

<p style="text-align: center;">WOMEN'S INTERAGENCY HIV STUDY QUESTION BY QUESTION SPECIFICATIONS FORM NP01: BASELINE NEUROPATHY SIGNS AND SYMPTOMS</p>

General Instructions:

1. Dates should be recorded in the MM/DD/YY format.
2. Times should be recorded in HH:MM format.
3. Remember to use leading zeros for the time and severity questions, e.g., 08:00 or 06.
4. Participants should remove shoes and socks.
5. This form should be completed before beginning the physical exam. Record the actual time you began NP01 in A6 "Time Module Began" and the actual time you ended the questionnaire in C5 "Time Module Ended."
6. A participant can refuse at any time. If she refuses a question or test, write "Refused" in the margin, initial this notation and any other comments, and then proceed to the next question.
7. If a participant rates a current symptom as 8 or higher, please refer her to her primary care provider or a neurologist for a full evaluation.
8. It is very important that the questions be read to the participant as written and in the correct order. Each participant in the study should hear *exactly* the same question. Using non-standardized changes – even one or two words – can affect the entire meaning of the question and lead to bias. Although some questions could be phrased differently or more simply, every word in the question serves a purpose and is specifically designed to achieve the research goals of the project. In order to combine the responses of all participants and analyze the data, there must be no variations in the way questions are asked.
9. The clinician can and should reconcile factual inconsistencies given by the participant within the context of the interview situation. For example, if the participant indicates that she is taking medication for neuropathy, please confirm that this was reported to the interviewer and recorded on F22MED.
10. If the participant reports multiple episodes of a bothersome symptom, ask her to provide a rating for the symptom when it was at its worst.
11. Be sure to follow-up with the participant after the exam to discuss problems not related to the questions on the form. For example, a participant may want to discuss swelling in her feet but this should be addressed after the exam.

SECTION B: NEUROPATHY SYMPTOMS

Our goal is to identify pain associated with distal sensory polyneuropathy (DSPN). This kind of pain is bilateral and affects at least the toes. It is described as burning, gnawing, aching, and shooting. Some pain should be present in the toes and/or feet to conclude that DSPN is present. Pain present in the calves or knees that is not also present in the toes and feet is unlikely to be due to DSPN.

In questions B1-B6, we are looking to characterize a specific type of pain that starts in the toes and may spread upward to the legs, and always occurs on both sides of the body simultaneously. The severity of pain on each side may differ; however, the pain must happen at the same time, bilaterally. If pain has fluctuated or disappeared at times, the participant should rate the pain when it was at its worst.

There are many types of pain that should be ruled out during the examination. Pain that is only in one side of the body, or spreads from the back down the legs should be excluded. Radicular pain – usually due to a herniated disc in the lumbosacral spine or to bony overgrowth from osteoarthritis in this region (although many other disorders can cause this syndrome) – may be the most difficult to separate from

pain due to neuropathy. Radicular pain typically starts in the back and radiates down the leg but we are not interested in this type of pain. Herniated discs usually cause unilateral pain and the pain is located in the back or at least buttocks. We are also not interested in leg pain due to venous thromboses (blood clots); arthritis in the knee, ankle, or foot; or foot problems due to podiatric causes such as corns and bunions. We are only interested in recording information about neuropathic pain of DSPN which starts in both toes and feet and may eventually extend into the leg.

HAND PARTICIPANT RESPONSE CARD NP01 TO RATE SEVERITY.

Please note that the symptom questions are structured to ask if the participant has EVER had a type of neuropathy first. After a symptom rating for the EVER question, ask about the same symptom within the last six months. B1, B3, and B5 are EVER questions. B2, B4, and B6 are IN THE LAST SIX MONTHS questions. For example, it is important to stress in B1 that you are asking about the participant's entire life history with pain, aching, or burning in her feet and legs. In B2, you would ask about pain, aching or burning during the last 6 months. Follow-up administration of neuropathy symptoms will not ask about a participant's lifetime history.

READ THE INTRODUCTION TO THE PARTICIPANT.

