

Diabetic Neuropathy in Korea

**: Proceedings of a consensus development
for the evaluation and management**

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Diabetic Neuropathy in Korea



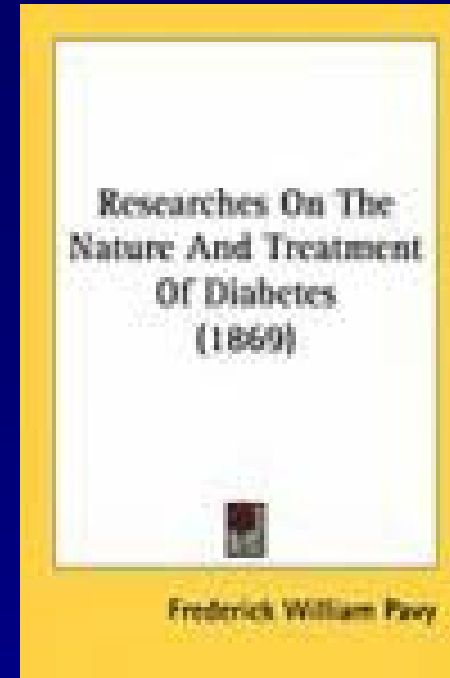
Korean Diabetic Neuropathy Study Group



Clinical Characteristics of diabetic Neuropathy in Korea



Guidelines for Management of Diabetic Neuropathy in Korea



Frederick William Pavy (1829-1911)

“heavy legs, numb feet, lighting pain and deep-seated pain in feet, hyperaesthesia, muscle tenderness, and impairment of patellar tendon reflexes”

Pavy also made a point that occurrence of neuropathic symptoms may precede that of clinical diabetes.



Indian physician **Susruta** (5th century AD),
“Their premonitory symptoms are-feeling of ***burning in the palms and soles***, body becoming ***unctuous and slimy and feel heavy***, urine is sweat, bad in smell, and white in color, and profound thirst...Complications include ***diarrhea, constipation, and fainting***”

Abd Allarh Ibn Sinna (Avicenna, 980-1037 AD),
He observed ***gangrene*** and the ‘***collapse of sexual function***’ as complications of diabetes.

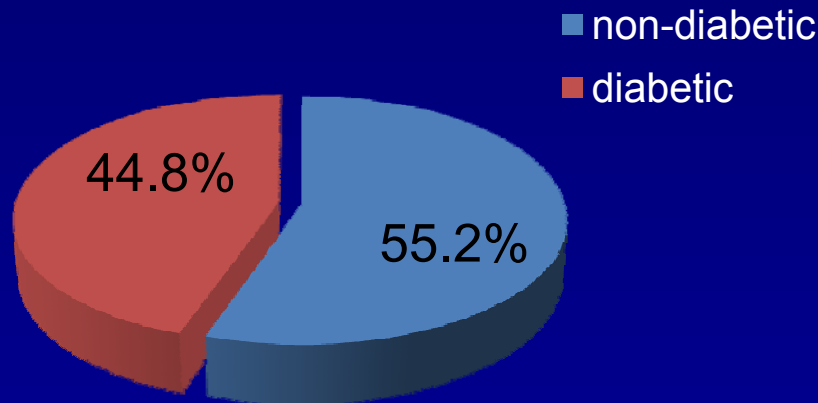


藤原道長 (**Fujiwara No Michigawa, 966-1028 AD**),
considered to be the first person to suffer from
diabetes (‘***water-drinking illness***’, mizu nomi yagi)
and autonomic neuropathy.

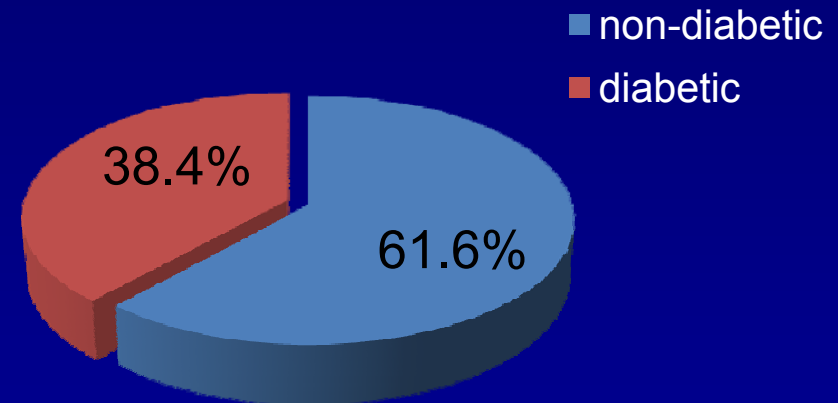
Diabetic Neuropathy in Korea

Foot diseases and diabetes

Foot amputation (N= 3,829, 2003)



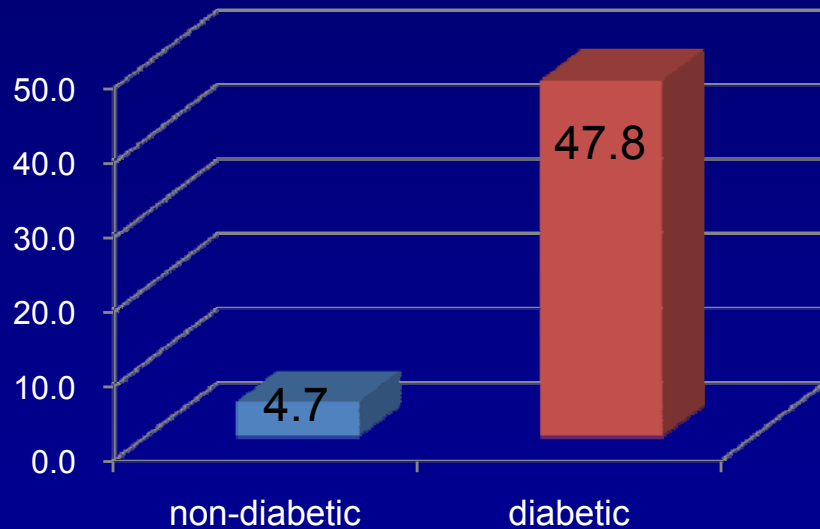
Foot ulcer (N= 8,495), 2003



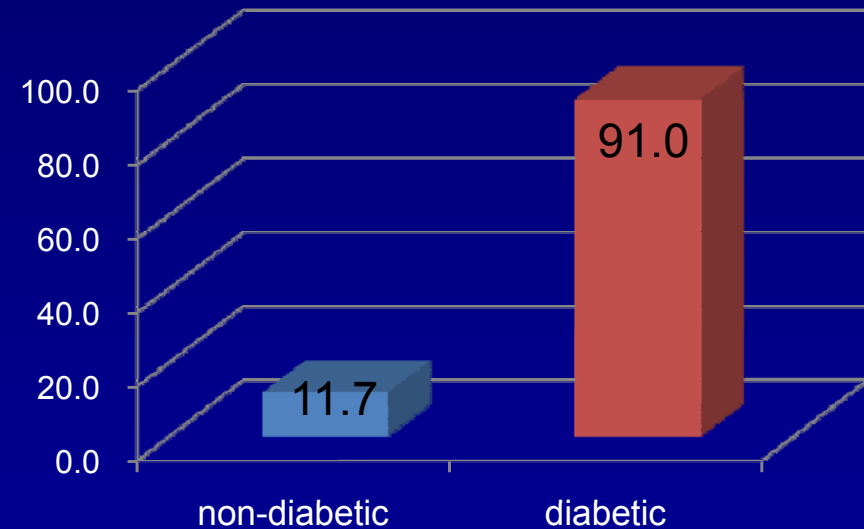
Analysis of the medical records sampled from the health insurance data regarding claims with foot amputation (Z894-899), ulcer of lower limb (L97), gangrene (R02), insulin-dependent diabetes (E10), non-insulin dependent diabetes (E11), malnutrition related diabetes (E12), other specified diabetes (E13) or unspecified diabetes (E14) as principal or secondary diagnosis between Dec 1994 and Dec 2002.

Foot disease in patients with diabetes

Foot amputation rate (2003)



Foot ulcer rate (2003)

