Supplemental Digital Content

Diabetic polyneuropathy and pain, prevalence, and patient characteristics: A cross-sectional questionnaire study of 5,514 patients with early type 2 diabetes.

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Supplementary Digital Content

Supplementary Table 1: *Full version of the questionnaire.*

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Supplementary Figure 1: *Frequency of "yes" responses to the MNSIq by the 4 possible neuropathy groups among the 5,249 patients with information on status of both DPN (defined by MNSIq) and painful DPN (defined by DN4 and pain location in both feet).*

Supplementary Figure 2: *The association of DPN and painful DPN with sleep disturbance – an example.*

Supplementary Table 1: *Questionnaire, full version*

HEIGHT

1.   Enter your height in centimetres: _____ cm

WEIGHT

2.   Enter your weight in kilograms: _____ kg

SMOKING

3.   Please tick the relevant item: ☐ Never smoked   ☐ Ex-smoker (stopped more than 6 months ago)   ☐ Smokes occasionally   ☐ Smokes daily

ALCOHOL INTAKE

4.   Please tick the relevant item: ☐ Less than 7 units per week (women)/14 units (men) per week   ☐ More than 7 units per week (women)/14 units (men) per week

PHYSICAL ACTIVITY

5.   How many days a week are you **physically active for at least 30 minutes per day?** One tick only.   (this includes moderate or hard physical activity with increased breathing, muscles exercise and use of strength, eg, recreational sports or competitive sports, heavy gardening, brisk walking, biking at moderate or fast pace or physically strenuous work. Both spare time and work activities are to be included)

Never	1 day	2 days	3 days	4 days	5 days	6 days	7 days
☐	☐	☐	☐	☐	☐	☐	☐

PHYSICAL ACTIVITY - *continued*

6. Do you engage in physical activity in your spare time, or participate in other activities that involve exercise?

☐ Yes ☐ No

7. Physical activity in your spare time in the past year. Tick off the box that best describes your level of activity:

☐ Exercising strenuously and practicing competitive sports regularly and several times a week

☐ Practising recreational sports or doing heavy gardening or similar at least 4 hours a week

☐ Walking, biking or other light exercise at least 4 times per week (Sunday strolls, light gardening and biking/walking to work should also be included)

☐ Reading, watching TV or other sedentary activity

WALKING/FALLS

8. Do you sometimes feel unsteady when walking?

☐ Yes ☐ No

9. Have you fallen in the past year?

☐ Yes ☐ No

If yes, how many times have you fallen in the past year?

☐ Once ☐ 2-4 times ☐ More than 4 times

10. Has your fall/falls made it necessary to contact your general practitioner?

☐ Yes ☐ No

11. Has your fall/falls made it necessary to contact the hospital

☐ Yes ☐ No

QUALITY OF LIFE

12. How will you rate your quality of life in the past 7 days? (one tick only)

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Worst possible quality of life   Best possible quality of life

SLEEP

13. How was your sleep quality in **the past 7 days**? Please respond to each item by marking one box per row.					
In the past 7 days…	Very poor	Poor	Fair	Good	Very good
My sleep quality was	☐	☐	☐	☐	☐
In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
I had difficulty falling asleep	☐	☐	☐	☐	☐
My sleep was refreshing	☐	☐	☐	☐	☐
I had a problem with sleep	☐	☐	☐	☐	☐

MENTAL HEALTH

14. How was your mental health **in the past 7 days?** Please respond to each statement by marking one box per row.					
In the past 7 days…	Never	Rarely	Sometimes	Often	Always
I felt uneasy	☐	☐	☐	☐	☐
My worries overwhelmed me	☐	☐	☐	☐	☐
I felt fearful	☐	☐	☐	☐	☐
I found it hard to focus on anything other than my anxiety	☐	☐	☐	☐	☐
I have felt worthless	☐	☐	☐	☐	☐
I have felt helpless	☐	☐	☐	☐	☐
I have felt depressed	☐	☐	☐	☐	☐
I have felt hopeless	☐	☐	☐	☐	☐

FEELING IN YOUR LEGS AND FEET

Please answer the following questions about the feeling in **your legs and feet.**

Check yes or no based on how you usually feel.