- B1. Indicate if the participant has ever had pain, aching or burning in both her feet and legs at around the same time. If the participant responds in the negative, then circle "2" and skip to B3.
- Have the participant use the scale on the NP01 response card. Ask her to rate the severity in her right foot and leg where 1 is mild and 10 is severe.
 - Have the participant use the scale on the NP01 response card. Ask her to rate the severity in her left foot and leg where 1 is mild and 10 is severe.
- B2. Indicate if the participant has had, in the last 6 months, pain, aching or burning in both her feet and legs at around the same time. If the participant responds in the negative, then circle "2" and skip to B3.
- Ask the participant to rate the severity in her right foot and leg.
 - Ask the participant to rate the severity in her left foot and leg.
- B3. Read the example. Indicate if the participant has ever had "pins and needles" in both her feet and legs at around the same time. If the participant responds in the negative, then circle "2" and skip to B5. Please be sure that the participant understands that the example provided in B3 is just an example. Do not record symptoms due to the example provided. **PROBE:** Do not record 'yes' if the participant has experienced "pins and needles" caused simply by sitting too long.
- Ask the participant to rate the severity in her right foot and leg.
 - Ask the participant to rate the severity in her left foot and leg.
- B4. Indicate if the participant has had, in the last 6 months, "pins and needles" in both her feet and legs at around the same time. If the participant responds in the negative, then circle "2" and skip to B5.
- Ask the participant to rate the severity in her right foot and leg.
 - Ask the participant to rate the severity in her left foot and leg.
- B5. Read the example. Indicate if the participant has ever had numbness in both her feet and legs at around the same time. If the participant responds in the negative, then circle "2" and skip to C1. Please be sure that the participant understands that the example provided in B5 is just an example. Do not record symptoms due to the example provided. **PROBE:** Do not record 'yes' if the participant has experienced numbness caused simply by Novocaine or Orajel.

- a. Ask the participant to rate the severity in her right foot and leg.
 - b. Ask the participant to rate the severity in her left foot and leg.
- B6. Indicate if the participant has had, in the last 6 months, numbness in both her feet and legs at around the same time. If the participant responds in the negative, then circle “2” and skip to C1.
- a. Ask the participant to rate the severity in her right foot and leg.
 - b. Ask the participant to rate the severity in her left foot and leg.

SECTION C: NEUROPATHY SIGNS

Gently assess whether or not simply handling the participant’s feet causes her pain. In these cases, be additionally careful when examining her feet and placing the tuning fork. Some participants may need assistance in removing their socks and shoes. Participants who have neuropathy may not feel the vibration at all. Participants with mild neuropathy will feel the vibration for less than ten seconds; they will be aware that the vibration is less strong on their toes than it was on the wrist. As the tuning fork testing and reflex testing is absolutely painless in participants without neuropathy and in some participants with neuropathy, the examiner should not forget that for some participants it will be painful.

Evaluation of Perception of Vibration: General Principles

Use a 128 Hz tuning fork to conduct the perception of vibration testing. One should strike the tuning fork hard enough that the sound of the impact of the two blades of the tuning fork is audible. Striking the part of the palm near the little finger and not near the thumb is less painful to some examiners. Others prefer striking the tuning fork against a hard object such as a table. When placing the tuning fork hold it on the stem, just below the bifurcation, i.e., the point where the two blades of the tuning fork meet. It is recommended that you hold the stem between your thumb and the outside of your index finger, like a chopstick.

The participant should be seated on the examining table. Refer to **Figure 1** for the correct placement of the tuning fork. Do not hold the toe with force or in an area that will dampen the participant’s sensation of vibration. If necessary, lightly hold the sides of the participant’s toe with your thumb and index finger to stabilize the foot. Some examiners prefer to bend over for the testing, others prefer to use a stool, and a select few prefer to get on the floor on their knees. Use the method that works best for you. The examiner may or may not use gloves. It will not affect the results of the testing.

The tuning fork can vibrate for an extended period of time. If the participant has a normal sense of vibration she will feel the vibration for well over 10 seconds. It is not necessary to hold the tuning fork to the participant’s toe until the tuning fork stops vibrating. It is only important to assess that the participant feels the vibration for greater than 10 seconds. If the participant feels the vibration for more than 10 seconds you can remove the stem of the tuning fork at 12 seconds.