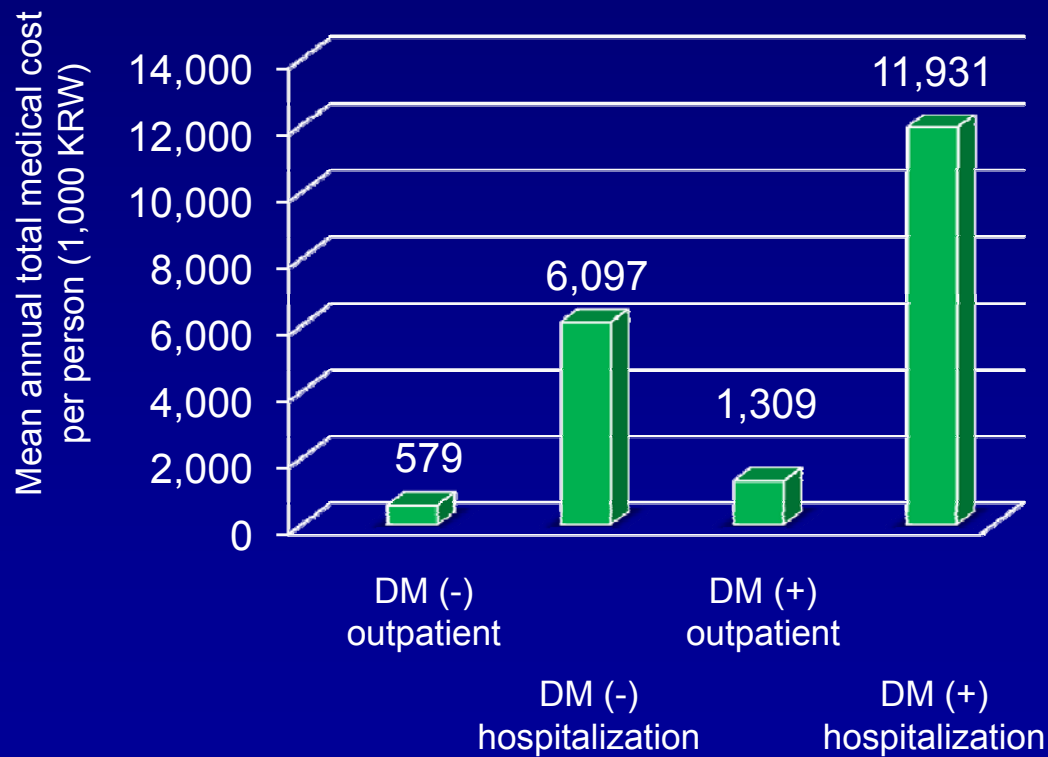


Per population of 100,000

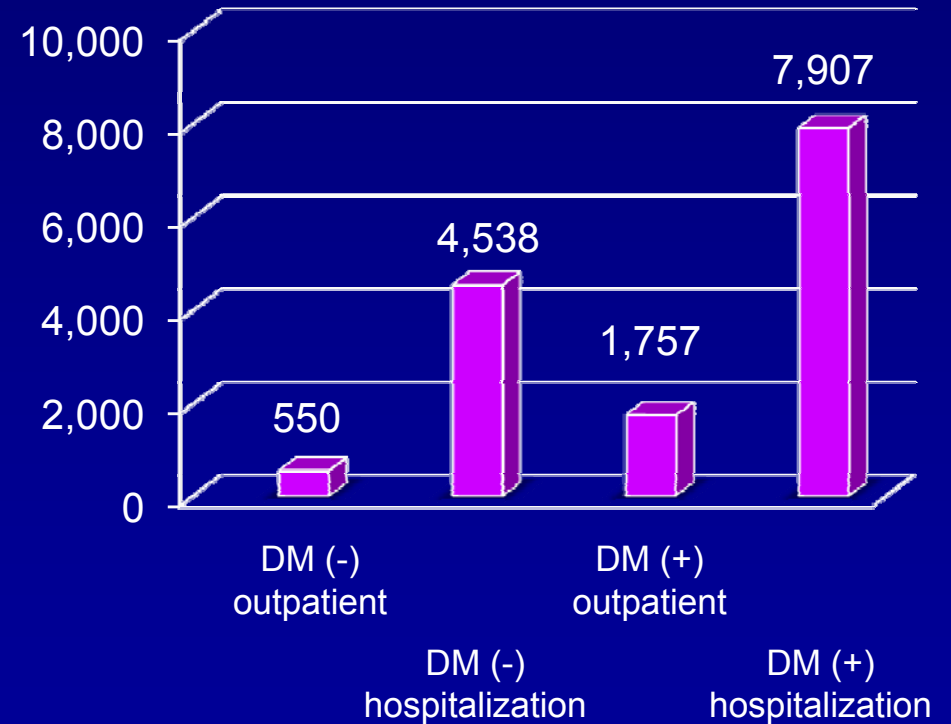
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Total medical cost in patients with diabetic foot disease

Foot amputation (2003)



Foot ulcer (2003)



Korean Diabetic Neuropathy Study Group

Subcommittee of KDA: Diabetic neuropathy study group

Director: Prof. Kyung Soo Ko, MD



Secretary: Hyuk -Sang Kwon MD

Advisory



Prof. Bong -Yun Cha, MD



Prof. Tae Sun Park, MD

Program

Ji Hyun Lee MD



Research

Jong Hwa Kim MD

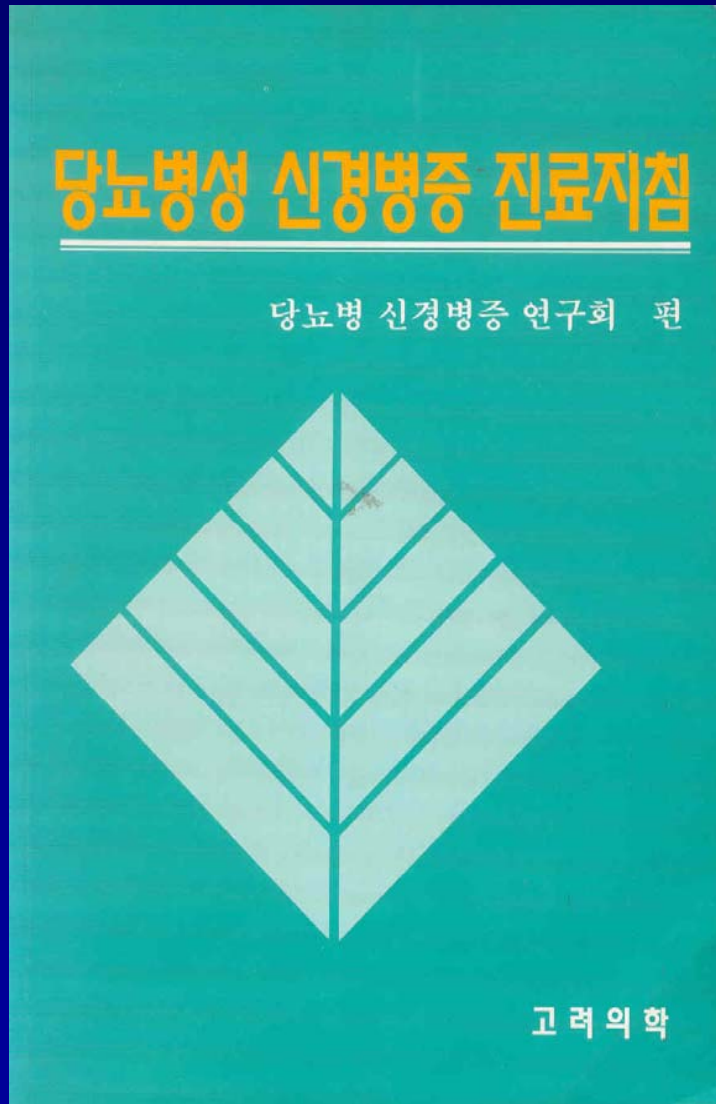


Publication

Jong Chul Won MD



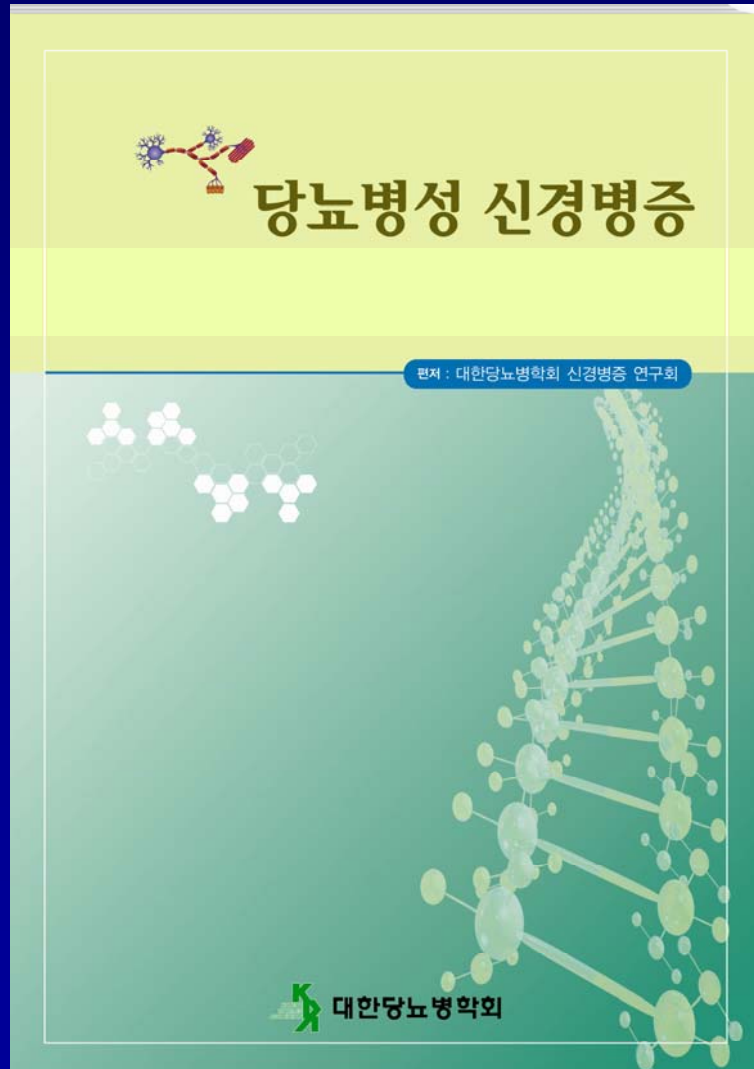
Guideline for management of diabetic neuropathy (1996)



Bo Wan Kim
Young Seol Kim
Yong Ki Kim
Hyun Man Kim
Ho Young Son
Hong Kyu Lee
Hyun Chul Lee
Min Young Jung

Korean Diabetic Neuropathy Study Group. 1996
(113 pages volume)

Textbook of Diabetic Neuropathy (Korean)

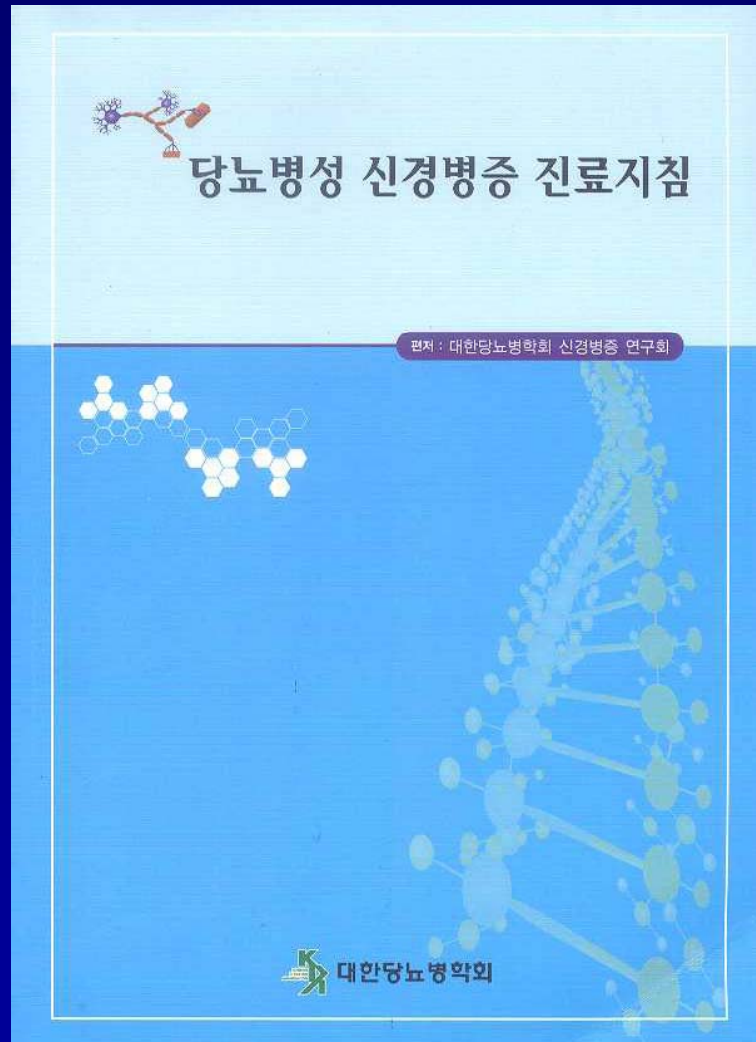


Prof. Bong Yun Cha MD

And 57 doctors and professors

Korean Diabetic Neuropathy Study Group. 2006
(309 pages volume)

