Diabetic polyneuropathy

what is it & how to prevent it and how to treat it?

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Disclosure

I have no actual or potential conflict of interest in relation to any product or service mentioned in this program or presentation.

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Learning Objectives

At the end of this presentation, you should:-

1. Understand what polyneuropathies are
2. Understand what diabetic polyneuropathy is & the symptoms
3. Describe the risk factors for developing polyneuropathy
4. Describe the treatment available
5. Understand the prognosis and implications of no intervention

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Pre questions

1. What is the difference between a polyneuropathy and mononeuropathy?

a. Mononeuropathy refers to focal involvement of a single nerve

b. Polyneuropathy is a homogeneous process affecting many peripheral nerves

c. Mononeuropathy is usually due to trauma, compression, or entrapment

d. Polyneuropathy usually affects the distal nerves most prominently

e. All of the above

2. What are the most common causes of polyneuropathy?

a. Alcoholism and Lupus

b. Diabetes and uremia/kidney failure

c. None of the above

d. All of the above

3. Polyneuropathy, peripheral neuropathy & neuropathy are the same

a. True

b. False

4. Codeine can be used to treat pain from polyneuropathy?

a. True

b. False

5. Risk factors associated with neuropathies are:

a. Hypertension

b. Smoking

c. Obesity

d. Type 2 Diabetes

e. All of the above

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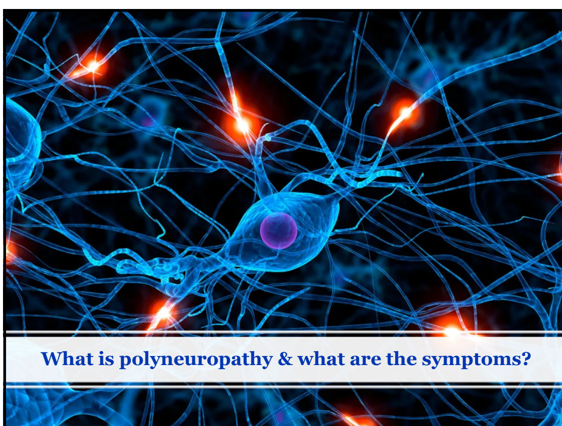

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Define polyneuropathy, neuropathy, peripheral neuropathy

Polyneuropathy - is a specific term that refers to generalized, relative actively homogeneous process affecting many peripheral nerves, with the distal nerves usually affected most prominently

Peripheral neuropathy - a less precise term that is frequently used synonymously with polyneuropathy. Can also be used to refer to any disorder of the peripheral nervous system including radiculopathies and mononeuropathies

Neuropathy used interchangeably with peripheral neuropathy and or polyneuropathy. Refers even more generally to disorders of the central and peripheral nervous system

Mononeuropathy - refers to focal involvement of a single nerve, usually due to a local cause such as trauma, compression or entrapment. Eg Carpal tunnel syndrome

mononeuropathy Multiplex - refers to simultaneous or sequential involvement of noncontiguous nerve trunks. The term can refer to multiple compressive neuropathies but often specifically it identifies multiple nerve infarcts due to a systemic vasculitic process that affects the vasa nervorum

Of note : diseases of central nervous system such as a brain tumor, stroke, or spinal cord lesion occasionally present with symptoms that are difficult to distinguish from polyneuropathy

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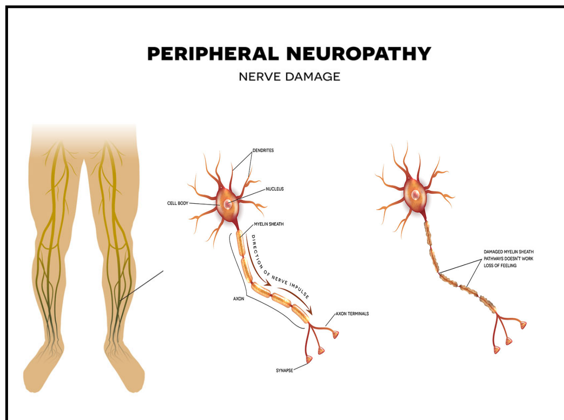

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There are other types of nerve damage....

