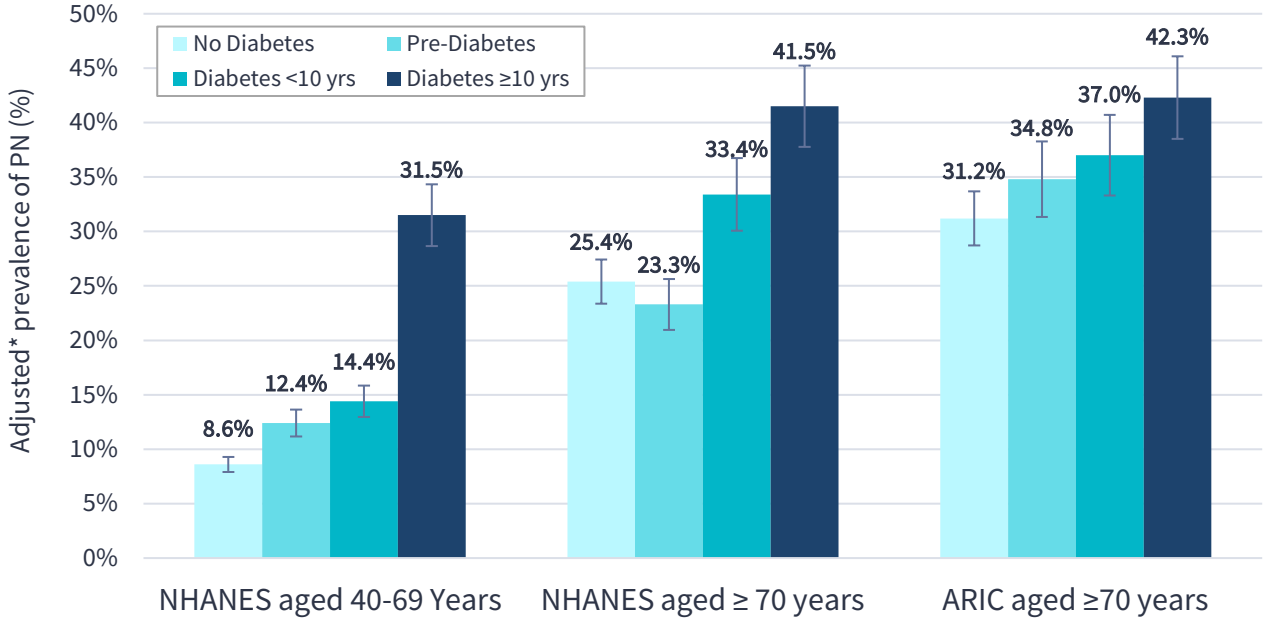


Peripheral neuropathy has a high population prevalence - 2x more common than PAD

Hicks et al. Sci Rep, 2021.: https://doi.org/10.1038/s41598-021-98565-w

NHANES: 1999–2004 National Health and Nutrition Examination Survey

ARIC: 2016-2017 Atherosclerosis Risk in Communities Study



*Age, sex and race-adjusted prevalence of peripheral neuropathy stratified by diabetes status in US adults aged 40-69 and ≥ 70 Years (NHANES, 1999-2004) and ARIC participants aged ≥ 70 years (Visit 6, 2016-2017).

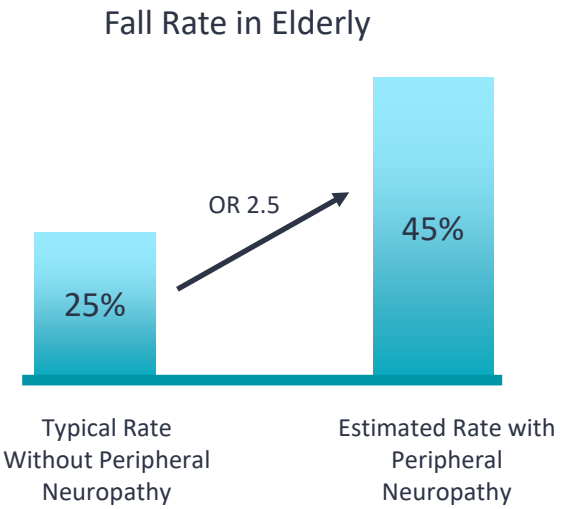
Peripheral neuropathy is an independent risk for falling and fall severity

Peripheral Neuropathy

- Decreased Sensation
- Altered Proprioception (sense of body position and movement)
- Weakness
- Neuropathic Pain

- Impaired postural stability
- Unstable gait

Increased Fall Risk (OR 1.5 – 2.5)
Increased Fall Severity



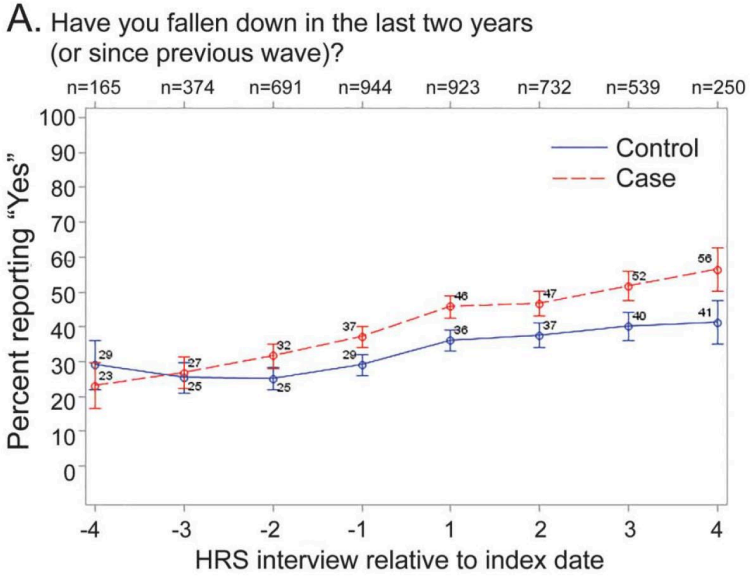
OR, odds ratio.

References: Richardson and Hurvitz. J Gerontol, 1995. Cheng et al. J Clin Nurs, 2002. Erlandson et al. J Acquir Immune Defic Syndr, 2019. Riskowski et al. Journal of Foot and Ankle Research, 2012.