Guideline for management of diabetic neuropathy (2007), updated



Prof. Bong-Yun Cha MD

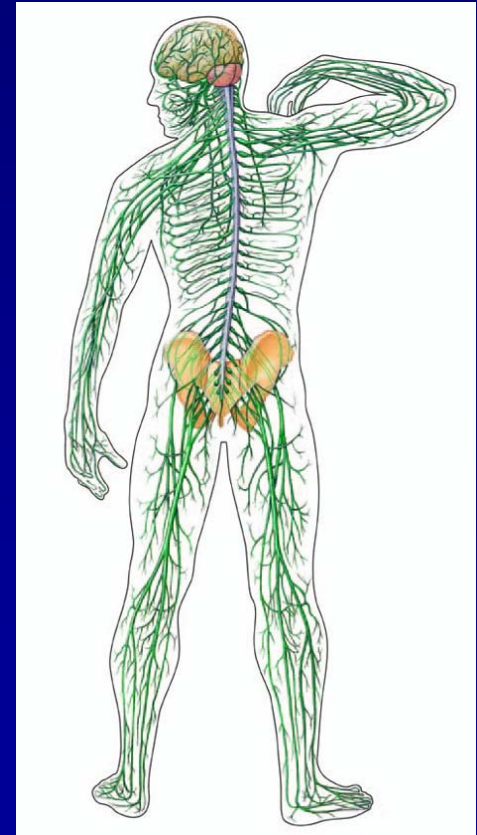
And 12 members of
Korean Diabetic
Neuropathy Study Group

Korean Diabetic Neuropathy Study Group. 2007
(65 pages volume)

Clinical study

- Diabetic distal symmetric peripheral neuropathy (DSPN) patients survey (2005), completed
 - PI: Prof. Bong-Yun Cha MD
 - Clinical characteristic of diabetic DSPN in Korea (31 hospitals)
- Burden of illness in painful diabetic peripheral neuropathy (2009), initiated
 - PI: Prof. Kyung Soo Ko MD
 - Patients reported outcomes (pain severity, patients functioning, sleep disturbance, impact on the quality of life) (40 hospitals)

Clinical Characteristics of Diabetic Neuropathy in Korea



Diabetic DSPN Patient Survey (1)

The survey aims to

1. Conduct a basic epidemiological study on diabetic neuropathy of Koreans,
2. Understand clinical characteristics of diabetic peripheral neuropathy of Koreans, and
3. Comprehend diagnosis criteria and treatment principals

DSPN: distal symmetric polyneuropathy

Diabetic DSPN Patient Survey (2)

Survey methods

- Face-to-face interview by experienced nurses
- Questionnaire and chart review to understand neuropathy symptoms due to diabetics, and basic neurological examination including deep tendon reflex test, tuning fork test and monofilament test for objective results

Areas surveyed

- Nationwide (31 Hospitals)

Subjects

- Diabetic patients who made out-patient visits to general hospitals

Samples

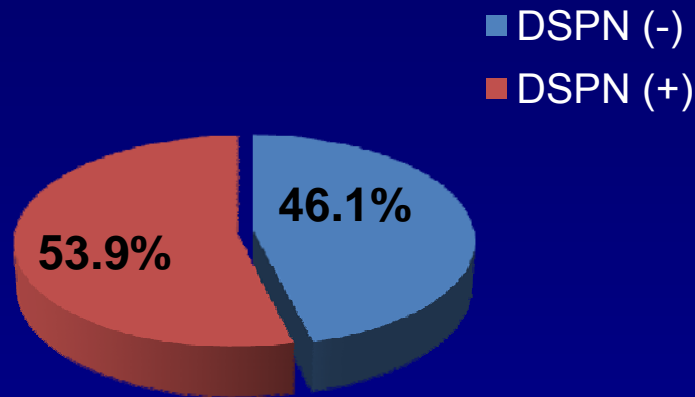
- N = 875 in total (male and female, 398 and 477, respectively)
* Neuropathy (+) : 472

Survey period

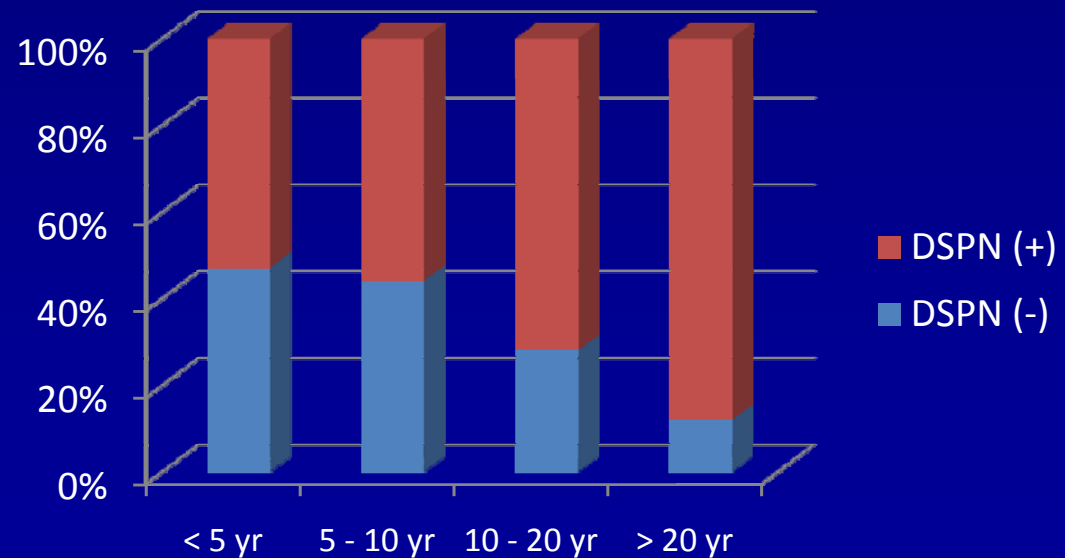
- 8/25/2005 ~ 10/25/2005

Diabetic neuropathy: Distal symmetric peripheral neuropathy

Presence of DSPN



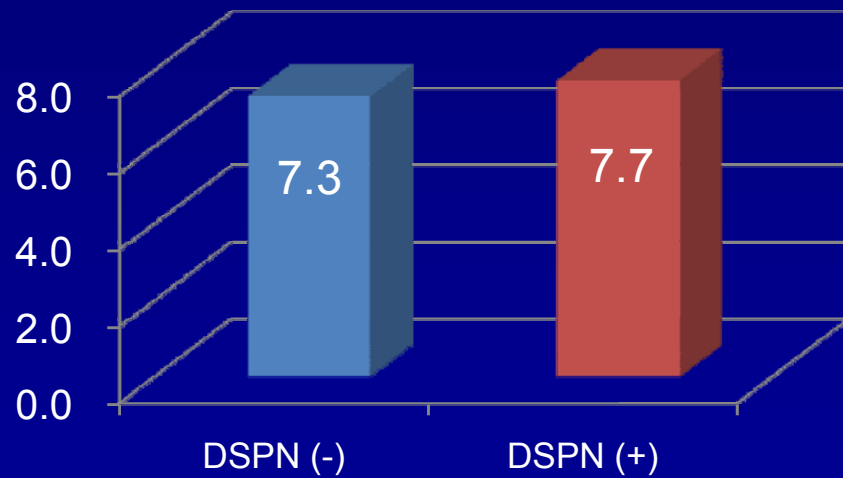
Duration of diabetes



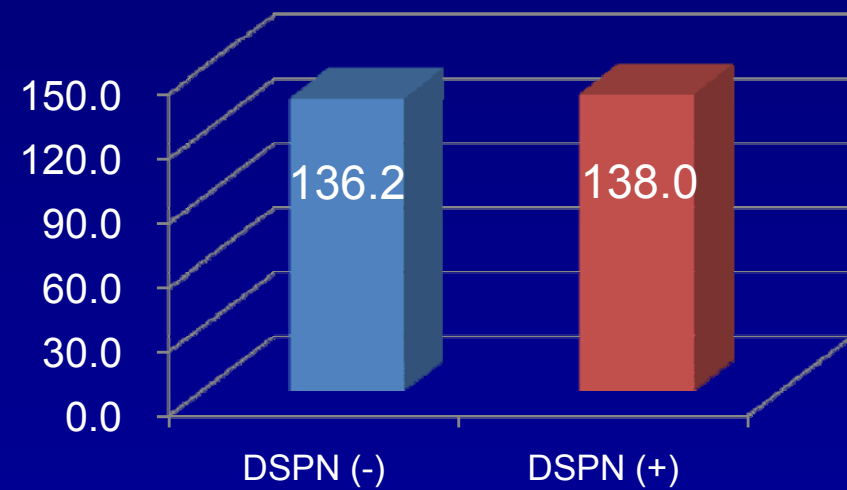
N = 875, (%)

Glycemic status of patients

A1C (%)



FPG (mg/dL)

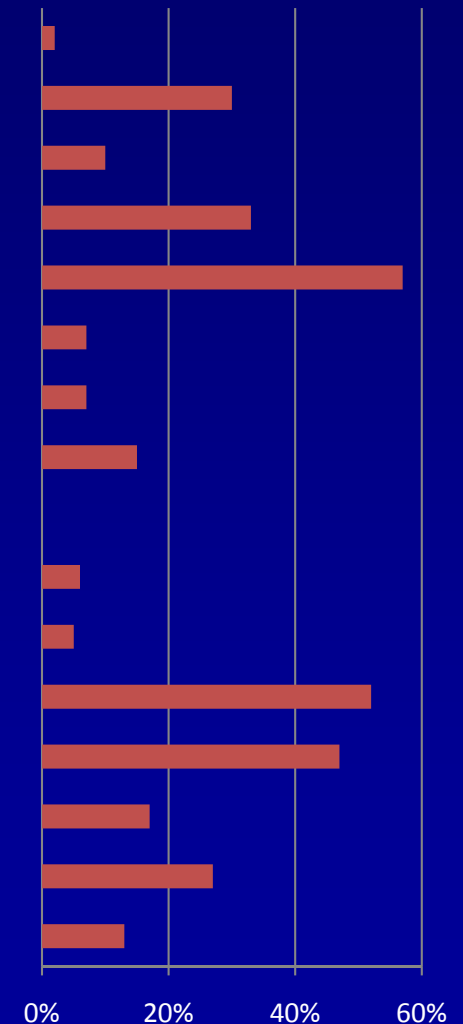


N = 875, (%)