Neuropathy Depends on the Type of Peripheral Nerve Affected

Sensory nerve damage
- Unusual sensations
- Pain from light touch
- Burning
- Numbness
- Tingling
- Balance problems

Motor nerve damage
- Muscle cramping
- Twitching
- Reflex abnormalities

Autonomic nerve damage
- Excess sweating
- Heat intolerance
- Getting full quickly
- Impotence
- Orthostatic hypotension (dizziness or fainting after standing up)

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What is polyneuropathy vs Mononeuropathy

- The peripheral nerves in the body can be affected by many things that can impair their health and function (a variety of toxic, inflammatory, hereditary, infectious, para-infectious factors) leading to clinical disorder of polyneuropathy.
- Causes include diabetes, alcohol abuse, HIV infection amongst other causes such as side effects of medications or genetic processes and sometimes idiopathic.
- The most common chronic axonal polyneuropathy including diabetes and or uremia.

MONONEUROPATHY

- Mononeuropathy Multiplex is an acute form and presents with multiple mononeuropathys (single nerve involvement) with involvement of entirely unrelated nerves eg. median nerve in the arm and the sciatic nerve in the leg

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Mononeuropathy	Polyneuropathy
Median nerve	**Hereditary disorders**
Carpal tunnel syndrome	Charcot-Marie-Tooth (CMT) disease
Ulnar nerve	Hereditary sensory neuropathy (HSN)
Tardy ulnar nerve palsy	**Inflammatory diseases**
Cubital tunnel syndrome	Guillain-Barré syndrome (GBS)
Radial nerve	Chronic inflammatory demyelinating polyneuropathy (CIDP)
Saturday night palsy	Vasculitis
Lateral femoral cutaneous nerve	**Infectious diseases**
Meralgia paresthetica	Leprosy
Sciatic nerve	HIV infection
Piriformis syndrome	**Systemic diseases**
Peroneal nerve	Diabetes mellitus
Captain chair palsy	Paraneoplastic
Strawberry picker palsy	Paraproteinemia
Tibial nerve	**Drugs and toxins**
Tarsal tunnel syndrome	Isoniazid
	Alcohol

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What are the symptoms?

- Characterized by symmetric distal sensory loss, burning or weakness
- Presentation varies depending on the underlying pathophysiology
- Abnormalities on physical exam are dependent on the type of polyneuropathy (axonal versus demyelinating), which classes of nerves are most involved (motor versus sensory)
- Other conditions can be confused with polyneuropathy such as central nervous system disorders including spinal cord processes, acute myopathies and neuromuscular junction diseases

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Symptoms? Pins & needles, pain & tingling

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Symptoms vary....

Typical
Peripheral Neuropathy Symptoms

- Loss of Feeling
- Hyper Sensitivity
- Freezing
- Sharp Jabbing Pain
- Tingling
- Burning Sensation
- Numbness

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Chronic & Acute axonal PN - symptoms progress?

- In **chronic & acute axonal polyneuropathy** including diabetes or end stage kidney disease/uremia, hypothyroid, few rheumatic diseases, Longstanding HIV infection, critical illness, amyloidosis, vitamin deficiencies, Lyme disease. Some toxins (alcohol, chemotherapy exposure, most heavy metals, some antibiotics eg Fluroquinolones, antiretrovirals and other medications) , Environmental eg. vibration induced nerve damage, prolonged cold exposure or hypoxemia and then idiopathic

The longer axons are affected first resulting in symptoms that begin in the lower extremities

Sensory symptoms usually precede motor symptoms.

Present with slowly progressive sensory loss and dysesthesias such as Numbness and burning sensation and pain in the feet , and mild gate abnormalities

with progression , mild weakness of the lower legs and hands symptoms may begin resulting in the classic "stocking and glove " distribution of sensory loss

in severe cases and numbness may continue to extend proximally affecting the intercostal nerves causing sensory loss over the sternum and eventually even getting to the top of the head with further progression

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Acute demyelinating PN - symptoms?

- **Acute demyelinating polyneuropathy** Usually autoimmune (Axonal forms also exist) such as Gillian Barre' syndrome has a very distinct presentation
  - effects predominantly *motor nerve fibers, so weakness* rather than sensory loss typically is the earliest sign
  - eventually however most patients will complain of some dysesthesias eg, numbness distally in the legs and arms.
  - Gait difficulties or hand clumsiness secondary to reduce proprioception are also common complaints
  - Courses variable , a 2 to 6 week period of decline is followed by stabilization and eventual improvement over several months
  - recovery depends upon the initial illness severity

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CIDP & Hereditary PN - symptoms?