Elevated risk of falls and pain precede peripheral neuropathy Dx by several years

Callaghan et al. Neurology, 2015: https://doi.org/10.1212/WNL.0000000000001714

Figure 1 **Comparison of the patient-oriented outcome trajectories between patients with neuropathy and propensity-matched controls**



"We found that older adults with neuropathy have more falls and pain and lower self-rated health compared to carefully matched controls without neuropathy. These differences were present 3–5 years prior to a neuropathy diagnosis and persist for several years after diagnosis."

"This finding may be partly explained by a delay in diagnosis in this highly prevalent condition, and also highlights the fact that neuropathy often develops slowly over time. Patients typically report neuropathic symptoms to their physician years after their insidious onset."

Clinical screening tests have low sensitivity

- Monofilament only detects loss of protective sensation

Perkins et al. Diabetes Care, 2001.

DPNCheck® **

**Corrected for false positive rate.*

***Referenced publication utilized traditional NCS. DPNCheck sural nerve conduction demonstrated to have high agreement with traditional NCS.*

Kural et al. 2018. Kamiya et al. 2021. Scarr et al. 2018. Lee at al. 2014.

DPNCheck® Overview

DPNCheck is a standardized and automated sural nerve conduction test

- Performed in minutes by medical assistant
- Gold standard NCS technology
- Device + single-patient use biosensor
- High diagnostic accuracy
- Validated in 30+ peer-reviewed studies
- 2M patients tested over 10 years

device display is simulated

Device Components

The device is powered by a 3V Panasonic CR123A battery. USB C Cable is provided for optionally uploading test results to Reporter PC application.

Device Configuration and Setup

Install Battery

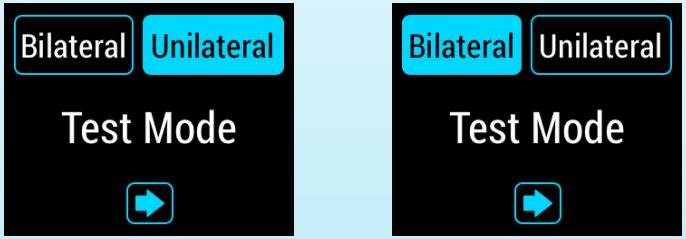
- Remove battery door with thumb/finger at arrow
- Insert the CR123A battery, match +/- to indicators

Apply Gray Foam

- Remove brown liner (stickier), align with device.
- Remove white liner and keep for protection of foam when not in use.

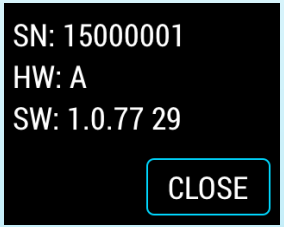
Device Configuration and Setup

Test Mode



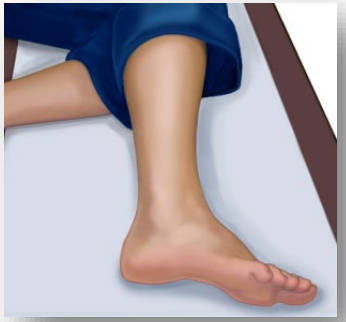
- Press button to power on device.
- Hold button 5 seconds, view Test Mode screen.
- Blue button shows selected. Change selection if needed

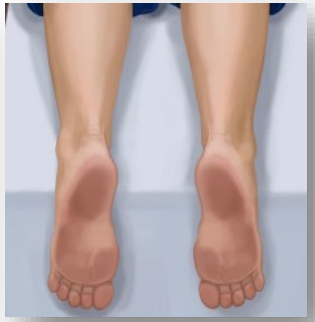
View Device Information

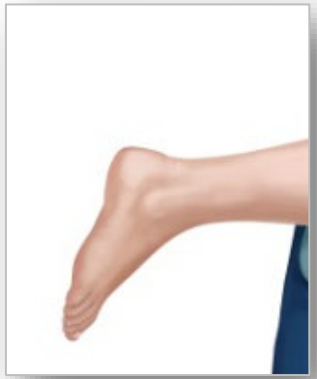


- Select Next from Test Mode screen, view Device information
- Serial number matches number printed on barcode inside battery compartment.

Step 1a: Position Patient







The patient should be in **comfortable** position that allows for relaxation of the leg and foot - it is important that the patient remains **relaxed** during the test.

Make sure you have **access** to the outer ankle bone and the calf.

Make sure you can **see the midline** of the calf.

Patient Positioning Techniques

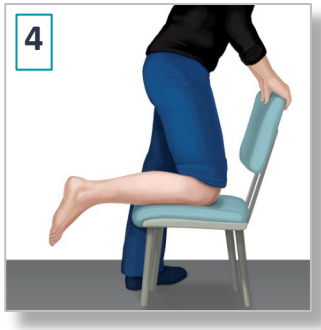
Lying Methods

Position – side

Position – side

Position - prone

Chair Method



Check Your Position

Tester:

- Patient's outer ankle bone and Achilles tendon are visible
- Stable grip on device

Patient:

- Fully relaxed upper and lower leg

Conditions above not met? Adjust position or try a different one.

