

71% of Men, 51% of Women With Diabetes Develop Neuropathy

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REVIEWED BY IRENE M. STRATTON, MSc

In 1998 the UKPDS reported that intensive blood glucose control decreased the risk of microvascular complications in patients with type 2 diabetes. At 12 years, 64% of men and 44% of women in the United Kingdom Prospective Diabetes¹ Study who were free of neuropathy at baseline developed at least one neuropathic abnormality.

Including those who had evidence of neuropathy at diagnosis, 71% of men and 51% of women have clinically significant neuropathy at 12 years.

Irene M. Stratton, MSc, presented data at the European Association for the Study of Diabetes in Munich on 5,102 patients in the UKPDS. Patients had newly diagnosed diabetes and had been followed for up to 25 years. Researchers defined clinical indices of neuropathy as mean great toe vibration sensory threshold >25, one or both ankle jerks absent and erectile dysfunction in men. Mrs. Stratton is a statistician in the Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism at the University of Oxford.

TABLE 1. CLINICAL INDICES OF NEUROPATHY AND RISK FACTORS

	RATE	AGE PER 5 YEARS	FEMALE	HBA1C PER 1%	HEIGHT PER 5 CM	WAIST PER 5 CM	ALCOHOL	CURRENT SMOKER	WEIGHT PER 5 KG
VST >25									
Prevalence	12.8	1.89	NS	NS	1.40	1.05	NS	NS	NS
Incidence	13.3	1.58	NS	1.10	1.22	NS	NS	1.29	1.08
ABSENT ANKLE JERKS									
Prevalence	14.5	1.28	2.09	1.06	1.17	1.14	NS	NS	NS
Incidence	22.2	1.11	NS	1.13	NS	1.11	NS	NS	NS
ERECTILE DYSFUNCTION									
Prevalence	20.4	1.41	N/A	NS	NS	NS	2.00	NS	NS
Incidence	34.3	1.19	N/A	NS	1.11	NS	1.27	NS	1.05

NS: not statistically significant
N/A: not applicable

UKPDS² AT A GLANCE

- The UKPDS (United Kingdom Prospective Diabetes Study) compared intensive glucose control with conventional control in a randomized trial.
- 5,102 patients were included and followed for a mean of up to 13 years; 42% of the patients were female.
- To determine treatment group assignment, patients were stratified by ideal bodyweight.
- Patients who were found not to be overweight received intensive treatment with insulin, sulphonylurea or diet, which was considered to be conventional treatment or the control group. Patients determined to be overweight were randomized to the above groups with the additional possibility of metformin.
- Investigators found that the risk of any diabetes-related outcome was 12% lower in patients who were assigned to the intensive blood-glucose control group versus those who were in the conventional control group ($P=.029$).
- Reporting in the *Lancet*, researchers said that the majority of risk reduction of the diabetes-related endpoint was attributable to a 25% reduced risk in microvascular outcomes.
- Experts said the improved microvascular outcomes and only borderline decrease in macrovascular disease, mirrored the results of the DCCT (Diabetes Control and Complications Trial) in type 1 diabetes.³
- The UKPDS revealed that, in the aggregate, intensive therapy improves health care status, thus providing important support for the glucose hypothesis, established by the DCCT for type 1 diabetes and suggested by the Kumamoto study of intensive insulin therapy in type 2 diabetes.⁴

THREE NEUROPATHIC INDICES ASSESSED

At entry into the study, investigators assessed three neuropathic indices and then again at 3-year intervals. Incident cases were defined as patients without neuropathy initially who had evidence of neuropathy at two consecutive visits up to 12 years after diagnosis.

For men, regular alcohol consumption increased the risk of incident and prevalent erectile dysfunction.

The investigators used logistic regression to determine prevalence of neuropathic indices and Cox proportional hazard models to examine incidence. The hazard ratios for age per 5 years, female gender, HbA1c per 1%, height per 5 cm, waist circumference per 5 cm, regular or heavy alcohol consumption, current smoking and weight per 5 kg are shown in the accompanying table where statistically significant ($P<.05$) (Table 1).

RISK INCREASED WITH AGE AT DIAGNOSIS

Thirty-six percent of men and 21% of women already have evidence of neuropathy when they are first diagnosed with type 2 diabetes. The risk of neuropathic abnormality increased with age at diagnosis and height. For men, regular alcohol consumption increased the risk of incident and prevalent erectile dysfunction.

The UKPDS² trial, published in 1998, found that intensive blood glucose control decreased the risk of microvascular complications in patients with type 2 diabetes. Patients randomized to intensive control had an 11% reduction in HbA1c compared with the conventional group and a 12% lower risk of any diabetes related outcome. ■

Irene M. Stratton, MSc, is a statistician in the Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism at the University of Oxford. She can be reached at irene.stratton@dtu.ox.ac.uk.



1. Stratton, Holman RR, Boulton AJM. Risk factors for neuropathy in UKPDS. Presented at the 40th Annual Meeting of the European Association for the Study of Diabetes. Sept. 5 to 9, 2004. Munich.
2. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet*. 1998;352:837-853.
3. Nathan D. Some answers, more controversy, from UKPDS. *Lancet*. 1998;352:854-858.
4. Ohkubo Y, Kishikawa H, Araki E, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabet Res Clin Pract* 1995; 28: 103-117.