

Consequences of Neuropathic Pain: Quality-of-life Issues and Associated Costs

Bill McCarberg, MD; Richard Billington, RPh

Abstract

Pain is the primary reason for patients seeking healthcare, and it has been estimated to result in more than \$100 billion per year in direct medical costs. Neuropathic pain (NP) alone has been associated with an approximately 3-fold increase in use of healthcare resources. The indirect costs associated with chronic pain result from increased absenteeism and decreased productivity at work, and they also have been estimated to total \$100 billion each year in the United States. NP contributes substantially to these costs. Results from one study indicated that employment was affected in 43% of patients with NP. Quality of life is also significantly reduced in such patients. Patients with chronic pain also have difficulty in initiating and maintaining sleep, and sleep deprivation has the potential to exacerbate pain. Sleep deprivation is also associated with both anxiety and depression, and both of these conditions can exacerbate sleep disturbances. Effective management of the patient with chronic pain, including NP, requires assessment and, if necessary, treatment of all comorbidities associated with this condition.

(Am J Manag Care. 2006;12:S263-S268)

Chronic pain results in high societal and patient burden. It has been estimated that 50 million people in the United States suffer from chronic pain, and it is the number one cause of disability in this country.¹ Results compiled by the American Pain Foundation (APF) document the high prevalence of chronic pain in the United States. Estimates from a large number of surveys reviewed by the APF indicate that 89% of people in the United States have

some pain at least monthly and that nearly 26 million Americans suffer from severe pain. People with moderate-to-severe pain have lived with their pain for an average of almost 1.5 years.² This article reviews the impact of chronic pain and neuropathic pain (NP) on society and individual patients.

.....
**IMPACT OF PAIN
ON SOCIETY**

The cost of pain or any other condition to society is generally divided into 2 parts: the direct costs associated with disease management and the indirect costs resulting from reduced productivity and worker absenteeism.

Direct Costs of Chronic Pain Management

The Centers for Disease Control and Prevention has estimated that total healthcare costs in the United States are \$1.4 trillion annually.³ Management of chronic pain contributes significantly to this total cost. Pain is the primary reason for seeking healthcare, and the direct medical costs for treatment of both acute and chronic pain have been estimated to exceed \$100 billion per year.⁴ Although total direct medical costs associated with all types of NP are not available, Berger and colleagues have provided an estimate of the excess direct medical treatment cost in people with NP.⁵ These investigators carried out a matched case-control study that included 55 686 patients with NP, most often back and neck pain with neuropathic involvement (62.3%), causalgia (12.1%), and diabetic peripheral neuropathy

Address Correspondence to: Bill McCarberg, MD, Chronic Pain Management Program, Kaiser Permanente, 732 North Broadway, Escondido, CA 92025. E-mail: bill.h.mccarberg@kp.org.

(DPN) (10.8%). Subjects with NP included in this study were more likely than controls to have other pain-related conditions and comorbidities, including fibromyalgia (6.0% vs 0.6% for control subjects), osteoarthritis (13.6% vs 3.6%), coronary heart disease (13.6% vs 6.5%), and depression (6.4% vs 2.3%). In the 2000 calendar year, total healthcare charges for patients with NP were \$17 355 versus \$5715 for controls.⁵ Thus, the presence of NP in a large cohort of patients is associated with an approximate 3-fold increase in healthcare costs versus those without NP.

Gordois and colleagues have provided information about the costs associated with DPN, a common cause of NP. Their results indicated that the total annual direct medical costs for the treatment of DPN and its complications were \$10.91 billion.⁶

Indirect Costs of Chronic Pain

The indirect costs associated with chronic pain have been estimated to total \$100 billion each year in the United States.¹ Both absenteeism and presenteeism (reduced productivity while at work) contribute to this cost.

The American Productivity Audit, a national survey of the United States workforce, was completed in 2002. This cross-sectional study was used to measure lost productive time associated with pain over a 2-week period in the summer of 2001. Survey results showed that 13% of the total workforce experienced a loss in productive time during a 2-week period as a result of pain. Workers who experienced lost productive time from a pain condition lost a mean of 4.6 hours per week. No difference in the proportion of the workforce losing ≥ 2 hours/week due to pain was observed as a function of subject sex, age, region of residence, type of occupation, duration of time in job, month of interview, or health insurance status. The majority (76.6%) of the lost productive time was explained by reduced performance while at work rather than absence. Lost productive time from common pain conditions among active workers costs an estimated \$61.2 billion per year. This amount accounts for 27% of the total estimated work-related cost of pain conditions

in the United States workforce.⁷ These results are consistent with other findings reported by the APF, which indicated that more than two thirds of all full-time employees (68%), the equivalent of more than 80 million workers, suffer from pain-related conditions. In addition, 14% of all full-time employees (>17 million) took sick days in 1995 as a result of pain conditions, which resulted in more than 50 million lost work days.²