	Yes	No
15. Are your legs and/or feet numb?	☐	☐
16. Do you ever have any burning pain in your legs and/or feet?	☐	☐
17. Are your feet too sensitive to touch?	☐	☐
18. Do you get muscle cramps in your legs and/or feet ?	☐	☐
19. Do you ever have any prickling feelings in your legs or feet ?	☐	☐
20. Does it hurt when the bed covers touch your skin?	☐	☐
21. When you get into the tub or shower, are you able to tell the hot water from the cold water?	☐	☐
22. Have you ever had an open sore on your foot?	☐	☐
23. Has your doctor ever told you that you have diabetic neuropathy?	☐	☐
24. Do you feel weak all over most of the time?	☐	☐
25. Are your symptoms worse at night?	☐	☐
26. Do your legs hurt when you walk?	☐	☐
27. Are you able to sense your feet when you walk?	☐	☐
28. Is the skin on your feet so dry that it cracks open ?	☐	☐
29. Have you ever had an amputation?	☐	☐

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PAIN

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30. Do you have constant or recurring pain?

☐ Yes   ☐ No

If yes, have had any of these types of pain in the past 3 months? (tick all that apply)

☐ Headache or facial pain

☐ Back pain, including low back pain and neck pain

☐ Shoulder pain

☐ Pain in the hands/arms

☐ Abdominal pain

☐ Pain in the legs

☐ Other pain (please note what kind of pain)_____

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31. Do you have constant or recurring pain **in your feet**

☐ Yes   ☐ No

If you have answered YES to question 31, please continue answering the rest of the questionnaire. The remaining questions are about pain in your feet.

If you have answered NO to questions 31, we thank you for your participation and kindly ask you to return the questionnaire in the attached reply envelope.

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32. Do you have pain in both feet?

☐ Yes   ☐ No

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33. Does the pain spread up your legs?

☐ Yes   ☐ No

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34. Do you have similar pain in your fingers/hands?

☐ Yes   ☐ No

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35. Do you wake up a nights due to pain in your feet?

☐ Yes   ☐ No

36. How long have you had pain in your feet?	Less than a month	1-3 months	More than 3 months, but less than a year	1-5 years	More than 5 years
	☐	☐	☐	☐	☐

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37. Please rate your pain intensity by marking the number that best describes your pain on average in your feet **in the past 24 hours**

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

No pain   Worst possible pain

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38. Please rate your pain intensity by marking the number that best describes your pain on average in your feet **in the past 7 days**

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

No pain   Worst possible pain

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39. Do you take pain medication for the pain in your feet?

☐ Yes, daily   ☐ Yes, but not daily   ☐ No

If yes, what kind of pain medication (tick more than one box if relevant)

☐ Over-the-counter medicine   ☐ Prescription medicine (medicine that has been prescribed by a doctor)

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40. The following questions are about how the pain in your feet interferes with your daily life.
Please respond to each question by marking one box per row.

In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
How much did pain interfere with your day to day activities?	☐	☐	☐	☐	☐
How much did pain interfere with work around the house?	☐	☐	☐	☐	☐
How much did pain interfere with your ability to participate in social activities?	☐	☐	☐	☐	☐

How much did pain interfere with your household chores?	☐	☐	☐	☐	☐

41. Please answer the following questions about the characteristics of the pain in your feet by marking one box per row.

Does the pain have one or more of the following characteristics?

	Yes	No
Burning	☐	☐
Painful cold	☐	☐
Electric shocks	☐	☐

Is the pain associated with one or more of the following symptoms in the same area?