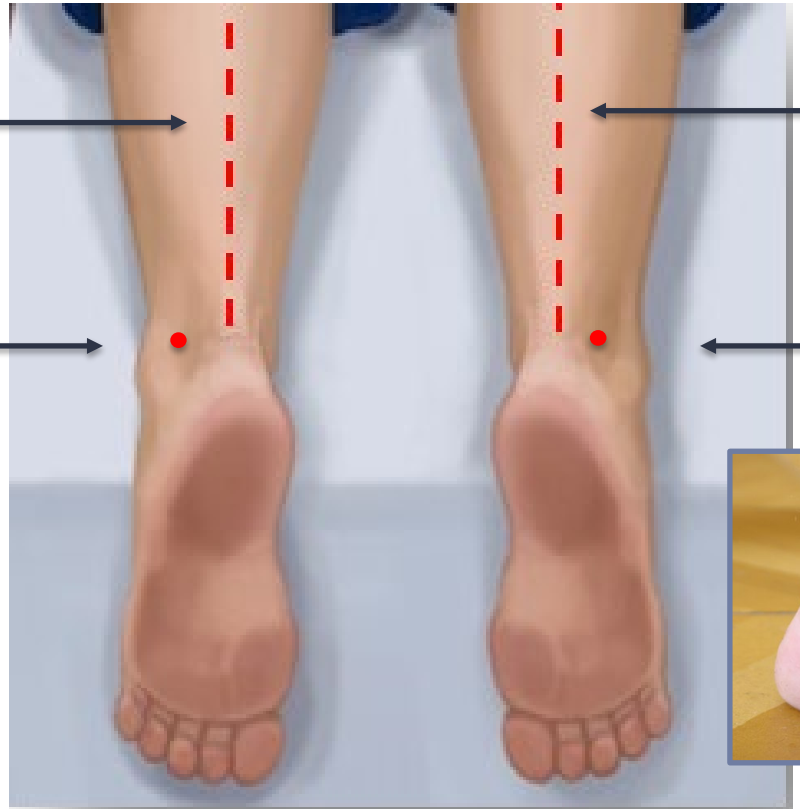
Anatomical Landmarks

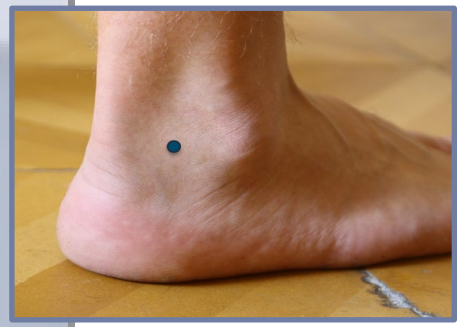
Midline to Calf

Midline to Calf

Between ankle bone and the Achilles tendon

Between ankle bone and the Achilles tendon





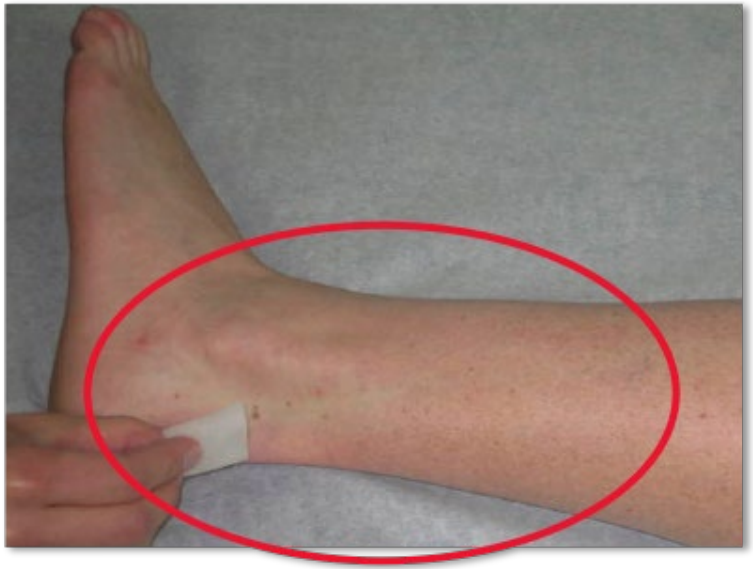
Preview: Device Alignment

The long probe should align with the outer ankle bone and placed between the ankle bone and the Achilles tendon.

Ensure that device is aligned to the midline.

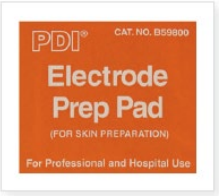
Ensure that blue arrow is pointing to the back of the knee.

Step 1a: Skin Preparation



Vigorously scrub the test area with the preparation pad provided.

Remove any dirt, lint, moisturizer, etc.