Additional analysis of a subset of 391 respondents in the American Productivity Audit with self-reported DPN indicated greater losses of productivity for this group than for either controls or participants with diabetes but without DPN. Approximately 28% of subjects without diabetes lost ≥ 2 hours per 2 workweeks as a result of health-related causes. The respective values for subjects with diabetes only and diabetes plus DPN were 34% and 52%.⁸

Results from a smaller-scale study of patients with painful DPN also indicated that this condition results in lost productivity to at least the same degree as all types of chronic pain considered together. About one third of the 140 subjects included in this survey (35%) reported some level of disruption in their employment status due to painful DPN, including reduced work time (15%), disability (12%), or becoming unemployed or taking early retirement (8%). Among those who were working for pay at the time of the survey, 59% reported being less productive at work at least some of the time.⁹ These results are consistent with those from a larger sample of 602 patients with NP who were recruited from general practitioners in 6 European countries. Employment status was affected in 43% of patients, and those who were employed missed a mean of 5.5 workdays during the past month.¹⁰

.....
**IMPACT OF CHRONIC PAIN
 ON QUALITY OF LIFE**

Results from numerous studies have demonstrated that chronic pain and NP both have significant negative effects on all quality-of-life domains. For example, Becker and

colleagues evaluated 150 patients with chronic nonmalignant pain (46% with NP) and noted that these patients were significantly below population norms for all domains of the Medical Outcome Study-Short Form (SF)-36 (Figure).¹¹ This was also the case for all Psychological General Well-being subscores.

Vinik and colleagues have demonstrated that quality of life is significantly reduced in patients with painful DPN. They used the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy to compare 262 patients with painful DPN, 86 patients with diabetes but without DPN, and 81 healthy controls. Study results indicated differences between patients with DPN and both control groups for all item groupings. Results also showed that total quality-of-life scores correlated with severity of neuropathy.¹²

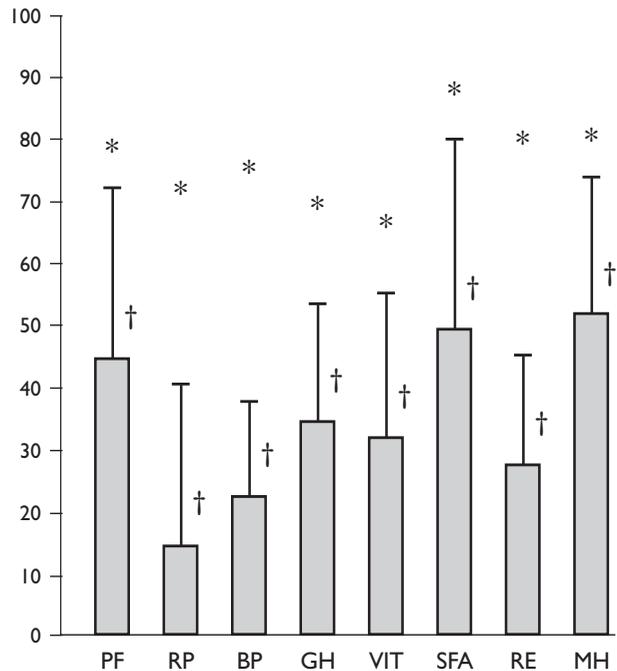
Benbow and associates also reported reduced quality of life in a comparison of 79 people with type 1 and type 2 diabetes versus 37 nondiabetic controls who were assessed using the Nottingham Health Profile (NHP). Subjects with neuropathy had significantly reduced quality of life in 5 of 6 NHP domains versus patients with diabetes but without DPN and healthy controls. The domains significantly affected by DPN were emotional reaction, energy, pain, physical mobility, and sleep.¹³

A prospective study of 105 patients with painful DPN also indicated significant negative impact of this condition on quality of life (Table 1). Results obtained using the Brief Pain Inventory indicated that pain substantially interfered with sleep (57.1% of patients), enjoyment of life (58.2%), recreational activities (56.1%), general activity (48.0%), mobility (57.0%), normal work (56.6%), and social activity (50.5%).¹⁴

.....
**COMORBIDITIES IN PATIENTS
 WITH CHRONIC PAIN**

As noted, people with NP are more likely than people without NP to have comorbidities, which include coronary heart disease and depression.⁵ Patients with NP are also likely to have increased anxiety and pain-

Figure. SF-36 Subscores for Patients With Chronic Pain



*Population values.

†P < .001.

SF-36 indicates Short Form-36; PF, physical functioning; RP, role physical; BP, body pain; GH, general health; VIT, vitality; SFA, social functioning; RE, role emotional; MH, mental health.