- Chronic Inflammatory demyelinating polyneuropathy (CIDP)
  - Eg. Secondary to lymphoproliferative disorders such as multiple myeloma or Waldenstrom's macroglobulinemia
  - Present with simultaneous weakness and generalized sensory loss
  - Exaggerations may be followed by periods of stability while in others there is a steady prolonged decline
- Hereditary polyneuropathies – the progression of the disease is very slow and insidious
  - neither patients or families appreciate the mark neurologic deficits or atrophy because of the slow progression
  - generally, do not complain of positive symptoms such as paresthesias or pain

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Diabetic polyneuropathy

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Diabetic polyneuropathy

- Generally considered predominantly axonal, however variable degrees of demyelination is often present on testing
- The mechanism underlying the development of diabetic neuropathy is extremely complex and likely relates to inflammatory, metabolic and ischemic effects

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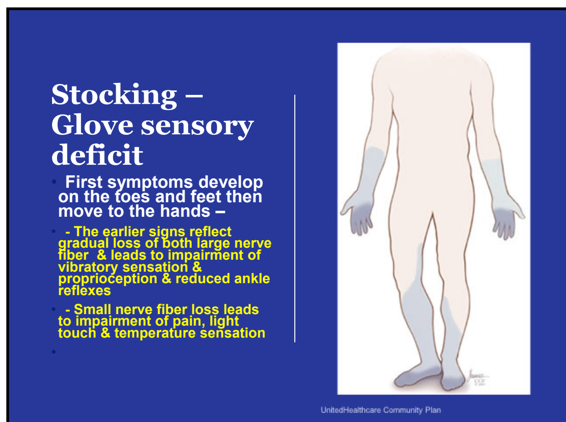

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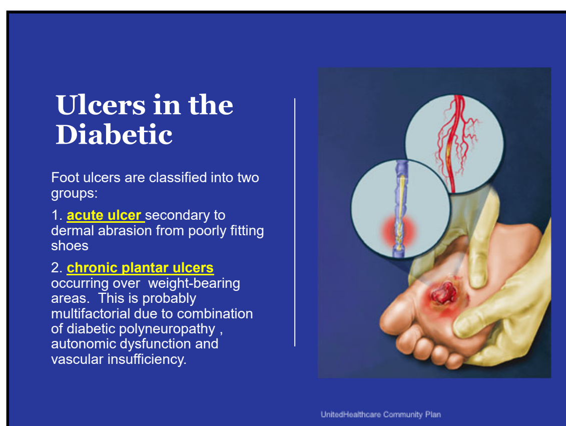

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Screening for and Diagnosing DM-PN

- The diagnosis of diabetic polyneuropathy is based primarily on clinical findings in the patient with diabetes – combination of typical symptoms with typical signs, typical signs on exam in the absence of symptoms, or with only the presence of a painful foot ulcer
- Is insidious in onset and can lead to formation of foot ulcers due to progressive loss of protective sensation , and muscle and joint disease
- the prevalence of diabetic polyneuropathy (and other microvascular and macrovascular complications) increases with disease duration
- should be suspected in any type 1 diabetic of more than 5 years duration and in all patients with type 2 diabetes
- polyneuropathy due to prediabetes should be suspected in any patient presenting with "idiopathic "painful polyneuropathy
- history and examination should focus on identifying the typical symptoms (eg. numbness, tingling, and pain starting in the toes with slow progression proximal spread) and signs (eg symmetric distal sensory loss) As well as identifying any atypical features that suggest another etiology
- simple screening tests have been developed to diagnose diabetic polyneuropathy in outpatient clinics and they include :
  - -Michigan neuropathy screening instrument
  - Michigan diabetic neuropathy score
  - Utah early neuropathy screening instrument
  - United Kingdom screening test

*(Screening for Diabetic polyneuropathy – Eva Feldman MD PHd, Jeremy Shefner MD PhD)

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Acute painful DM neuropathies that can confuse the diagnoses:

- **Treatment -induced diabetic polyneuropathy** - this presents in the setting of rapid glycemic control
- **Diabetic neuropathic cachexia-** a polyneuropathy that occurs in the setting of unintended severe weight loss
- **Diabetic lumbosacral polyradiculopathy (or diabetic amyotrophy)** – which typically presents with acute, asymmetric, focal onset of pain followed by weakness involving the proximal leg with associated weight loss

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Is it polyneuropathy or peripheral artery disease?

- Both may have bilateral distal symmetric pain in the toes and the feet
- although the exam of decreased sensation or loss of deep tendon reflexes, implies neuropathy it may not be exclusive
- **specific clues of neuropathy include :**
  - **location of the pain** eg. Feet more than Calves
  - **the quality of the pain**
  - **the timing of the pain** eg. present at rest and improves with walking

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How to inquire? What to ask the patient?