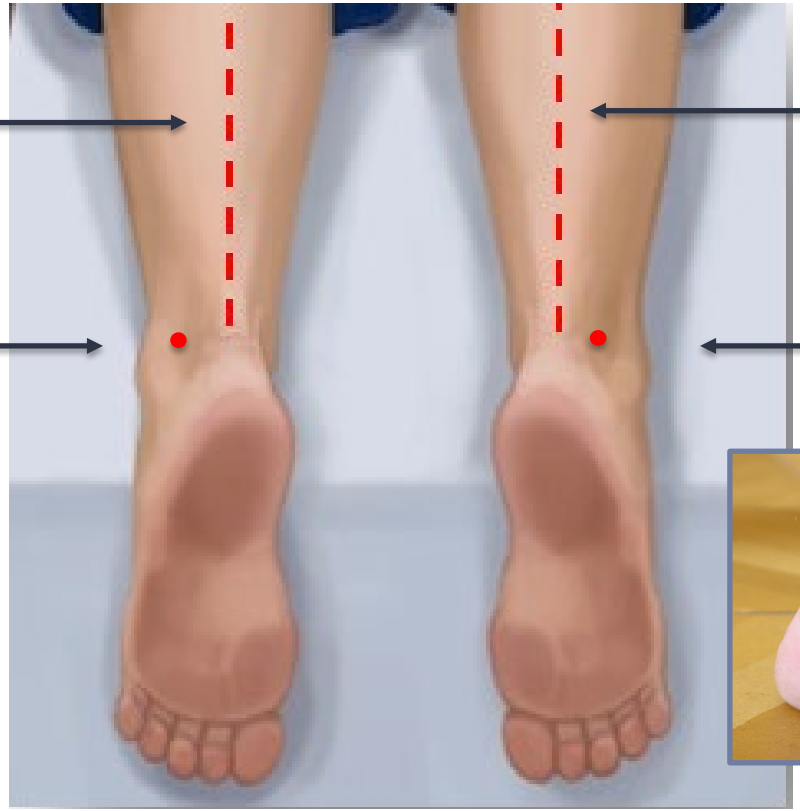


alcohol

Step 1b: Mark Anatomical Landmarks

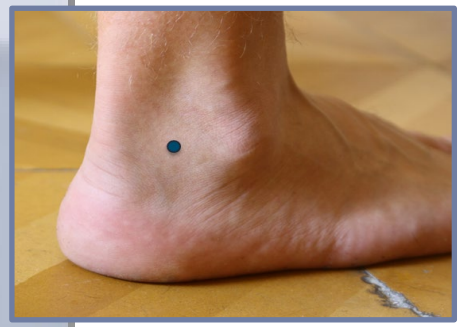
Midline to Calf

Between ankle bone and the Achilles tendon



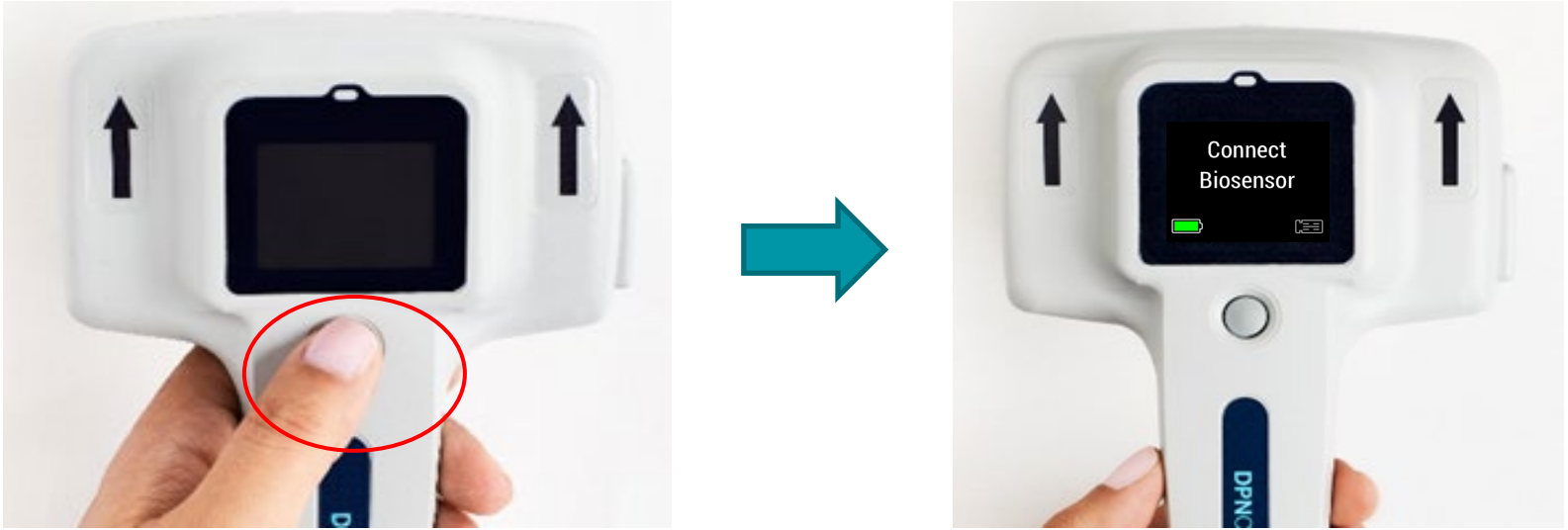
Midline to Calf

Between ankle bone and the Achilles tendon



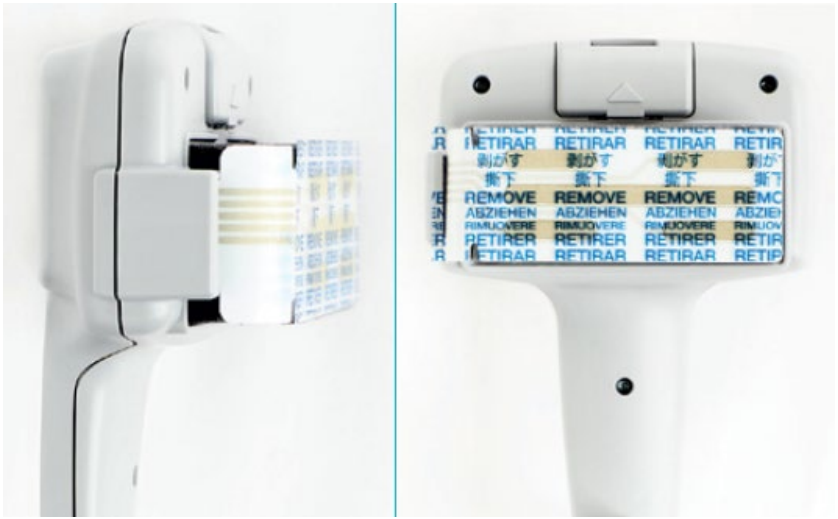
Use a skin marker to draw the marks shown in the image.

Step 2: Power On



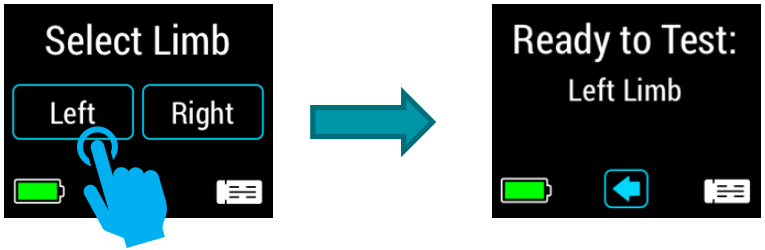
- Power on the device by pressing the power button
- The display will prompt you to connect the biosensor

Step 3: Insert Biosensor

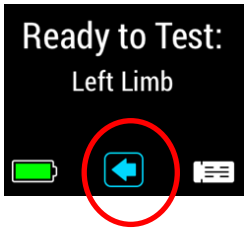


- Remove the white liner from gray foam (if not already done) and set aside for later use.
- **Fully** insert the biosensor into the port.
- Align the biosensor to the foam
- The display will prompt you to select the limb (next slide).
- *Tip: Align the biosensor with the foam on all sides, "REMOVE" label side faces up.*

Step 4: Select Limb



- Select the leg to be tested on the touch screen.
- Once selected, “Ready to Test:” will be displayed followed by the limb selected (and green LED will illuminate).
- The back arrow allows you to return to the previous screen if needed.