Subjective symptoms: MNSI

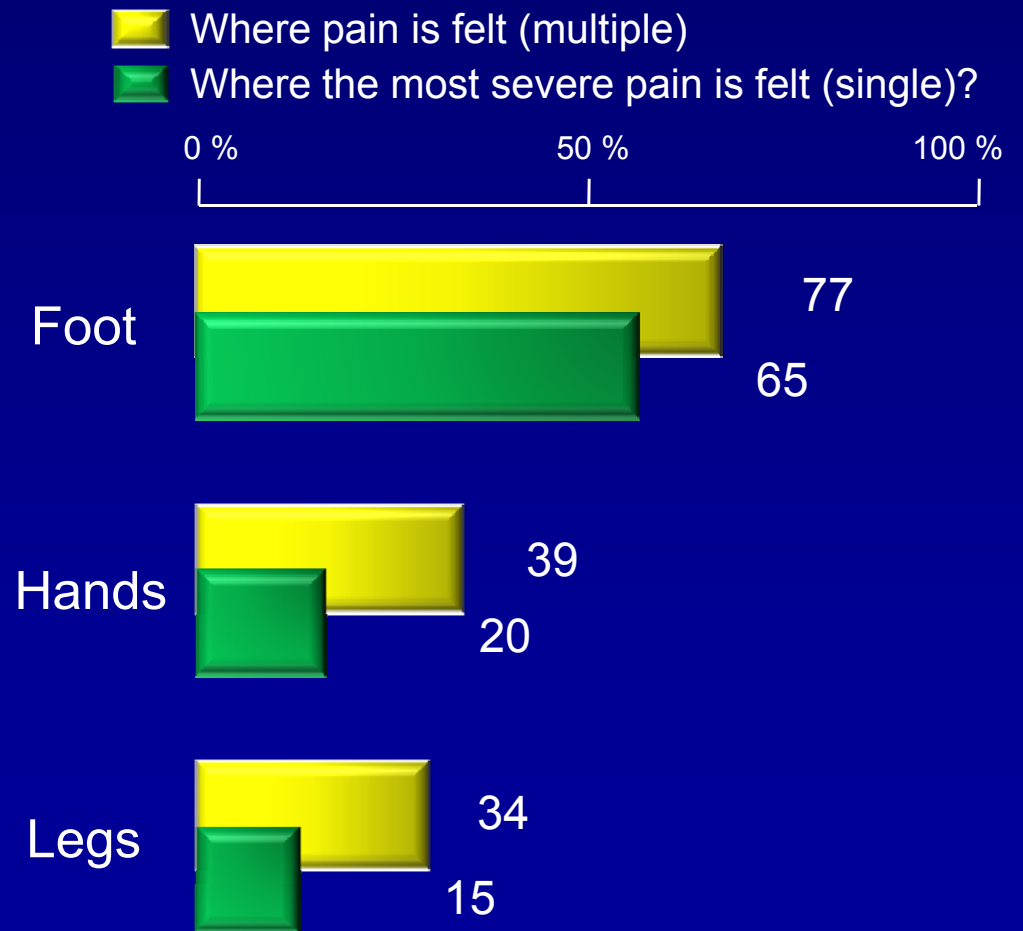
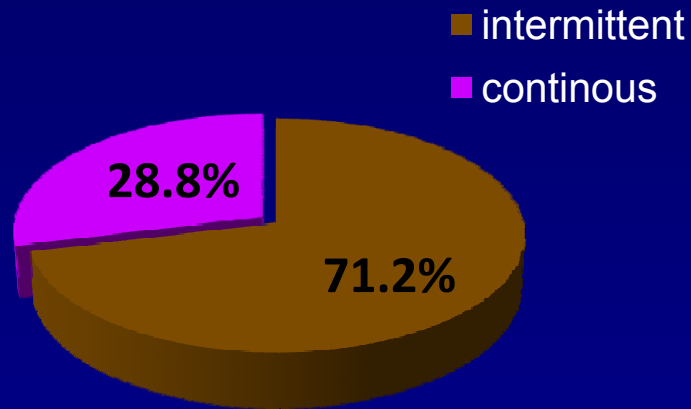
MICHIGAN NEUROPATHY SCREENING INSTRUMENT

1. Are your legs and/or feet numb?
2. Do you ever have any burning pain in your legs and/or feet?
3. Are your feet too sensitive to touch?
4. Do you get muscle cramps in your legs and/or feet?
5. Do you ever have any prickling feelings in your legs or feet?
6. Does it hurt when the bed covers touch your skin?
7. When you get into the tub or shower, are you able to tell the hot water from the cold water?
8. Have you ever had an open sore on your foot?
9. Has your doctor ever told you that you have diabetic neuropathy?
10. Do you feel weak all over most of the time?
11. Are your symptoms worse at night?
12. Do your legs hurt when you walk?
13. Are you able to sense your feet when you walk?
14. Is the skin on your feet so dry that it cracks open?
15. Have you ever had an amputation?



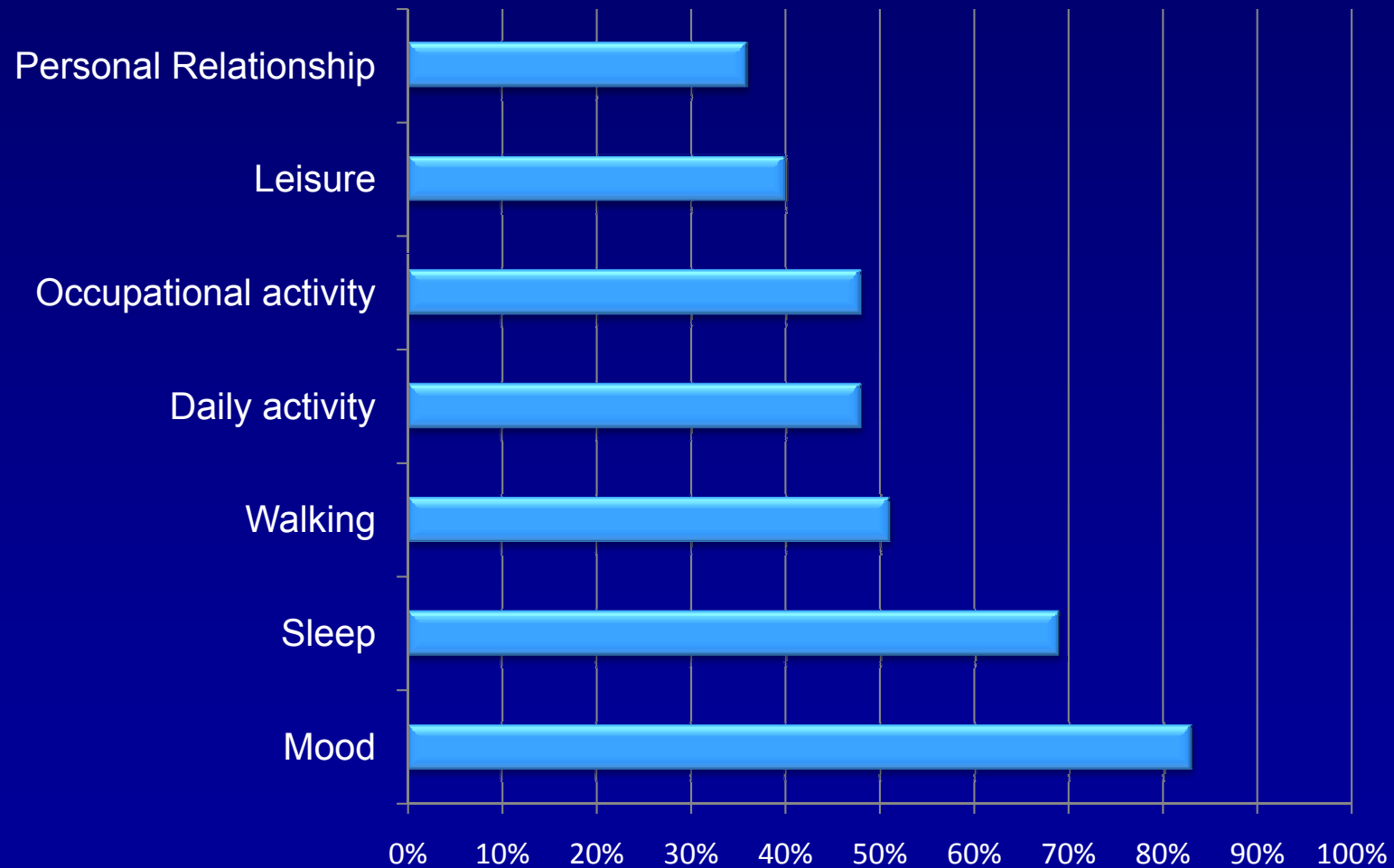
N = 472, (%)

DSPN: Duration and location



N = 472, (%)