Source: Reprinted with permission from Reference 11.

associated interference with sleep.¹⁵⁻¹⁷ The combination of pain, interference with sleep, depression, and anxiety can greatly interfere with patients' ability to function.

Sleep Deprivation

Sleep deprivation can be particularly devastating in patients with chronic pain, who often have difficulty initiating and maintaining sleep. Sleep deprivation has been associated with a decreased pain threshold, muscle aches, and stiffness in normal volunteers, and loss of sleep might thus be expected to exacerbate the underlying cause of sleep deprivation in patients with chronic pain. Sleep deprivation has also been associated with both anxiety and depression, and both of these conditions can, in turn, result in sleep disturbances.¹⁸ Loss of sleep can

Table 1. BPI Results for Patients With Painful DPN

Activity	Score (SD)*	Percent with substantial interference†
General activity	4.33 (3.15)	48.0
Mood	4.04 (3.02)	43.4
Mobility	4.63 (3.13)	57.0
Normal work	4.70 (3.21)	56.6
Relations	3.13 (2.90)	36.1
Sleep	5.38 (3.25)	57.1
Enjoyment of life	5.00 (2.89)	58.2
Self-care	3.31 (2.96)	35.1
Recreational activities	4.77 (3.55)	56.1
Social activities	4.25 (2.61)	50.5

*BPI score is based on a 1-10 rating.

†As defined by a BPI score of ≥5.

BPI indicates Brief Pain Inventory; DPN, diabetic peripheral neuropathy; SD, standard deviation.

Source: Adapted with permission from Reference 14.

influence the prognosis for many diseases, and sleep deprivation has been shown to increase the risk for impaired glucose tolerance and diabetes.¹⁹

.....

**MANAGING THE WHOLE PATIENT
WITH CHRONIC PAIN**

Effective management of the patient with chronic pain, including NP, requires assessment and, if necessary, treatment of all comorbidities associated with this condition. Physicians should evaluate all aspects of pain, sleep, and mood in patients with chronic pain. Several instruments have been developed to aid clinicians in gathering qualitative and quantitative information from patients with chronic pain. These include the Pittsburgh Sleep Quality Index, Hamilton Depression Rating Scale, Beck Depression Inventory (BDI), SF-36, NHP, and Treatment Outcome for Pain Survey, a version of the SF-36 specifically developed for pain clinics. A sleep diary is also a reliable approach to obtaining information about sleep disturbance in patients with chronic pain.¹⁸

All patients with chronic pain should be screened for depression with a simple

instrument, such as the BDI. A preliminary screen for depression can be accomplished by asking 2 simple questions: (1) During the past month, have you often been bothered by feeling down, depressed, or hopeless? and (2) During the past month, have you often been bothered by having little interest or pleasure in doing things?¹⁸

The triad of chronic pain, sleep disturbances, and depression/anxiety is particularly important and must be fully addressed if the patient is to be restored to optimal functionality. Pharmacologic treatment strategies that reduce pain frequently result in concurrent improvements in common pain-associated comorbidities, and therapy should be selected on the basis of its impact both on pain and on these conditions.²⁰

Effective treatment of pain can significantly improve quality of life, and clinical trial results for at least some agents that have been approved for the treatment of NP and DPN document this. Duloxetine, gabapentin, and pregabalin have all been shown to improve quality of life in patients with NP,²¹⁻²³ and both gabapentin and pregabalin have also been demonstrated to improve sleep in patients with NP.^{22,23} Results from these and a selection of other studies that evaluated effects of medical therapy on quality of life in patients with DPN or postherpetic neuralgia (PHN) are summarized in **Table 2**.

.....

CONCLUSION

Effective treatment that addresses pain and comorbidities can enhance outcomes for patients with chronic pain. Some agents used for the treatment of NP, particularly newer medications approved for painful DPN and PHN, have the potential to produce improvements in pain and comorbidities, particularly sleep disturbance, and to enhance quality of life. Even the most effective therapies may not provide complete pain relief in many patients with NP, and a better measure of treatment outcome may be improvements in functionality and quality of life, which reflect the impact of treatment on a wide range of variables.