	Yes	No
Tingling	☐	☐
Pins and needles	☐	☐
Numbness	☐	☐
Itching	☐	☐

Supplementary Table 2: *Age, gender, and diabetes duration among responders and non-responders*		
	Non-responders[a]	Responders[b]
Age, mean (SD)	59.6 (12.8)	64.1 (10.9)
Female gender, n(%)	495 (40.8)	2,355 (42,7)
Diabetes duration, median (IQR)	4.6 (3.4-5.9)	4.6 (3.5-5.7)
[a]N = 1212: The 971, who never returned a questionnaire + the 225 who returned a blank questionnaire + the 16 who returned multiple questionnaires and were excluded (diabetes duration, n = 1,203) [b]N = 5,514: Those, who returned a fully or partly filled questionnaire		

Supplementary Table 3: *Prevalence of possible DPN (defined by MNSIq≥4) and possible painful DPN (defined by DN4≥3 + pain location in both feet) with 95% confidence intervals in total and stratified according to sex and age among all patients (N = 5,514) who returned a filled out questionnaire.*

	Possible DPN			Possible Painful DPN		
	Responses	Events	Prevalence, % (95% CI)	Responses	Events	Prevalence, % (95% CI)
Total	5,359[a]	962	18.0 (16.9-19.0)	5,372[b]	536	10.0 (9.2-10.8)[c]
Sex						
Female	2,274	503	20.2 (18.6-21.9)	2,278	258	11.3 (10.1-12.7)
Male	3,085	459	16.3 (15.0-17.7)	3,094	278	9.0 (8.0-10.0)
Age, years						
<55	1,129	241	21.3 (19.0-23.9)	1,130	124	11.0 (9.2-12.9)
55 - 65	1,481	194	19.9 (17.8-22.0)	1,478	163	11.0 (9.5-12.7)
65 - 75	1,034	172	16.6 (14.4-19.0)	1,034	93	9.0 (7.3-10.9)
≥ 75	1,715	255	14.9 (13.2-16.6)	1,730	156	9.0 (7.7-10.5)

Abbreviations: MNSIq, Michigan neuropathy screening questionnaire; DPN, diabetic polyneuropathy; DN4, Douleur Neuropathique en 4 Questions, CI, confidence interval.

[a] 5,359 persons had sufficient answers to determine MNSIq-defined DPN status.

[b] 5,372 persons had sufficient answers to determine DN4-defined painful DPN status.

[c] Including 2.4% (n = 130) with MNSIq <4 and 0.4% (n=20) with unknown MNSIq status.

Supplementary Table 4: *Prevalence of possible DPN (defined by MNSIq≥4) and possible painful DPN (defined by DN4≥3 + pain location in both feet) with 95% confidence intervals in total and according to questionnaire interval*

	Possible DPN		Possible Painful DPN	
	Distribution of responses	**% (95% CI)**	**Distribution of responses**	**% (95% CI)**
Total	5,359	18.0 (16.9-19.0)	5,372	10.0 (9.2-10.8)
Questionnaire interval^a				
T1	4,478	17.8 (16.7-19.0)	4,482	10.0 (9.1-10.9)
T2	478	17.8 (14.5-21.5)	488	8.4 (6.1-11.2)
T3	403	19.4 (15.6-23.6)	402	11.7 (8.7-15.2)

Abbreviations: MNSIq, Michigan neuropathy screening questionnaire; DPN, diabetic polyneuropathy; DN4, Douleur Neuropathique en 4 Questions, CI, confidence interval

[a]According to time period: T1: response received in the time interval between first questionnaire and first reminder, T2: response received in the time period from first reminder to second reminder, T3: response received in the time period from second reminder to closure of questionnaire survey.