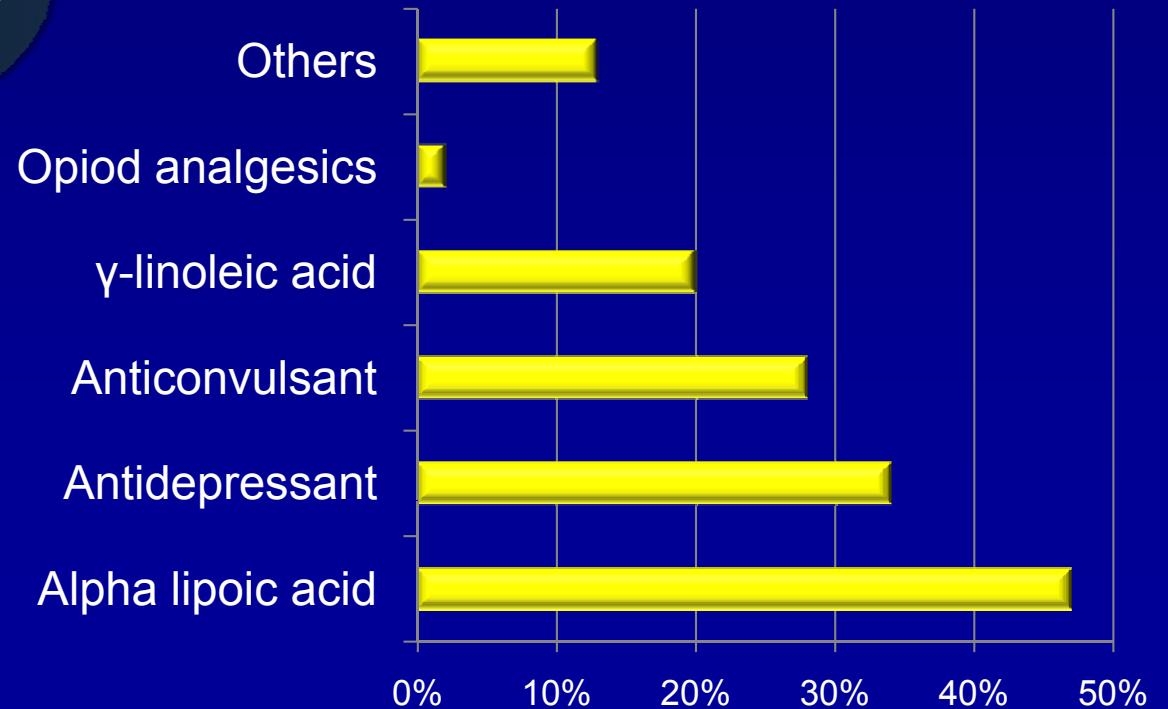
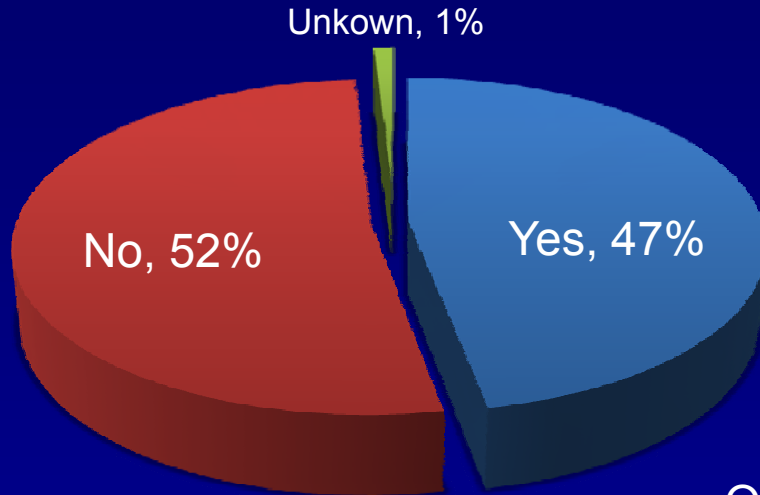
DSPN: Impact on the quality of life



N = 472, (%)

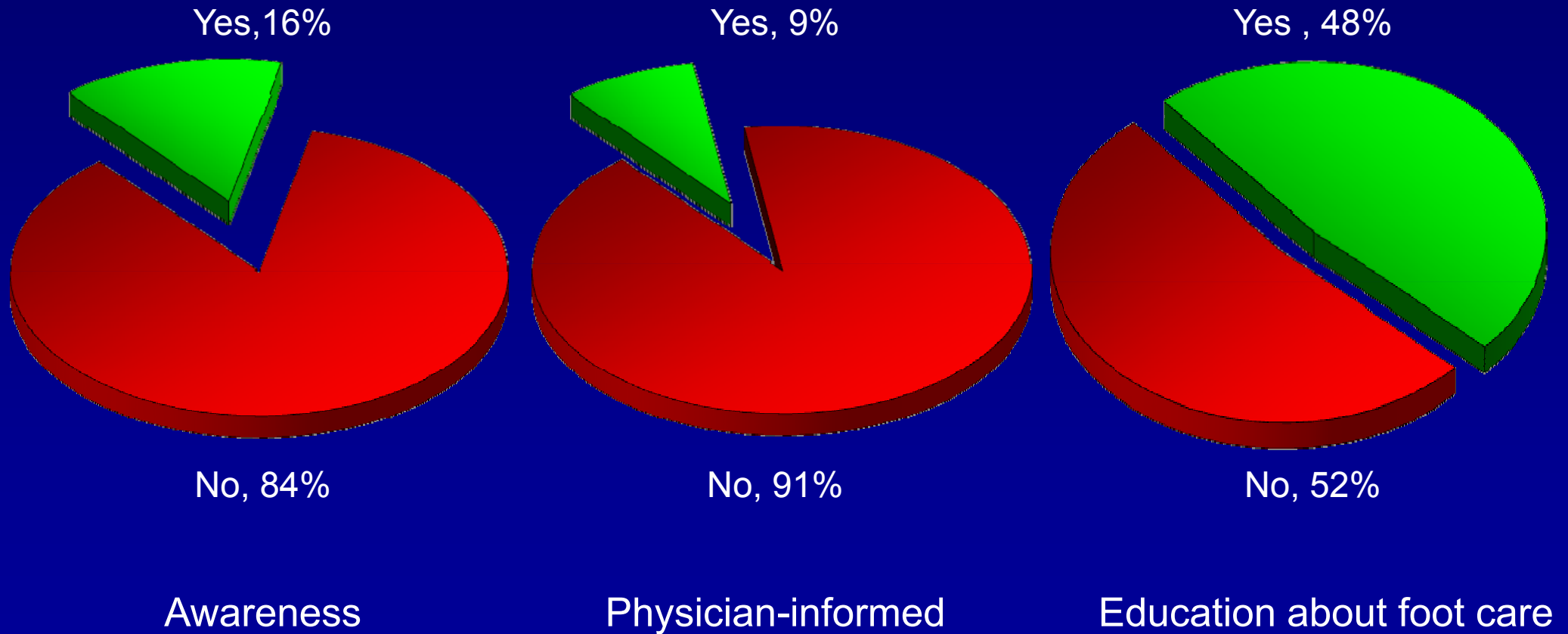
DSPN: Treatment

N = 472, (%)



N = 222, (%)

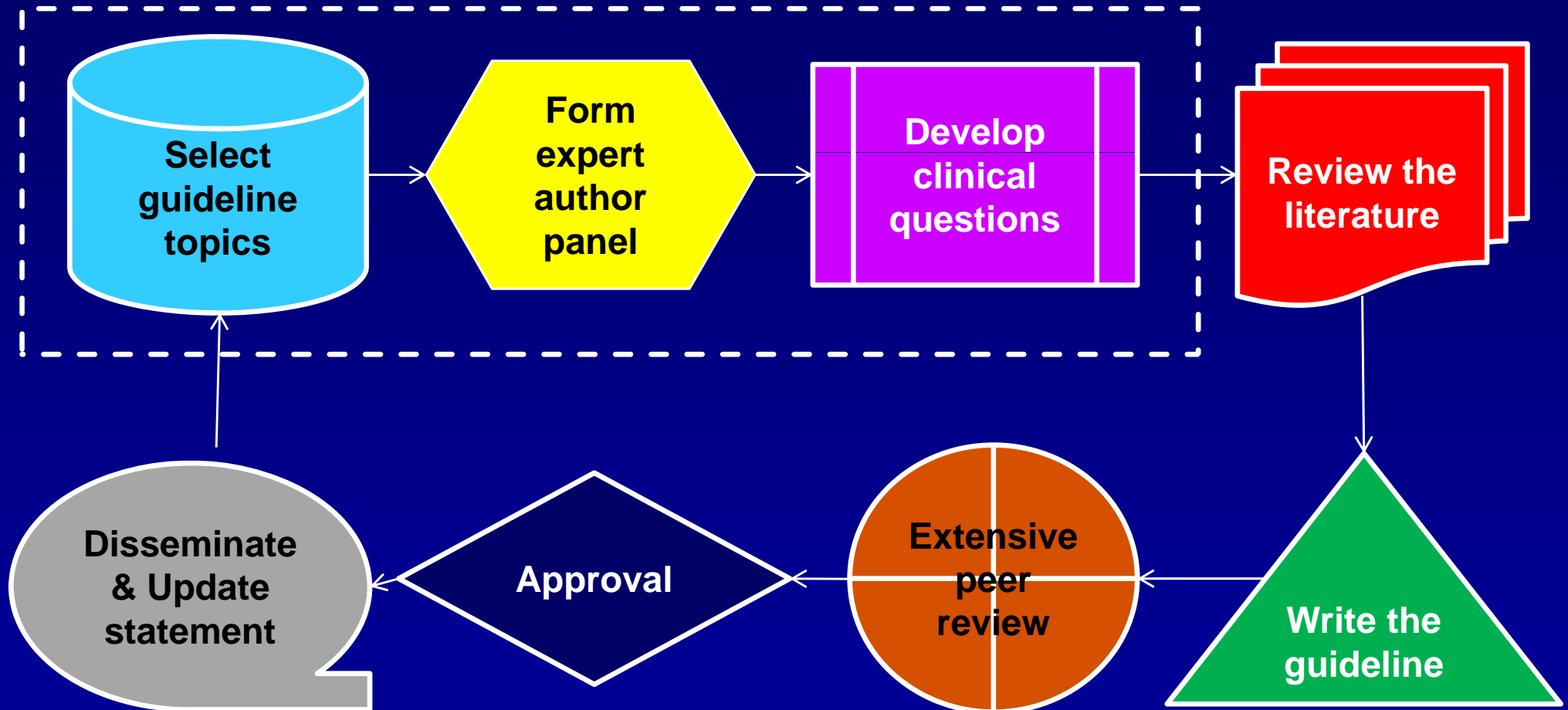
DSPN: Awareness



N = 875, (%)