It is very important to establish a vibration control for every participant. This allows the participant to understand what you mean by “vibration.” Demonstrate first on her wrist and ask, “What do you feel?” It is important to consistently ask this exact question and see if the participant feels the sensation we are expecting. She should describe the feeling as a buzzing or tingling, not merely pressure. She may also imitate the sound of the sensation. Do not bias the participant by asking the question differently, e.g., “Do you feel the buzzing?” This type of question wording gives away the answer. The participant should tell you that the vibration stops when you remove the tuning fork. There is a little art to this as some participants will “tune out” and forget to tell you when they stop feeling the vibration. This may lead you to infer that they still feel the buzzing. One should test this at the wrist by purposely withdrawing the tuning fork after a few seconds. If the participant correctly stated that the buzzing stopped, repeat at the wrist and time how long she feels the vibration.

Timing can be awkward but it is significantly more accurate than counting. Many clinicians in the WIHS will be conducting this test and it is important to standardize the timing aspect of this exam across all

WIHS sites. One method is to place a stopwatch on the floor, within eyesight, and let it run. Watch the stopwatch and use this as a counter. You can also use a digital wristwatch that displays the seconds or a wristwatch with hands. The watch should be on the wrist that is not applying the tuning fork. You can also reference a clock with hands that is within eyesight. With a little practice, one can master viewing the timer and placing the tuning fork.



Figure 1. Evaluating Perception of Vibration. Press the 128 Hz tuning fork firmly (but not too hard) against the distal interphalangeal joint of the great toe. A normal response is for the participant to feel vibration (not just pressure) for more than 10 seconds.

- C1a & b. Indicate the length of time that the participant felt the vibration in her right (C1a) and left (C1b) great toe at the distal interphalangeal joint. Use a stop watch or timer to accurately measure the length of time.

Instructions for Evaluation of Perception of Vibration

1. Establish a vibration control. Inform the participant that the tuning fork will make a loud, clanging sound but that is normal. The sound of the discs hitting each other may startle the participant so it is best to warn her in advance.
 - a. Place the stem of the tuning fork on the participant's wrist.
 - b. Ask the participant, "What do you feel?"
 - c. If the participant tells you that she feels vibration, then go on to test the great toes.
 - d. If the participant doesn't tell you that she feels vibration, ask her, "Do you feel a vibration or buzzing on your wrist?" If the participant still responds in the negative, test her perception of vibration on her forehead.
 - e. Proceed when the participant feels vibration.
2. Testing vibration in the toes.
 - a. Ask the participant question C1, watch the timer, and place the stem firmly against the distal interphalangeal joint of the great right toe.
 - b. Record the result in C1a for the right toe.
 - c. Repeat for the left toe and record the result in C1b.
3. If you do not think that the participant understood you the first time, repeat the test and use the new time.
4. Should it become necessary, you can test the attention of the participant. Strike the tuning fork. Outside of the participant's range of vision, subtly hold the discs to stop the vibration and then apply the stem. She should indicate that she does not feel vibration.

Circle the correct value for the length of time that the participant felt the vibration:

0	Greater than 10 seconds	Normal perception of vibration
1	6-10 seconds	Mild loss
2	5 seconds or less	Moderate loss
3	No feeling	
-9	Unable to evaluate	

Evaluation of Deep Tendon Reflexes: General Principles

Use a large Queen's Square hammer to conduct the deep tendon reflex testing. Refer to **Figure 2** for correct placement of the hammer and the appropriate way to hold the participant's foot. Hold the hammer about two-thirds of the way down the handle, near the red plastic tip. Be sure that the participant is seated and that you are seated or otherwise in a stable, balanced position. Hold the foot slightly away from the examining table if you need room to swing the hammer. Gloves are optional and their use will not affect results.

The examiner should practice until a "swinging" movement of the hammer is mastered. Use your wrist to start the motion and then loosen your grip slightly so that the weight of the hammer leads the motion. If you loosen too much, you may lose control of the hammer. The movement of the hammer is stopped when the hammer strikes the participant's tendon; the examiner does not provide the braking of the hammer. Never strike the participant with excessive force and be mindful that, for some participants, any amount of contact with their feet is painful.