Supplementary Table 5. *The difference between the estimates for possible DPN (defined by MNSIq) and possible painful (defined by DN4 and pain location in both feet) with corresponding 95% confidence intervals.*

	Quality of Life (NRS 0-10)		Depression T-scores		Sleep disturbance T-scores		Anxiety T-scores	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Possible DPN	-1.16 (-1.31 ; -1.01)**	-0.85 (-1.00; -0.71)**	4.18 (3.53; 4.84)**	2.95 (2.30; 3.59)**	4.65 (4.04; 5.27)**	3.46 (2.86; 4.06)**	3.97 (3.31 ; 4.64)**	2.82 (2.17; 3.48)**
Possible Painful DPN	-0.85 (-1.04; -0.67)**	-0.57 (-0.76; -0.39)**	3.35 (2.51; 4.18)**	2.12 (1.30; 2.93)**	2.22 (1.44 ; 3.00)**	1.05 (0.30; 1.81)**	2.73 (1.89; 3.58)**	1.61 (0.78; 2.44)**
Difference, 95% CI	-0.30 (-0.59; -0.01)*	-0.28 (-0.56; 0.00)	0.84 (-0.45; 2.13)	0.83 (-0.41; 2.07)	2.43 (1.21; 3.64)**	2.41 (1.25; 3.57)**	1.24 (-0.05; 2.55)	1.21 (-0.05; 2.48)

Abbreviations: MNSIq, Michigan neuropathy screening questionnaire; DPN, diabetic polyneuropathy; DN4, Douleur Neuropathique en 4 questions; OR, odds ratio; CI, confidence interval. [a]Model 1: Adjusted for age, sex, diabetes duration, BMI, and DPN or painful DPN, respectively. [b]Model 2: Adjusted for age, sex, diabetes duration, BMI, number of pain locations other than extremities (head/face, lower or upper back, shoulders, stomach, or "other location" [category capturing locations not listed here]), and DPN or painful DPN, respectively.
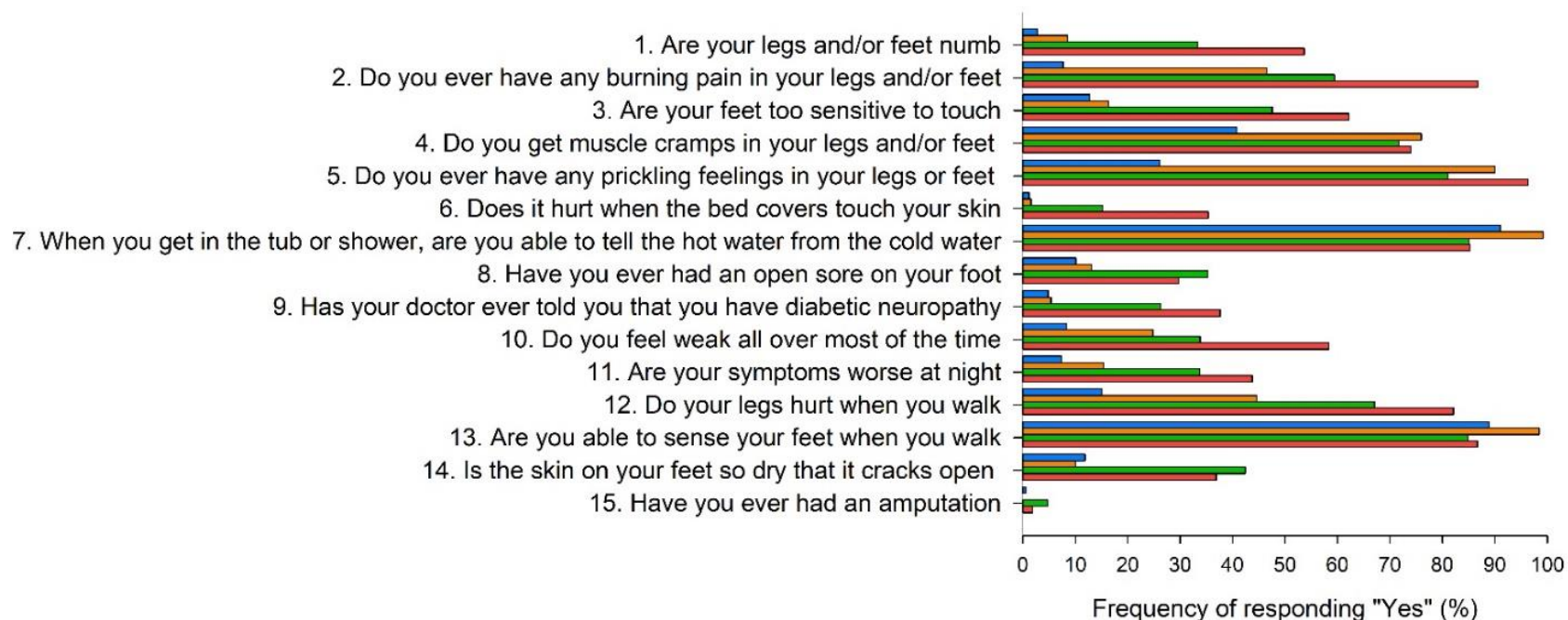
*P-value < 0.05, **P-value<0.001