Guidelines for Management of Diabetic Neuropathy in Korea

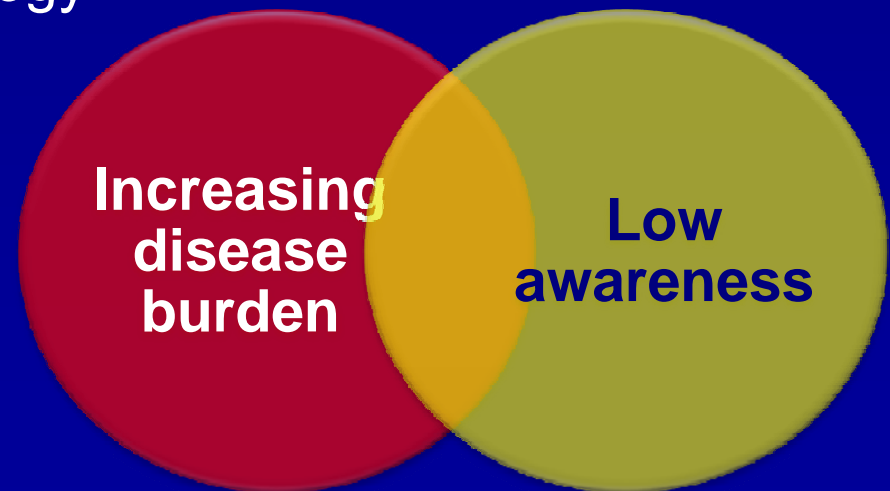
Guideline development process



Select guideline topics



- ✓ Members' needs
- ✓ Prevalence of condition
- ✓ Health impact of condition for the individual and others
- ✓ Socioeconomic impact
- ✓ Extent of practice variation
- ✓ Quality of available evidence
- ✓ External constraints on practice
- ✓ Urgency for evaluation of new practice technology



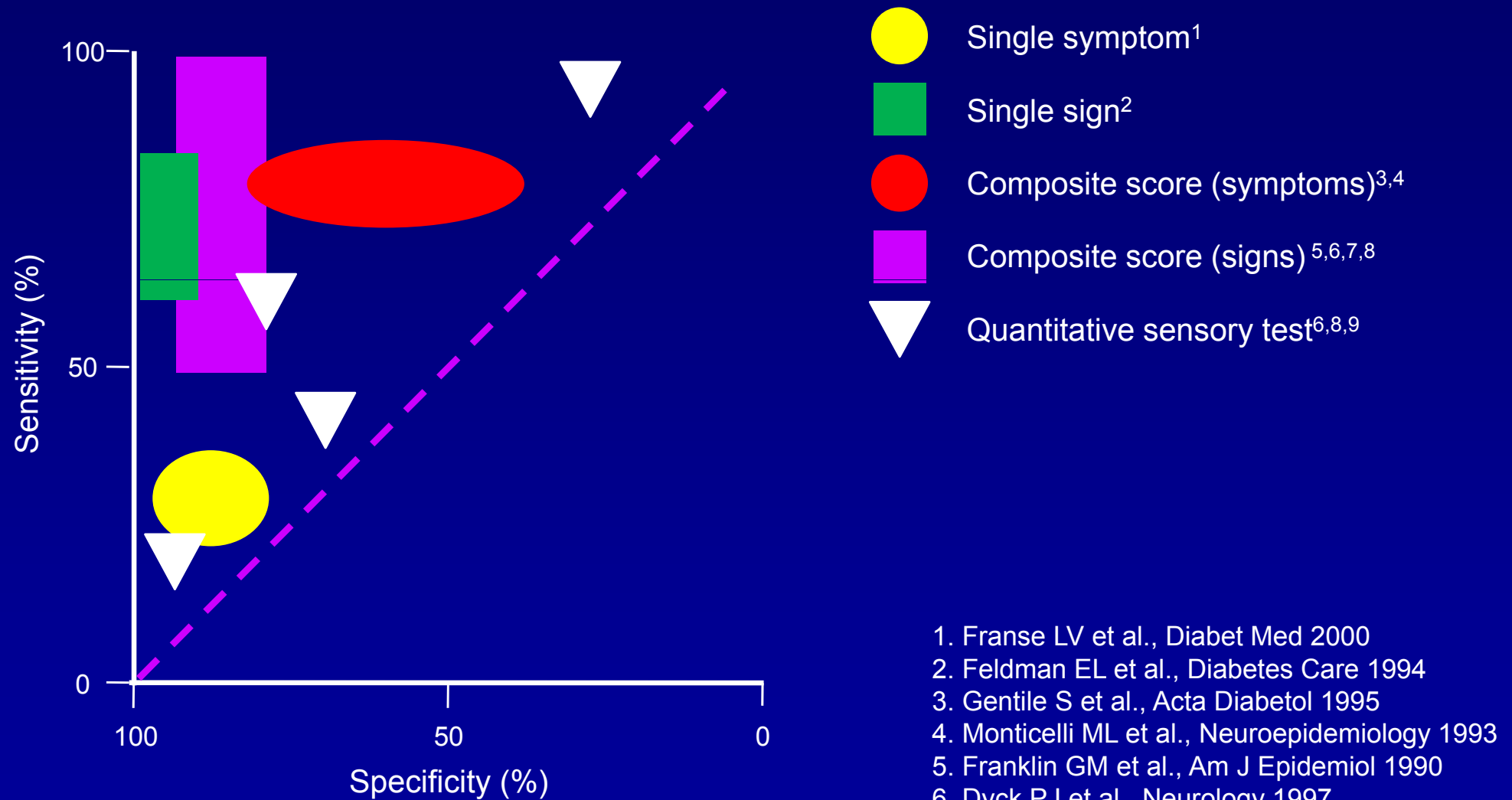
Symposium: Diagnosis and treatment of painful diabetic neuropathy

Oct 7 2009. Professors: Endocrinology, Neurology, Anesthesiology (Korean Pain Management Study Group)

Object: review the current practice for management of painful diabetic neuropathy and clinical question development

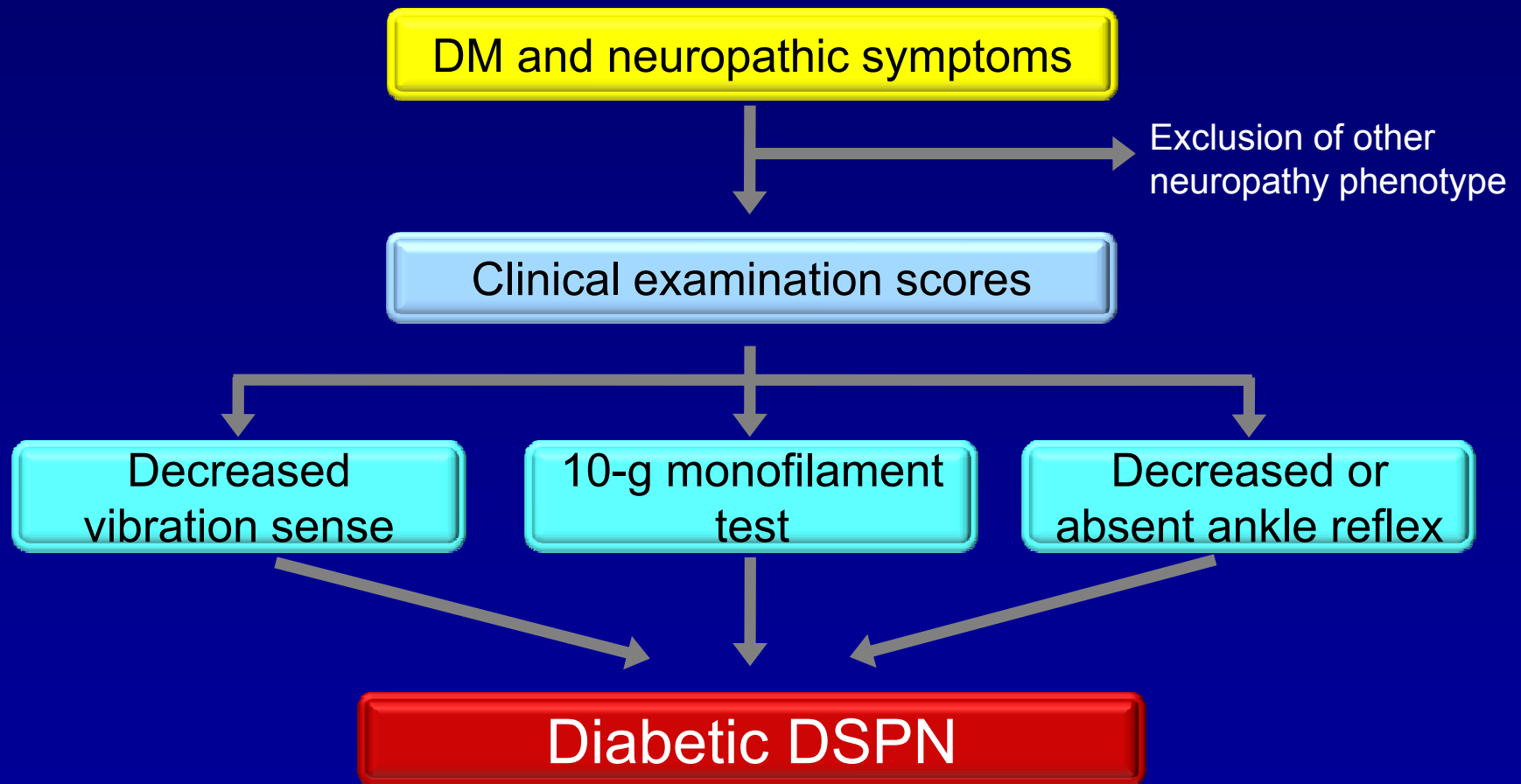


Diagnostic accuracy for the presence of distal symmetric polyneuropathy



1. Franse LV et al., Diabet Med 2000
2. Feldman EL et al., Diabetes Care 1994
3. Gentile S et al., Acta Diabetol 1995
4. Monticelli ML et al., Neuroepidemiology 1993
5. Franklin GM et al., Am J Epidemiol 1990
6. Dyck PJ et al., Neurology 1997
7. Valk GD et al., Diabet Med 1992
8. Dyck PJ et al., Neurology 1992
9. Maser RE et al., Diabetes Care 1992

Diagnosis of diabetic DSPN



AACE Guideline (1)

American Association of Clinical Endocrinologists (AACE) medical guidelines for clinical practice for the management of diabetes mellitus. Microvascular complications

All patients with T2DM should be assessed for neuropathy at the time of diagnosis (**grade A**); **annual examinations** should be performed thereafter in all patients. Screening may include:

History and examination eliciting signs of autonomic dysfunction
Testing for heart rate variability, if indicated, which may include expiration-to-inspiration ratio and response to the Valsalva maneuver and standing.

Inspect the patient's feet at every visit (grade B).