Step 5: Apply Gel

- Apply a small amount of Signa gel to each probe*.
- The head of the probe should be covered with gel.
- *Tip: Remove excess gel that may lead to gel smearing between the probes.*

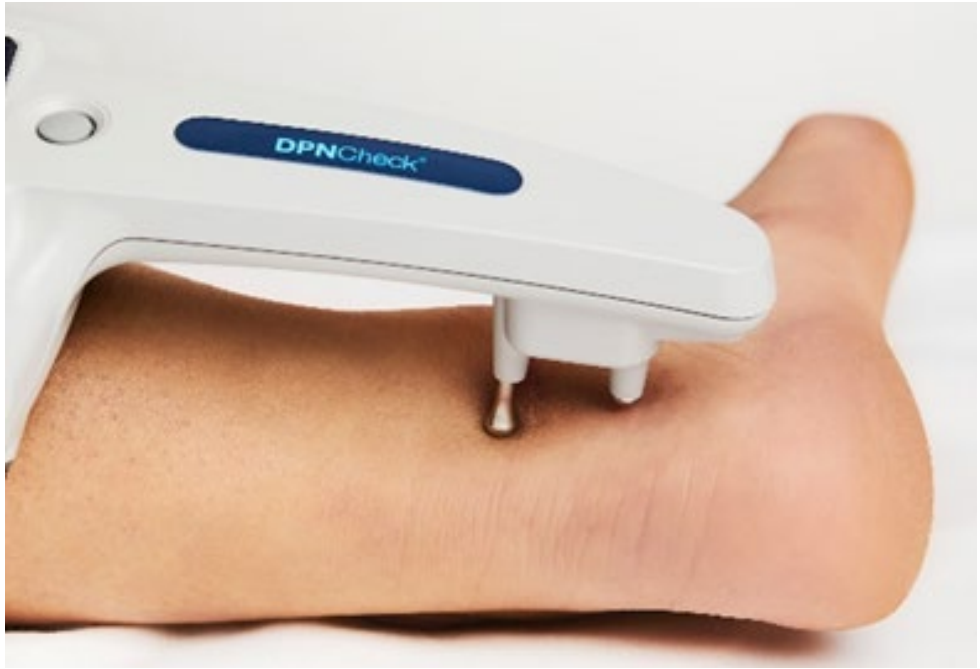
**Note: Must use the Signa gel provided with biosensors.*

Step 6: Remove Biosensor Backing

- Remove the backing from the biosensor*.

**Note: Save the foam liner or biosensor liner to protect the foam when device is not in use.*

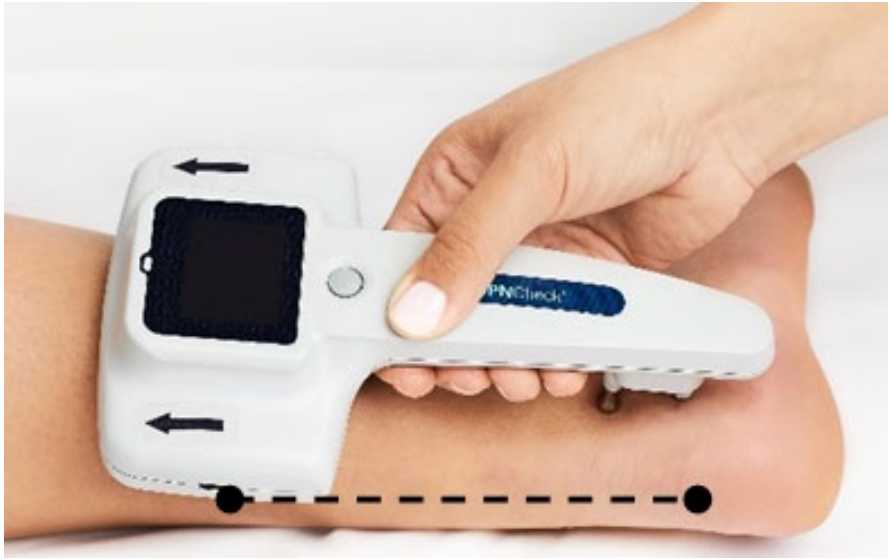
Step 7: Place Probes



- Place the long probe at the mark made between center of outer ankle bone and Achilles tendon.
- Do not press down yet.

- *Tip: The probes should be behind and not over the ankle bone.*

Step 8: Place Biosensor



- Align the edge of the biosensor to the mark made along the center of the Achilles tendon.
- Arrow closest to Achilles will point toward back of the knee.
- Do not press down yet.

Step 9: Finalize Placement and Contact

- Check your placement
  - Is long probe **behind** Ankle Bone?
  - Is edge of biosensor along **center** of Achilles?
- Check that gel has not smeared between probes
- Press down on **probes** – both probes contact fully
- Press down on **foam** – biosensor contacts fully
- Make sure your **grip is stable** and **pressure is even** - hold with two hands if needed

Step 10: Start Test

- Press the button to start.
- The display will show “Testing”.
- During the test, the LED blinks green when each stimulus is delivered.
- Maintain constant pressure during the test.
- Test time will vary but generally lasts for 10-15 seconds.

Step 11: View Results

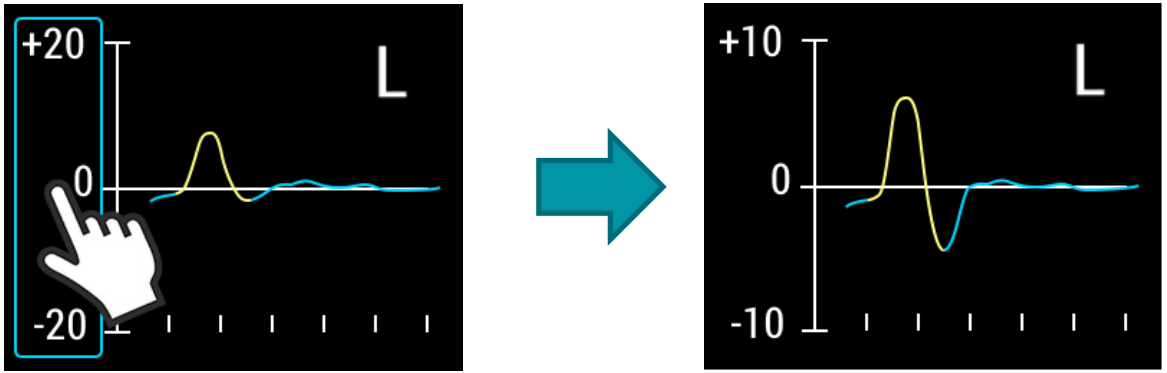
- Once results are displayed, the test is complete.
- Remove device from the leg.
- **Amp** shows the amplitude of the sural nerve response in microvolts.
- **CV** shows the conduction velocity of the sural nerve response in meters per second.
- **Limb** tested shown in upper right of screen.

Optional Review: Waveform

- To view the waveform of the measured sural response, press area where Amp and CV results are displayed.
- When you touch that area, it will highlight with an outline.
- Once you remove your finger, the waveform will display.
- Press in the waveform area to return to the Amp/CV results.