Supplementary Table 6. *The association between neuropathy and a) quality of life, b) depression, c) sleep and d) anxiety among the 5,249 patients with sufficient information to determine status of both possible DPN (defined by MNSIq) and possible painful DPN (defined by DN4 and pain location in both feet). Sensitivity analysis – without adjustment for BMI.*

	Quality of Life (NRS 0-10)		Depression T-scores		Sleep disturbance T-scores		Anxiety T-scores	
	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]	Model 1[a]	Model 2[b]
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Possible DPN	-1.26 (-1.40 ; -1.11)**	-0.92 (-1.07; -0.78)**	4.42 (3.77; 5.07)**	3.09 (2.46; 3.74)**	4.75 (4.14 ; 5.36)**	3.49 (2.90; 4.07)**	4.04 (3.38 ; 4.70)**	2.83 (2.18; 3.50)**
Possible painful DPN	-0.86 (-1.05 ; -0.67)**	-0.57 (-0.76; -0.39)**	3.37 (2.54; 4.20)**	2.13 (1.32; 2.94)**	2.25 (1.48 ; 3.03)**	1.09 (0.34; 1.85)**	2.79 (1.95 ;3.63)**	1.68 (0.85; 2.50)**
Number of other pain locations								
1	-	-0.62 (-0.75; -0.49)	-	1.39 (0.81; 1.97)	-	1.97 (1.42; 2.51)	-	1.29 (0.70; 1.88)
2	-	-1.02 (-1.15; -0.88)	-	3.61 (3.00; 4.22)	-	3.93 (3.36; 4.51)	-	3.47 (2.84; 4.09)
3	-	-1.35 (-1.52; -1.19)	-	5.66 (4.93; 6.39)	-	5.28 (4.59; 5.96)	-	5.15 (4.40; 5.89)
4	-	-1.86 (-2.09; -1.62)	-	7.74 (6.69; 8.78)	-	6.51 (5.55; 7.46)	-	6.88 (5.82; 7.94)
5	-	-1.60 (-2.16; -1.03)	-	8.21 (5.80; 10.62)	-	7.03 (4.77; 9.29)	-	7.40 (4.87; 9.93)

Abbreviations: MNSIq, Michigan neuropathy screening questionnaire; DPN, diabetic polyneuropathy; DN4, Douleur Neuropathique en 4 questions; OR, odds ratio; CI, confidence interval. [a]Model 1: Adjusted for age, sex, diabetes duration, and DPN or painful DPN, respectively. [b]Model 2: Adjusted for age, sex, diabetes duration, number of pain locations other than extremities (head/face, lower or upper back, shoulders, stomach, or "other location" [category capturing locations not listed here]), and DPN or painful DPN, respectively.