Perform an annual comprehensive foot examination (grade B)

AACE Guideline (2)

American Association of Clinical Endocrinologists (AACE) medical guidelines for clinical practice for the management of diabetes mellitus. Microvascular complications

Consider treatment with **duloxetine** or **pregabalin**, both of which are indicated to treat diabetic neuropathy (**grade C**).

Tricyclic antidepressants; topical capsaicin; and antiepileptic drugs such as carbamazepine, gabapentin, pregabalin, topiramate, and lamotrigine may provide symptomatic relief, but must be prescribed with knowledge of potential toxicities (**grade C**).

KDA Guideline



Annual examination with pin-prick test, temperature/vibration sense, and 10-g monofilament

Most patients with painful diabetic neuropathy need to be treated with **alpha lipoic acid, γ -linoleic acid, TCA, anticonvulsant, SSRI ect.**

JDS Guideline



The simultaneous presence of diabetes and peripheral neuropathy¹ strongly suggest diabetic neuropathy.

Mild cases may be improved simply by glycemic control.

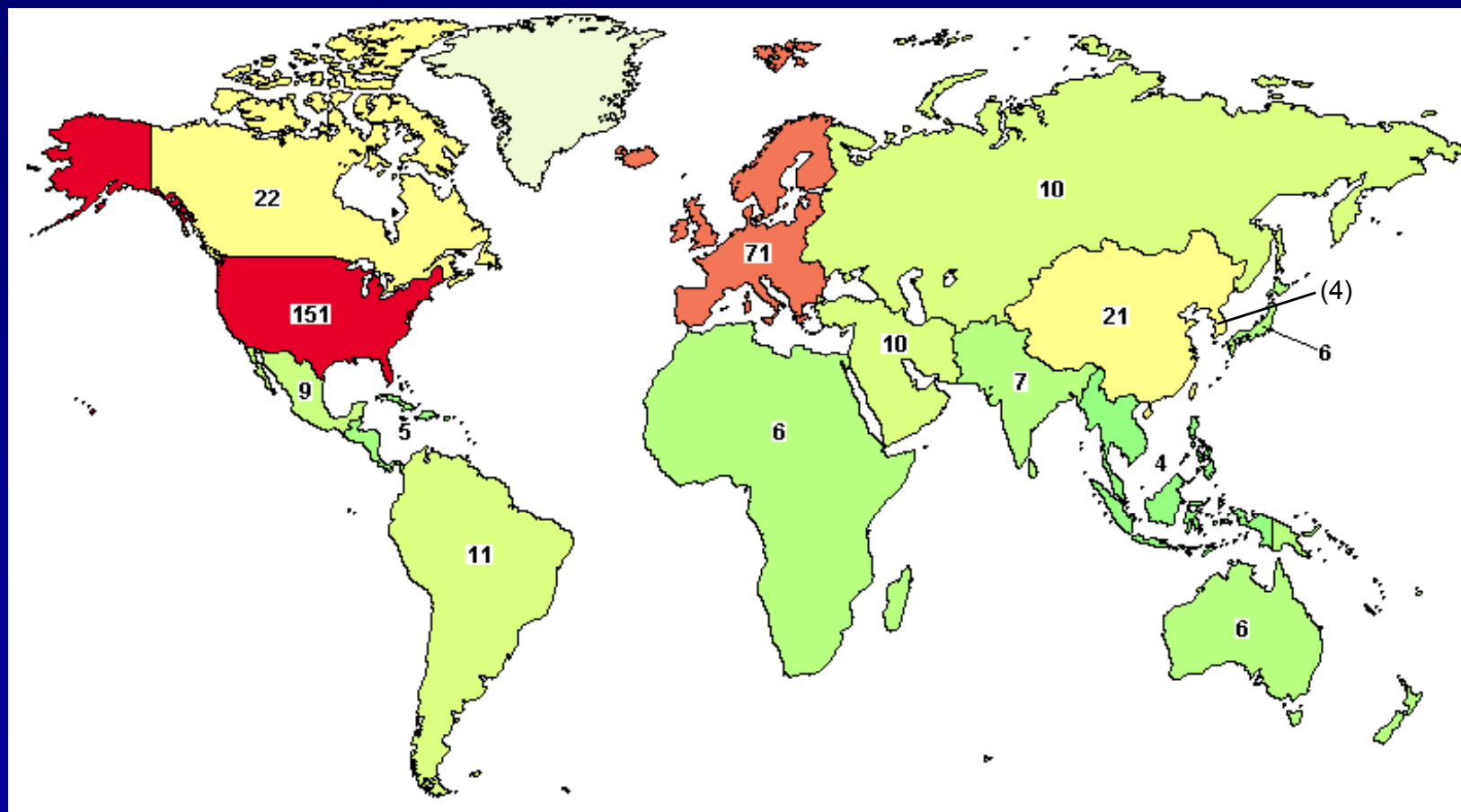
NSAID, AR inhibitor (epalrestat) and antiarrhythmics (mexiletine), anticonvulsants (carbamazepine), and antidepressants may be effective, but chronic cases may be difficult to treat.

1. Numbness in both lower limbs, dolor, hypoesthesia or parasthesia, and absence of the Achilles tendon reflex.

JDS. *Treatment Guide for Diabetes*.2007

Clinical trials for “Diabetic Neuropathy”

Map of 290 studies found by search of: diabetes and neuropathy



<http://clinicaltrials.gov> accessed at Nov 2 2009

Clinical trials in Korea

Found 4 studies with search of diabetes and neuropathy (Nov 2, 2009)

Completed **A Study To Evaluate Pregabalin In Patients With Painful Diabetic Peripheral Neuropathy (DPN)**

Placebo, pregabalin

Recruiting **An Efficacy and Safety Study of Carisbamate in the Treatment of Nerve Pain in Diabetics**

Placeb, Carisbamate 1,200 mg/d, Carisbamate 800 mg/d, Pregabalin 300 mg/d

Completed **Pregabalin Peripheral Neuropathic Pain Study**

Has Results

Placebo, pregabalin

Completed **Study Evaluating the Safety and Efficacy of a Once-daily Dose of Tigecycline vs Ertapenem in Diabetic Foot Infections With a Substudy in Patients With Diabetic Foot Infections Complicated by Osteomyelitis.**

Has Results

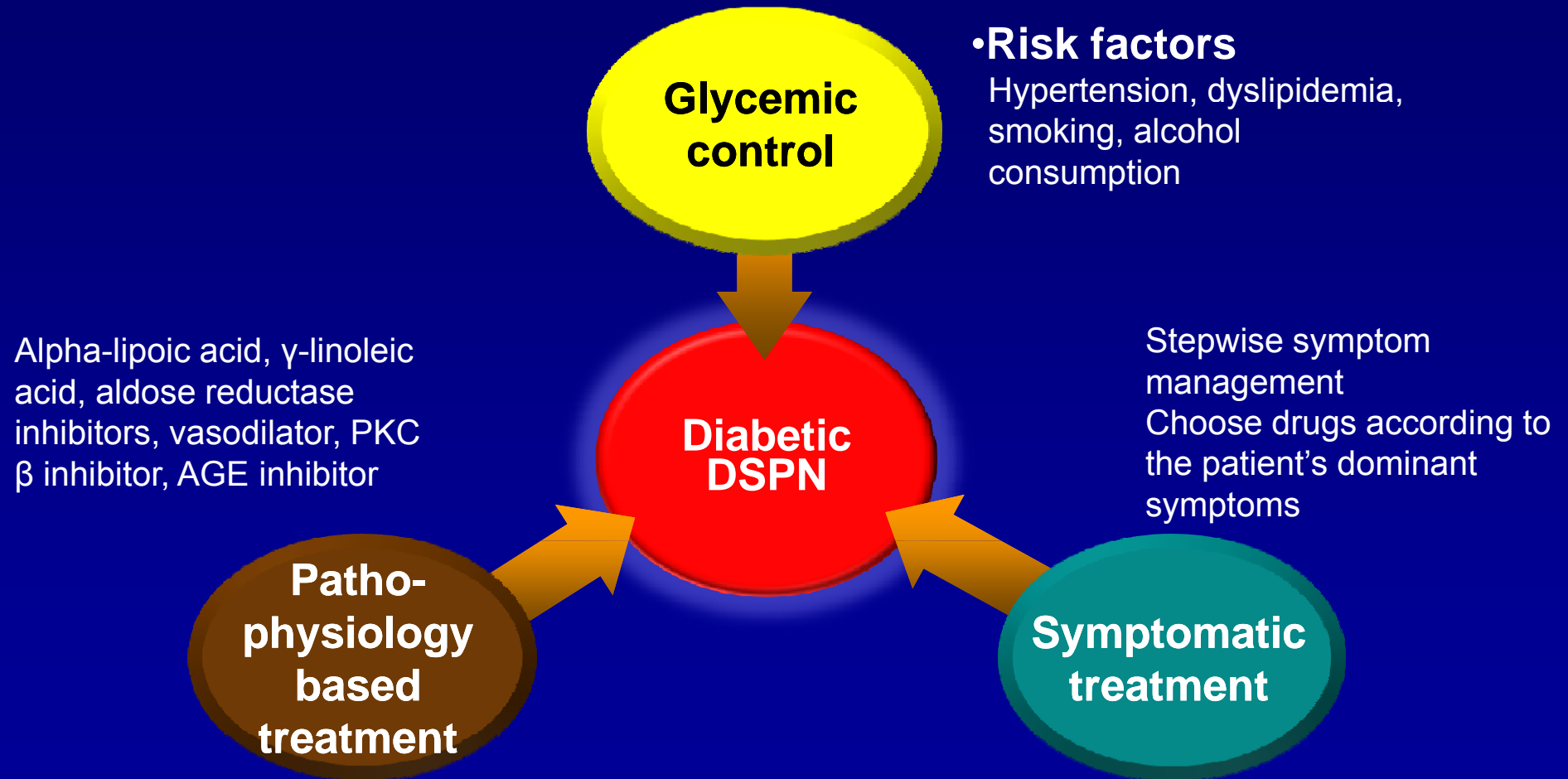
Tigecycline, Ertapenem

Clinical trials in Japan

Found 6 studies with search of diabetes and neuropathy (Nov 2, 2009)