Optional Review: Waveform

- For small amplitude waveforms, scaling may be adjusted.



Test Complete

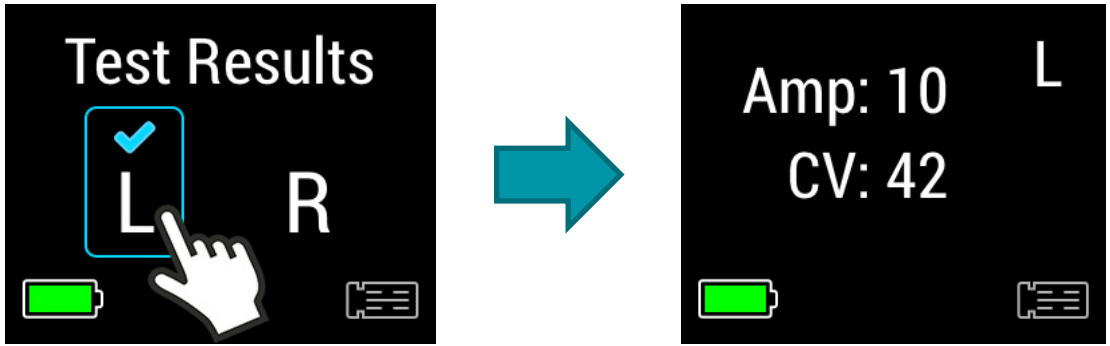
- When results are shown, the test is complete.
- Record the results directly from the device, or upload to the Reporter application.
- To start a new test right away, press the button or insert a new biosensor.
- Device will power off after 1-2 minutes of inactivity.

Testing Protocol

- The test will provide a nerve conduction result the first time in most patients.
- If the first test does not provide a result, the test should be repeated.
  - Pressing the test button again is usually all that is required.
- If the repeat test does not provide a result, the opposite leg should be tested.
  - The same biosensor may be used on both legs.
- There will be a small percentage of patients that you will not be able to obtain results on.

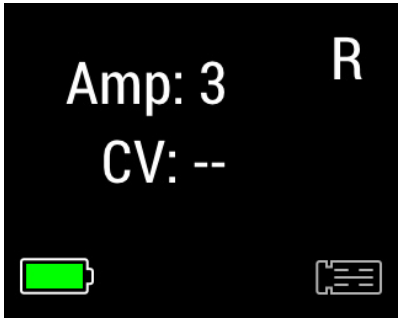
Review Results

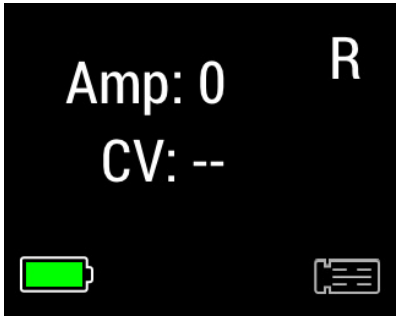
- After device powers off, you can still review your most recent results:
  - Power on device with no biosensor connected to show Home screen.
  - Blue outline and checkmark indicate which limb has a result.
  - Press button or touch limb to navigate to results.
  - Press button to return to Home screen.



Low Amplitude Results

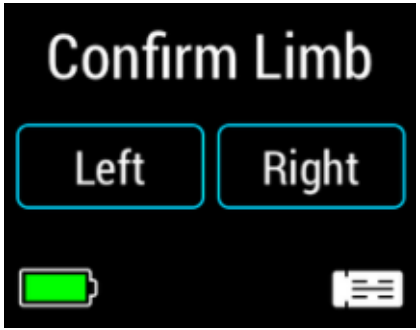
- In some cases where amplitude of sural nerve response is low, only Amp will be reported.
- These are valid test results.

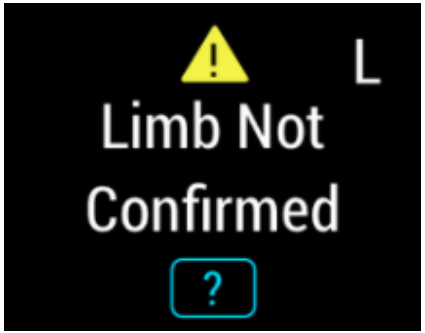




Confirming Limb

- In some cases, you may be prompted to confirm the limb during the test.
- If limb matches original selection, results are reported.
- If limb does not match original selection, test must be repeated.



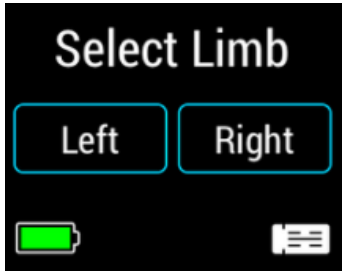


Error Results

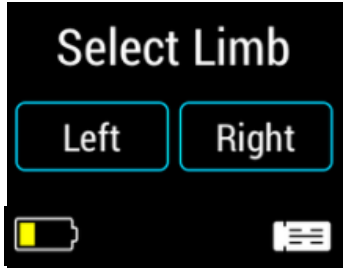
- DPNCheck 2.0 has a number of internal checks to ensure that data quality is sufficient for reporting results.
- Error message will be shown if results cannot be reported.
- Help info screen ? contains troubleshooting information (also included in Reference Guide card).

Battery

- DPNCheck 2.0 uses the Panasonic CR123A battery (replacements can be ordered through NeuroMetrix).
- Single battery should last at least 100 tests.
- Battery icon shows when to replace.



Battery OK

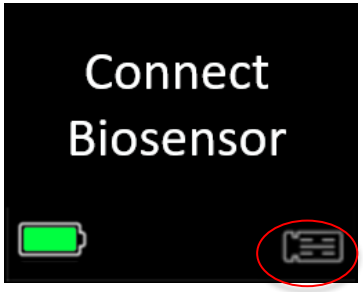


Battery Low,
Replace soon

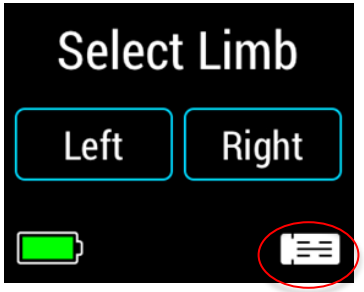
Replace Immediately*
**When battery very low, device may not power on.*

Biosensor Icon

- DPNCheck 2.0 indicates proper biosensor connection



No Biosensor Connected



Biosensor Connected

Cleaning/Re-Use

- The biosensor may be used to test other leg on the same patient if needed.
- The biosensor must be changed between patients.
- The device probes should be cleaned between patients
  - Wipe away excess gel
  - Isopropyl Alcohol wipes may be used to clean/disinfect probes
  - Check temperature lens between probes for gel and wipe away
- The foam does not contact the patient and should not need cleaning unless contaminated. Replace the foam when no longer sticky.
- A soft cloth or wipe with water or isopropyl alcohol may be used to clean the unit exterior as needed; do not use abrasive cleaners or strong solvents.