- **Where did the symptoms start?** – Symptoms of DM-PN typically start in the toes
- **What are the symptoms?-** numbness, tingling, and pain are typical early symptoms
- **Are these symptoms worse at night, is it painful when bedsheets touch the feet? is the pain stabbing, burning, or lightning like ?**
- **Is there any weakness present?** – weakness typically develops late and usually first effects to ext and ankle dorsi flexion
- **How have symptoms changed overtime?** – proximal spread is typical
- **What is the pace of symptom progression?** Slow progression is typical
- **Are there any differences from 1 foot to the other?** –symmetry of symptoms is typical
- **(For patients with hand symptoms), how much of the legs were involved by the time hand symptoms occurred?-** Symptoms typically ascend from the toes to the knees before affecting the fingertips
- **Are Autonomic symptoms present?** (eg. Lightheadedness, Constipation, urinary retention, change in sweating patterns, blurred vision, abdominal bloating)? – Prominent autonomic involvement is atypical especially early in the disease course
- **Is there a history of alcohol use ?** – prolonged excessive alcohol use is a common cause of symmetric polyneuropathy
- **Is there a family history** of similar symptoms or a family history of high arches or hammer toes? - Suggest hereditary neuropathy, high arches or hammertoes suggests Charcot-Marie-tooth disease
- **What other medical problems are present ?** – Many other medical conditions are associated with peripheral neuropathy

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Risk factors

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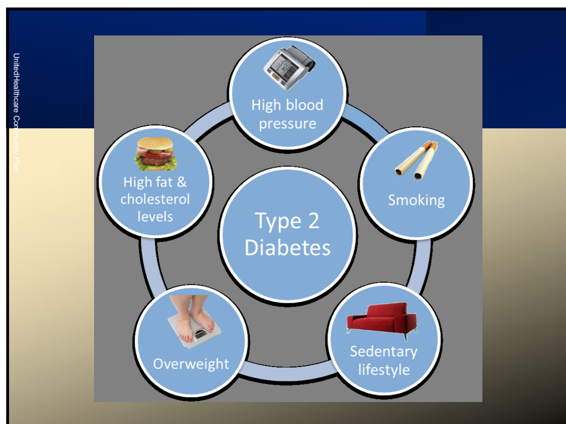

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Modifiable Risk factors

- Diabetes type 2 at onset and Diabetes type 1 after 5 years
- Presence of cardiovascular risk factors : obesity, cigarette smoking, hypercholesterolemia, high blood pressure
- B12 deficiency
- Alcoholism

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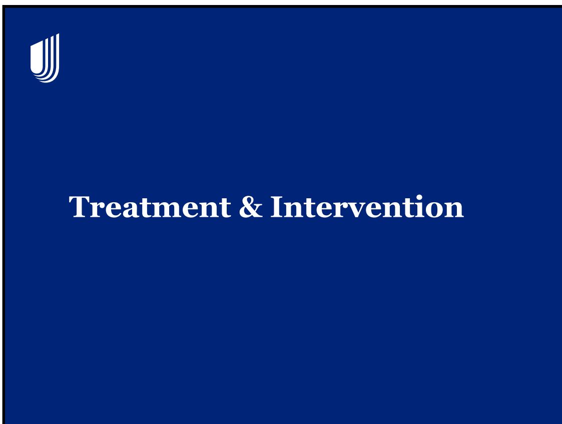

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Treatment & Intervention

- ***Lifestyle interventions and modifications*** are essential to prevent onset and progression, especially in people with prediabetes and type 2 diabetes
- ***Vascular disease prevention Goals*** include :
  - ✓ achieving a normal body weight
  - ✓ attaining individualized glycemic, blood pressure and lipid goals
  - ✓ 150 minutes of moderate to vigorous aerobic activity and two to three sessions of resistance training weekly
  - ✓ surgical treatment of diabetes type 2 (bariatric surgery) – has been shown to reduce neuropathy incidence as well as microvascular complications
- ***Vascular risk factor treatment***, as above including avoidance of cigarette smoking and excess alcohol consumption
- ***Foot care*** is essential , daily foot inspection for:
  - dry or cracking skin
  - fissures
  - planter callus formation
  - signs of early infection between the toes and around the toenails
  - regular foot exam to detect peripheral neuropathy
- ***Safety and fall prevention*** home and environmental modifications
- ***B12 deficiency*** – Metformin reduces intestinal absorption of B12 and should be suspected & checked with worsening neuropathy symptoms in patients treated with metformin

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Treatment and Intervention – Pain management