Recruiting	A Long-Term Study To Evaluate Safety And Efficacy Of Pregabalin For Pain Associated With Diabetic Peripheral Neuropathy pregabalin
Completed	Randomized, Double-Blind, Multicenter, Placebo-Controlled Study Of Pregabalin For Pain Associated With Diabetic Peripheral Neuropathy placebo, pregabalin
Completed	A Study for the Treatment of Painful Diabetic Neuropathy Duloxetine hydrochloride, placebo
Recruiting	A Long-Term Study for the Treatment of Painful Diabetic Neuropathy Duloxetine hydrochloride
Terminated	ASP 8825 - Study in Patients With Painful Diabetic Polyneuropathy ASP8825, placebo
Active, not recruiting	OlmeSartan and Calcium Antagonists Randomized (OSCAR) Study Olmesartan medoxomil, Calcium channel blockers (amlodipine, azelnidipine)

Treatment of diabetic DSPN



Undetermined treatment

- Additional Therapies
 - Topicals :
 - Capsaicin, lidocaine 5% patch
 - Acupuncture
 - NMDA receptor antagonists
 - Antiarrhythmics
- Physical Therapy
- Steroid injections
- Surgical decompression
- Nerve ablation
- Medications

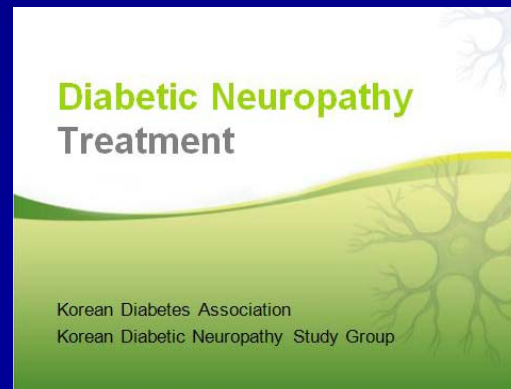
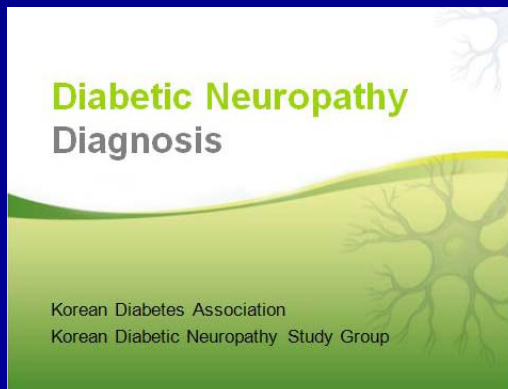
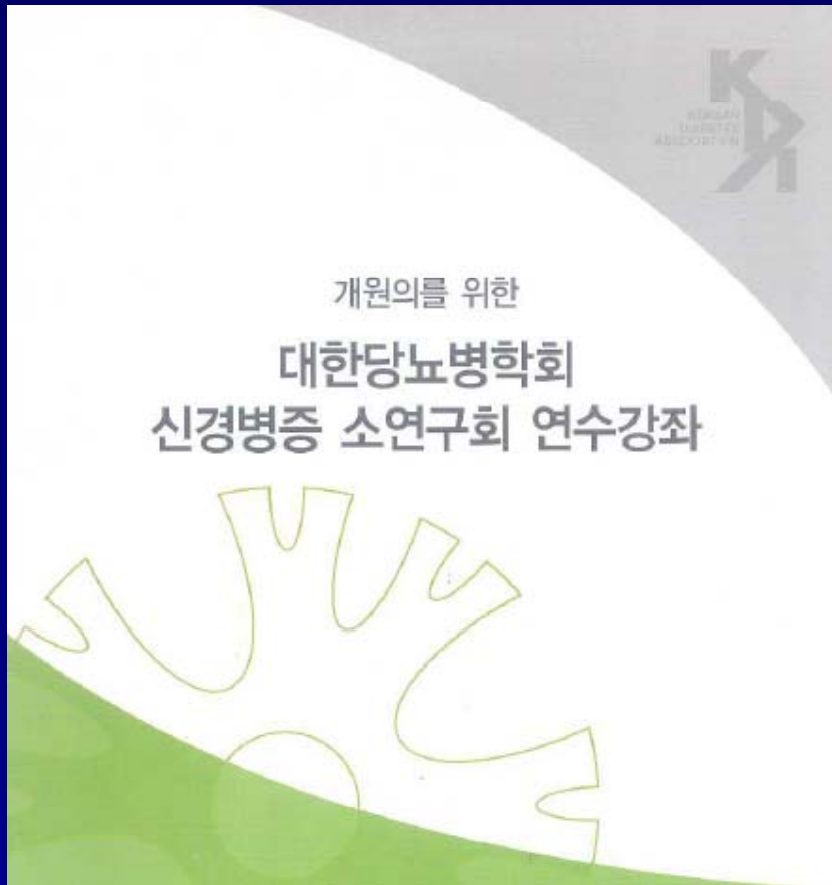


Questions about diabetic neuropathy will be answered

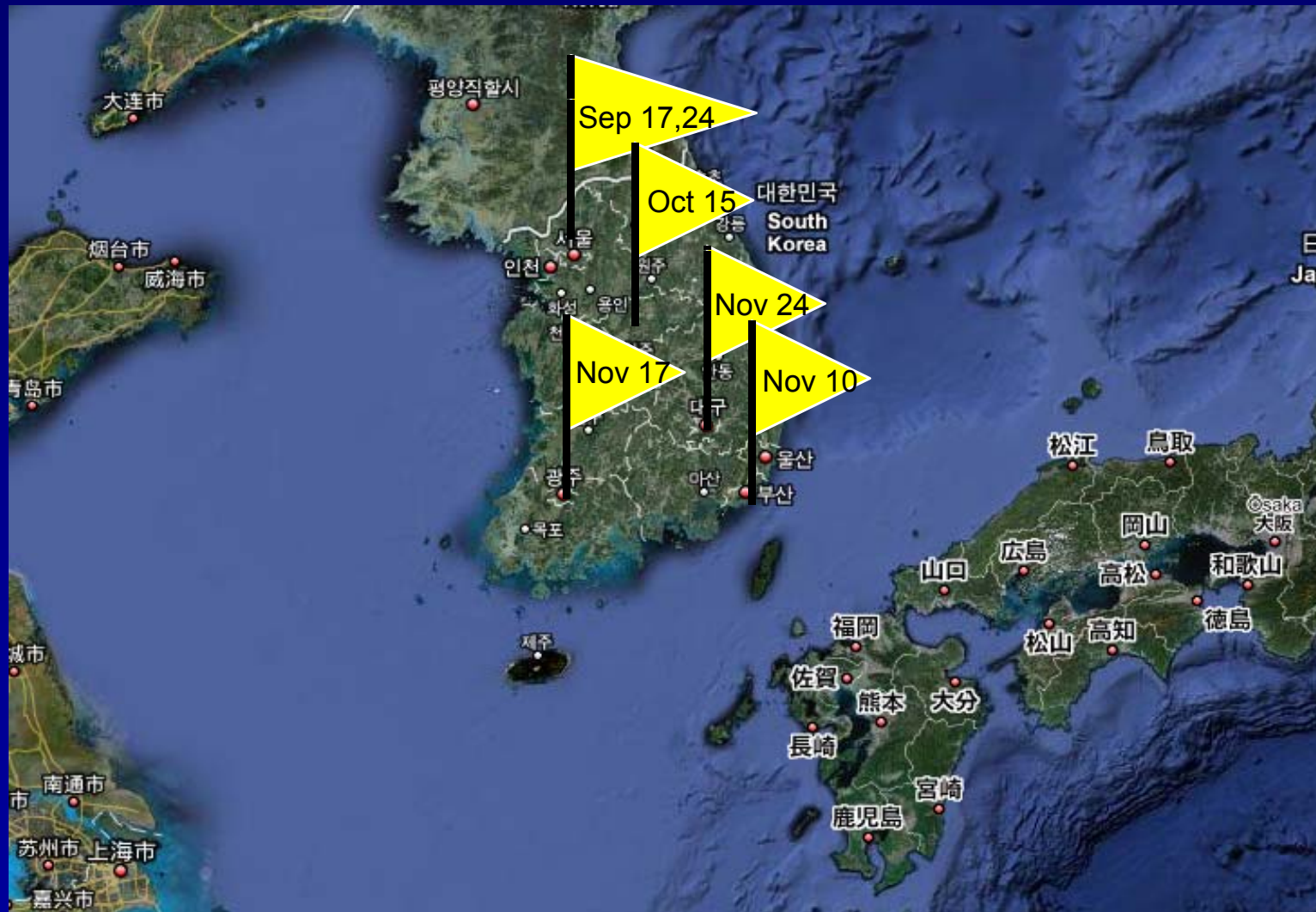


Clinical question development

- 1) Role of electro-physiologic study in the diagnosis of DSPN.
- 2) Role of non-pharmacological treatment in patients with medically intractable neuropathic pain.



Training course for primary physician: Management of diabetic neuropathy



Brochures for patients

これからは 楽にしてください。

これからは 自由になってください。。。

糖尿病性神経病変 これ以上
耐えないで 医者と 相談し
てください



이제는
편안해지세요!
당뇨환자 4명 중 1명은 당뇨병성 신경병증으로 인한
통증으로 고통받고 있습니다.

손, 발 저림
찌릿찌릿함
따끔거림
통증으로 인한 수면장애

당뇨병성 신경병증통증, 더 이상 참지 말고
의사 선생님과 상담하세요!



이제는
자유로워지세요!
당뇨환자 4명 중 1명은 당뇨병성 신경병증으로 인한
통증으로 고통 받고 있습니다.

손, 발 저림
찌릿찌릿함
따끔거림
통증으로 인한 수면장애

당뇨병성 신경병증통증, 더 이상 참지 말고
의사 선생님과 상담하세요!

Summary and future direction

- Foot diseases in diabetic patients in Korea were 10-folds more common compared with those on non-diabetics
- Comprehensive examination composed of composite symptom score and simple neurologic examinations should be performed annually
- When treating patients with diabetic DSPN, consider treatment with pathophysiology-based approach and, in some cases, symptomatic treatment is required
- Roles or indications of electrophysiologic study and non-pharmacologic treatment will be determined
- The strategies for dissemination of current management guideline is urgent

Acknowledgement

In je univiersity

Kyung Soo Ko MD

Catholic University, Seoul

Bong-Yun Cha MD

Hyuk Sang Kwon MD

Chonbuk University, Jeonju

Tae-sun Park MD

Catholic University, Daegu

Ji-Hyun Lee MD

Sejong Hospital, Bucheon

Jong-Wha Kim MD

All members of Korean Diabetic
Neuropathy Study Group

Pfizer, Korea

Thank you for your attention!