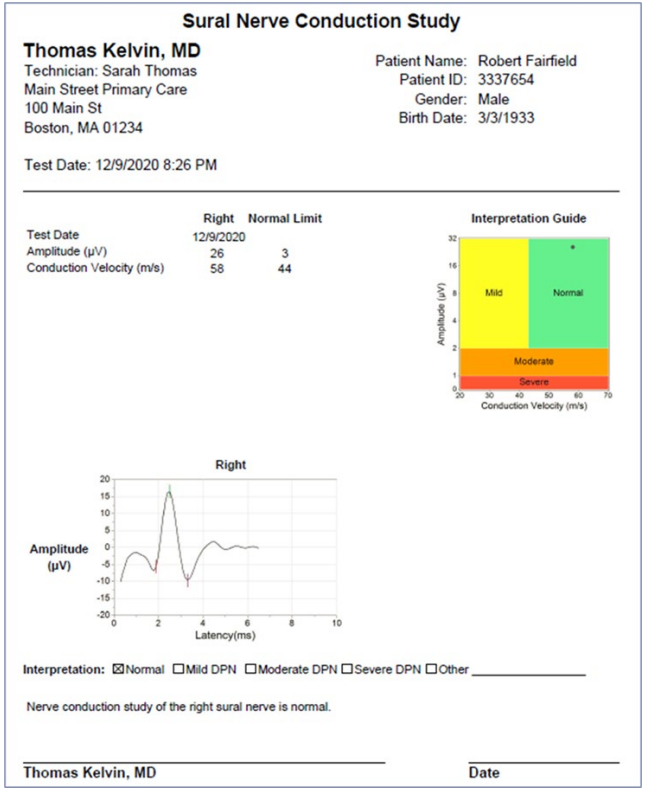
Documentation & Reporting

Reporting Documentation & Interpretation

- **Report Generation Software:**
  - Generate report (PDF, HL7 or XML)
  - Automatic comparison to normal limits
  - Archive data

- **NCS waveforms and values provide detailed documentation of neuropathy status**

- **Currently relies on manual data entry, development underway for EHR integration solution.**



Sural Nerve Conduction Study

Thomas Kelvin, MD
Technician: Sarah Thomas
Main Street Primary Care
100 Main St
Boston, MA 01234

Patient Name: Robert Fairfield
Patient ID: 3337654
Gender: Male
Birth Date: 3/3/1933

Test Date: 12/9/2020 8:26 PM

	Right	Normal Limit
Test Date	12/9/2020	
Amplitude (μV)	26	3
Conduction Velocity (m/s)	58	44

Interpretation Guide

Right

Interpretation: ☒Normal ☐Mild DPN ☐Moderate DPN ☐Severe DPN ☐Other _____

Nerve conduction study of the right sural nerve is normal.

Thomas Kelvin, MD

Date

Resources

- DPNCheck 2.0 User Manual (Model NC-040) is available on the website: www.dpncheck.com/dpncheck-user-manual

- The following materials are provided with your DPNCheck device:
  - Reference Guide with quick-start instructions
  - Patient Positioning Guide
  - Interpretation Guide (without age/height adjustment)

Contact Information

For immediate help when testing contact:

NeuroMetrix Customer Service @ (888) 786-7287

Questions and discussion

APPENDIX:
Documentation & Research

DPNCheck® has been clinically validated

- Published data on thousands of patients

Over 30 peer-reviewed clinical studies and review articles

DPNCHECK DETECTS DIABETIC PERIPHERAL NEUROPATHY WITH HIGH SENSITIVITY AND SPECIFICITY

Study Publication	Type 2	Type 1	No Diabetes	Total	Reference Diagnosis	Sensitivity	Specificity
Binns-Hall et al. 2018	231	5	0	236	Clinical	0.84	0.68
Papanas et al. 2019	0	53	0	53	Clinical	0.96	0.93
Chatzikosma et al. 2016	114	0	46	160	Clinical	0.91	0.86
Hirayasu et al. 2018	92	0	0	92	Clinical	0.85	0.86
Lee et al. 2014	28	16	0	44	NCS	0.95	0.71
Kural et al. 2018	168	0	0	168	NCS	0.82	0.85
Scarr et al. 2018	0	68	71	139	NCS	0.86	0.79
Total	**633**	**142**	**117**	**892**		**0.88***	**0.82***

*Summary sensitivity and specificity determined by bivariate meta-analysis.

9 out of 10 polyneuropathy cases detected

Half of peripheral neuropathy is coded as non-specific, but may have an identifiable etiology

HCC075	Coded comorbidities that may be causative for peripheral neuropathy*	G6289/ G629 (Unspecified Polyneuropathy)	2019 Claims Data
No	Rheumatoid Arthritis	Yes	0.71%
No	Substance Dependence	Yes	0.61%
No	AIDS/ HIV	Yes	0.03%
No	Cancer	Yes	0.89%
No	Unspecified Diabetes	Yes	0.71%
No	Cirrhosis/ End-Stage Liver	Yes	0.13%
No	Dialysis	Yes	0.76%
Possible Yes	**At least one comorbidity**	**Yes**	**2.81%**
No	**No comorbidity***	**Yes**	**2.58%**

*Additional potential causes include metabolic syndrome, hypoxic conditions, nutritional deficiencies

Total Unspecified/ General Neuropathy **5.39%**

ghg

Source: Gorman Health Group analysis, 2021

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APPENDIX:
Gorman Health Group Analysis

CODING:
Gorman Health Group analysis of polyneuropathy coding in Medicare Advantage (2021)