- approximately 15 to 20% of patients have pain in the feet , described as burning or stabbing
- pain may be self limited and spontaneously resolve within two years of onset in up 50% of patients
- Pain medications are not useful for non painful symptoms such as numbness
- **Opioids & Topiramate (Topimax) are not recommended**
- First line : - 2-3 month titration trial typically required, Combination therapies are additive
  - **several antidepressants** (best using patients with comorbid depression diagnosis):duloxetine*, venlafaxine; amitriptyline, desipramine, nortriptyline (esp useful with comorbid insomnia, excluding dx of CAD);
  - **gabapentinoid anti seizure medications**:- pregabalin and gabapentin (Helpful with comorbid complaints of restless leg syndrome) * renal dosing required

Second line :

- **Capsaicin** cream 0.075%, High concentration Capsaicin 8% patch - administered by health care professional over 2-3 hours can be repeated in 3 months - but generally poorly tolerated
- **Lidocaine** 12hr patch 5%
- **transcutaneous electrical nerve stimulation (TENS)**
- **spinal cord stimulation**

Other therapies –

- **alpha lipoic acid (ALA)** 600mg natural supplement – for those intolerant of the 1st & 2nd line options
- **Valproic acid & carbamazepine**

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But really, IT'S SIMPLE……………………

DIABETES CONTROL

DIABETES MANAGEMENT

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Prognosis

- Every 17s someone is diagnosed with diabetes in the US
- Incidence of diabetics with a diabetic foot ulcers (DFU)= 3.1-11.8% (1-3.4M in USA) (Diabetic foot ulcers and their recurrence – NEJM) or 5% & lifetime risk 15% (ncbi.nlm.nih)
- Incidence of diabetics in USA who get leg amputations = daily 230 Americans (ajmc)

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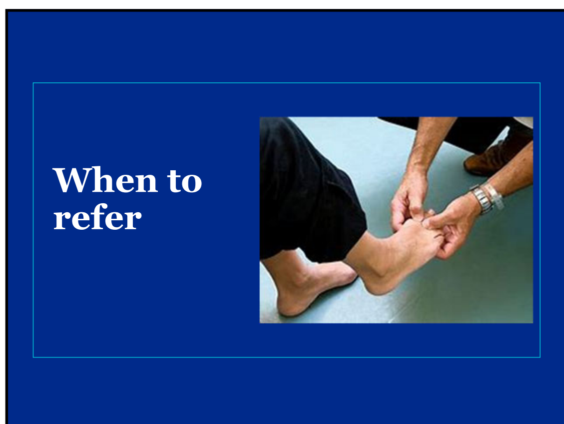

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When to refer & who to refer to ?

•Patients with *typical symptoms* and signs of diabetic symmetric polyneuropathy ie. slow progressing, predominant sensory loss, distal onset, symmetric etc

•initial referral to a podiatrist & then a neurologist; With progressive symptom- initial referral to neurologist is important

•Those with *atypical symptoms* need to be referred to the PCP for evaluation or neurologist

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Post questions

1. What is the difference between a polyneuropathy and mononeuropathy?

a. Mononeuropathy refers to focal involvement of a single nerve

b. Polyneuropathy is a homogeneous process affecting many peripheral nerves

c. Mononeuropathy is usually due to trauma, compression, or entrapment

d. Polyneuropathy usually affects the distal nerves most prominently

e. All of the above

2. What are the most common causes of polyneuropathy?

a. Alcoholism and Lupus

b. Diabetes and uremia/kidney failure

c. None of the above

d. All of the above

3. Polyneuropathy, peripheral neuropathy & neuropathy are the same

a. True

b. False

4. Codeine can be used to treat pain from polyneuropathy?

a. True

b. False

5. Risk factors associated with neuropathies are:

a. Hypertension

b. Smoking

c. Obesity

d. Type 2 Diabetes

e. All of the above

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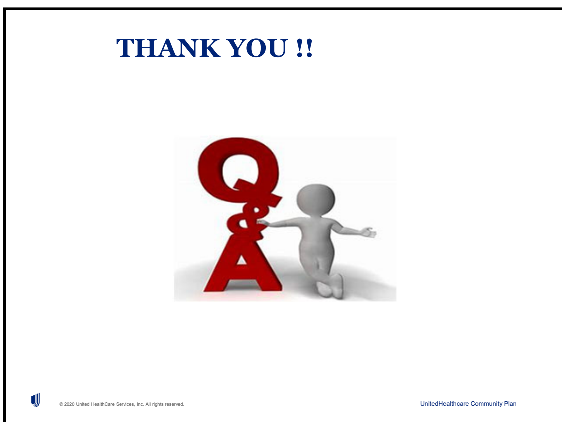

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