**P-value<0.001

Supplementary Figure 1: *Frequency of "yes" responses to the MNSIq by the 4 neuropathy groups among the 5,249 patients with information on status of both possible DPN (defined by MNSIq) and possible painful DPN (defined by DN4 and pain location in both feet).*
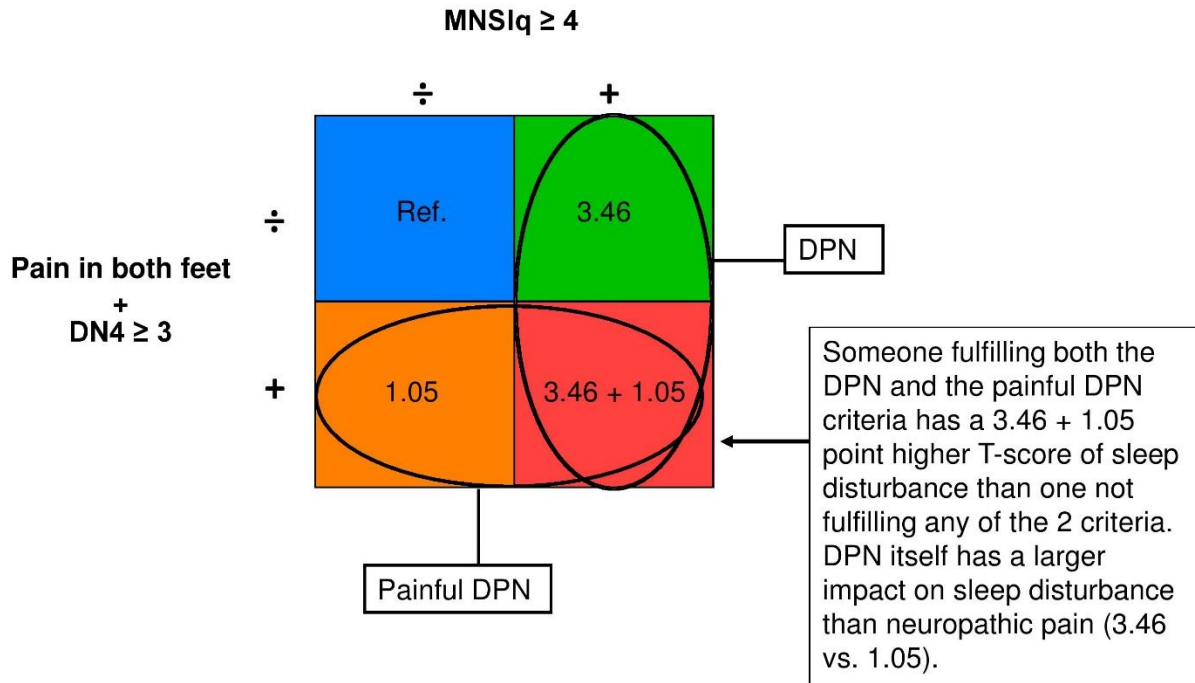

Abbreviations: MNSIq: Michigan Neuropathy Screening Instrument questionnaire, DN4: Douleur Neuropathique en 4 Questions.

Of note: Answering "no" to item 7 and 13 count as 1 point, while answering "yes" to item 1-3, 5-6, 11-12, 14-15 each count as 1 point. Thus, a low frequency of "yes"-responses to item 7 and 13 is associated with a higher likelihood of DPN. Item 4 and 10 are per definition not included in the score.

Blue: MNSIq<4/DN4<3 or no pain, Orange: MNSIq<4/DN4≥3 and pain, Green: MNSIq≥4/DN4<3 or no pain, Red: MNSIq≥4/DN4≥3 and pain

Supplementary Figure 2: *The association of possible DPN and possible painful DPN with sleep disturbance – an example*

Abbreviations: MNSIq: Michigan Neuropathy Screening Instrument questionnaire, DN4: Douleur Neuropathique en 4 Questions.
The estimates are all found in table 5. All estimates are adjusted for age, gender, diabetes duration, BMI, and pain in other locations than extremities.