- Analysis of claims data from 4 MA plans (2018-2020 data sets)
- Recommended best practices for polyneuropathy documentation and coding

ghg

Half of peripheral neuropathy is coded as non-specific, but may have an identifiable etiology

- Analysis of coding data from 4 Medicare Advantage plans
- Prevalence of peripheral neuropathy by ICD-10 codes **~15%**
  - Diabetic PN (~10%) and non-diabetic PN (~5%)
- Most non-diabetic peripheral neuropathy coded as non-specific (G6289, G629)
  - At least 50% may have an identifiable etiology
  - Potential causes often coded in these patients (e.g., RA, alcoholism, AIDS/HIV, kidney disease/dialysis)
- Peripheral neuropathy documentation is often incomplete
  - Lack of specificity, status and current treatment
  - Use of auto-populated EMR defaults

HCC075	Coded comorbidities that may be causative for peripheral neuropathy*	G6289/ G629 (Unspecified Polyneuropathy)	2019 Claims Data
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Possible Yes	At least one comorbidity	Yes	2.81%
No	No comorbidity*	Yes	2.58%
		Total Unspecified/ General Neuropathy	5.39%

*Additional potential causes include metabolic syndrome, hypoxic conditions, nutritional deficiencies

ghg

Source: Gorman Health Group analysis, 2021

Peripheral Neuropathy - HCC & ICD-10

CMS HCC	CMS HCC DESCRIPTION	Coeff
18	Diabetes with Chronic Complications (Diabetic Neuropathies)	.302
75	Myasthenia Gravis/Myoneural Disorders and Guillain-Barre Syndrome/Inflammatory and Toxic Neuropathy	.472

Inflammatory & Toxic Neuropathies	
G611	Serum neuropathy
G6181-G619	Inflammatory Neuropathies
G620	Drug-induced polyneuropathy
G621	Alcoholic polyneuropathy
G622	Polyneuropathy due to other toxic agents
G6281	Critical illness polyneuropathy
G6282	Radiation-induced polyneuropathy
G63	Polyneuropathy in diseases classified elsewhere
G651-G652	Sequelae of other inflammatory; toxic neuropathy
Diabetic Neuropathy	
E1140	Type 2 diabetes mellitus with diabetic neuropathy, unspecified
E1142	Type 2 diabetes mellitus with diabetic polyneuropathy
E1143	Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy
*Assign appropriate diabetes type for first 3 characters (E08 due to underlying condition; E09 Drug or Chemical Induced; E10 Type 1; E13 Other specified type	

ghg

Source: Gorman Health Group analysis, 2021

Peripheral neuropathy should be coded with specificity if underlying cause is identified

- **Accurate assignment of ICD10 code is dependent upon the underlying cause for the peripheral neuropathy, which also impacts HCC qualification**
  - Idiopathic (G603) and unspecified neuropathies (G629) are not included in the risk adjustment models
  - Unspecified or idiopathic codes are often reported when a specific cause should be identified via clinical work-up

- **ICD10 guidelines assume a causal relationship between peripheral neuropathy and diabetes only**
  - Causational or linking verbiage is needed for all other specific types of neuropathy

Inflammatory & Toxic Neuropathies	
G611	Serum neuropathy
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Rheumatoid Polyneuropathies	
M0550 – M0559	Rheumatoid polyneuropathy with rheumatoid arthritis (site specificity needed, or unspecified site)

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ghg

Source: Gorman Health Group analysis, 2021

Avoid these common peripheral neuropathy coding pitfalls:

- Omitting a coexisting/underlying peripheral neuropathy diagnosis 1x per year in an otherwise uncomplicated patient when managed with neuropathy medications or other neuropathy interventions
- Failing to assign code combinations of diabetes and another specific neurological manifestation
  - Peripheral neuropathy may have multiple underlying causes
  - Diabetic peripheral neuropathy may be exacerbated by other events or conditions (e.g., chemotherapy, alcoholism)
- Defaulting to unspecified/idiopathic peripheral neuropathy when likely to be associated with a known underlying condition/cause following clinical work-up
- Conflicting documentation within the review of symptoms (ROS) or physical exam
  - Many EHR templates auto-populate as 'normal'
  - It is important to update these fields when assigning diagnosis codes in the Assessment and Plan if clinically indicated
  - Patients with peripheral neuropathy may not report symptoms due to asymptomatic disease or lack of recognition due to slow progression

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ghg

Source: Gorman Health Group analysis, 2021

There are gaps in capturing risk associated with non-diabetic peripheral neuropathies (HCC 75)

HCC 75 captures peripheral neuropathy from common non-diabetic reasons:

- Metabolic syndrome, nutritional (B12 deficiency)
- Immune (Rheumatoid arthritis), infectious (COVID-19, HIV, Lyme disease)
- Chemotherapy Induced Peripheral Neuropathy, toxic (alcohol)
- Uremia, liver disease, chronic hypoxia (sleep apnea, COPD)

Why such a significant gap in HCC 75 detection?

- Peripheral neuropathies often do not have clear signs and symptoms
- Physicians are not sufficiently focused on signs and symptoms of peripheral neuropathy in non-diabetic patients
- Traditional clinical screening tools (e.g., monofilament) are inadequate
- Peripheral neuropathy work-up may be incomplete

Undocumented PN creates clinical and financial risk

- Skin trauma, foot ulcers
- Increased fall risk
- Increased hospitalization rates
- **Decreased quality of life**

ghg

Source: Gorman Health Group analysis, 2021

Accurate RAF assessment requires complete and specific coding

EXAMPLE

Complete and Accurate Coding	
72 year old male	0.394
Hypertension - I10	0
Alcohol dependence, in remission, F1020, HCC 55	0.329
Alcoholic polyneuropathy, G621, HCC 75	0.472
Total RAF	1.195
PMPM	$ 850.00
Year	$ 12,189.00

Some conditions coded, lacking specificity	
72 year old male	0.394
Hypertension - I10	0
Alcohol dependence, in remission, F1020, HCC 55	0.329
Polyneuropathy, unspecified - G62.9	0
Total RAF	0.723
PMPM	$ 850.00
Year	$ 7,374.60

No conditions coded	
72 year old male	0.394
Hypertension - I10	0
Alcohol Abuse, in remission - F1011	0
Numbness and Tingling (Parasthesia of Skin) - R202	0
Total RAF	0.394
PMPM	$ 850.00
Year	$ 4,018.80

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