Test that the participant is relaxed by letting her foot fall and seeing if it dangles loosely. You can also tap the bottom of her foot gently to see if she is tensing her foot. Encourage the participant to relax. Many people will remain in control of their reflexes and will not relax.

Some participants will have a very obvious, brisk reflex. Others will have more subtle reflexes. A normal response is for the ankle to plantar flex downward after a short delay and the muscle, in this case the gastrocnemius, in the posterior of the calf will contract. The biggest problem is when no or very little reflex is elicited. If you are not sure whether you are getting a reflex, you can put your hand over the calf when you strike the reflex (you may need someone to dorsiflex the participant's ankle) and feel for the contraction. If you don't find a reflex, it could be because the reflex was absent or decreased or because the technique used to conduct the reflex testing is inadequate. The examiner should check her technique by eliciting a knee, elbow or forearm reflex. If there is not a delay, then this may only be a mechanical response, i.e., simply striking the ankle may cause some movement that has nothing to do with a reflex. Most of the time with DSPN, the ankle reflex is lost, but other reflexes are present. By eliciting a knee reflex and not eliciting an ankle reflex, one gains confidence that bad technique is not the cause of the absent reflex. Furthermore, the Jendrassik maneuver (see **Figure 3**) may help elicit the reflex; reassuring the examiner that her technique was acceptable.



Figure 2. Evaluating Deep Tendon Reflexes. You should be able to elicit ankle reflexes in most patients when they are sitting on a chair in the normal way (on their posterior). The examiner dorsiflexes the ankle from its passive position to a ninety degree angle between the foot and ankle.

- C2a & b. Ask the participant question C2. Swing the reflex hammer behind the foot so that it directly strikes the Achilles tendon above the heel. Observe the calf muscle for a contraction. A true reflex manifests as a slight delay then a jump downward led by the ball of the foot. You may repeat this a second time to confirm the presence or absence of the reflex. Indicate the results of the ankle reflex test in the right (C2a) and the left (C2b) foot.

Circle the correct value for results of the evaluation:

- 0 Absent reflex
- 1 Hypoactive reflex
- 2 Normal, Increased, or Clonus reflex
- 9 Unable to evaluate

If the participant has, for example, one foot in a cast or an amputated foot, then record and initial this information in the margin. Circle -9 for that foot. If you cannot obtain a reflex even after multiple attempts, circle 0. Some individuals do not have a reflex but this is not necessarily an indication of a neurologic problem.

- C3. Based on the results in questions C2a and C2b, indicate if both the right and left ankle reflexes are equal to 2, i.e., normal, increased or clonus. If both the left and right are normal, then circle "1" and skip to question C5. If no, meaning that the participant had at least one ankle reflex recorded as "0", "1", or "-9", then circle "2" and go to question C4. If the participant had a normal, increased, or clonus reflex for *both* feet, then the exam is finished. If the participant had an absent or hypoactive reflex in one or both feet, proceed to C4 and repeat the reflex test while the participant performs the Jendrassik maneuver. You should repeat the reflex test for both the right and left foot even if only one foot had a normal reflex *without* the Jendrassik maneuver.

- C4a & b. If you must proceed to question C4, demonstrate how the participant should hold her hands (see **Figure 3**). Tell her that on the count of three she should close her eyes and pull tightly. Count to three and when you are sure that the she is tensing her hands, swing the hammer. If the participant has long fingernails and cannot lock her fingers, she can clasp opposite forearms with her hands. Encourage the participant to pull hard while you swing the hammer. Indicate the results of the ankle reflex test in the right (C4a) and the left (C4b) foot.



Figure 3. Jendrassik maneuver. If no reflex is elicited in C1a or b, use this technique. Have the participant interlace her fingers as shown, and tell the participant that on the count of three, she should pull outwards. Strike the Achilles tendon when she is pulling outwards.

C5. Record the time that the neuropathy questions and measurements in NP01 were completed.