Table 2. Results From a Selection of Clinical Trials That Evaluate the Effect of Medical Treatments for DPN or PHN on Quality of Life

Reference	Treatment	Number of patients	Quality-of-life measure	Positive effect of treatment on quality of life (yes/no)
DPN				
Capsaicin Study Group	Capsaicin	277		Yes
Goldstein et al	Duloxetine	457	SF-36 EQ-5D	Yes
Backonja	Gabapentin	165	SF-36	Yes
Gilron	Gabapentin Morphine Gabapentin + morphine	35	SF-36	Yes (for all treatments)
White	Lidocaine patches 5%	49	BPI pain interference scale	Yes
Watson	Oxycodone	36	SF-36	Yes
Lesser	Pregabalin	338	SF-36	Yes
Rosenstock	Pregabalin	146	SF-36	Yes
Harati	Tramadol	131		Yes
PHN				
Rice	Gabapentin	334	SF-36	Yes
Rowbotham	Gabapentin	229	SF-36	Yes
White	Lidocaine patches 5%	11	BPI pain interference scale	Yes
Sabatowski	Pregabalin	238	SF-36	Yes

DPN indicates diabetic peripheral neuropathy; PHN, painful postherpetic neuralgia; SF-36, Short Form-36; BPI, Brief Pain Inventory. Sources: References 21-23; Capsaicin Study Group. *Diabetes Care*. 1992;15:159-165; Backonja M, et al. *JAMA*. 1998;280:1831-1836; Gilron I, et al. *N Engl J Med*. 2005;352:1324-1334; White WT, et al. *Pain Med*. 2003;4:321-330; Watson CP, et al. *Pain*. 2003;105:71-78; Rosenstock J, et al. *Pain*. 2004;110:628-638; Harati Y, et al. *Neurology*. 1998;50:1842-1846; Rowbotham M, et al. *JAMA*. 1998;280:1837-1842; Sabatowski R, et al. *Pain*. 2004;109:26-35.

REFERENCES

1. Pal S. Prevalence of chronic pain and migraine. *Pharmacist*. 2005;3:12-15.
2. American Pain Foundation. Pain Facts. Available at: <http://www.painfoundation.org/print.asp?file=LibrarySurveys.htm>. Accessed May 3, 2006.
3. Centers for Disease Control and Prevention. Chronic disease-overview. 2005. Available at: <http://www.cdc.gov/washington/overview/chrondis.htm>. Accessed May 3, 2006.
4. Eksterowicz N. It's the decade of pain control and research: are we really making a difference? *Nurse Reporter*. 2004;1:18-24.
5. Berger A, Dukes EM, Oster G. Clinical characteristics and economic costs of patients with painful neuropathic disorders. *J Pain*. 2004;5:143-149.
6. Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA. The health care costs of diabetic neuropathy in the United States. *Diabetes Care*. 2003;26:1790-1795.
7. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain

- conditions in the US workforce. *JAMA*. 2003;290:2443-2454.
8. Stewart WF, Ricci JA, Chee E, Brandenburg N. Work related costs of diabetic neuropathic (DPN) pain in the US: results from the American Productivity Audit. Poster presented at: The 24th Annual Scientific Meeting of the American Pain Society; March 30-April 2, 2005; Boston, Mass.
9. Tolle T, Xu X, Sadosky AB. Painful diabetic neuropathy: a cross-sectional survey of health state impairment and treatment patterns. *J Diabetes Complications*. 2006;20:26-33.
10. McDermott AM, Toelle TR, Rowbotham DJ, Schaefer CP, Dukes EM. The burden of neuropathic pain: results from a cross-selective survey. *Eur J Pain*. 2006;10:127-135.
11. Becker N, Bondegaard Thomsen A, Olsen AK, Sjogren P, Bech P, Eriksen J. Pain epidemiology and health related quality of life in chronic non-malignant pain patients referred to a Danish multidisciplinary pain center. *Pain*. 1997;73:393-400.
12. Vinik EJ, Hayes RP, Oglesby A, et al. The development and validation of the Norfolk QOL-DN, a new measure of patients' perception of the effects of diabetes

and diabetic neuropathy. *Diabetes Technol Ther.* 2005;7:497-508.

13. Benbow SJ, Wallymahmed ME, MacFarlane IA. Diabetic peripheral neuropathy and quality of life. *QJM.* 1998;91:733-737.

14. Galer BS, Ganas A, Jensen MP. Painful diabetic polyneuropathy: epidemiology, pain description, and quality of life. *Diabetes Res Clin Pract.* 2000;47:123-128.

15. Gore M, Brandenburg NA, Dukes E, Hoffman DL, Tai KS, Stacey B. Pain severity in diabetic peripheral neuropathy is associated with patient functioning, symptom levels of anxiety and depression, and sleep. *J Pain Symptom Manage.* 2005;30:374-385.

16. Barkin RL, Barkin SJ, Barkin DS. Perception, assessment, treatment, and management of pain in the elderly. *Clin Geriatr Med.* 2005;21:465-490.

17. Harden N, Cohen M. Unmet needs in the management of neuropathic pain. *J Pain Symptom Manage.* 2003;25(5 suppl):S12-S17.

18. Nicholson B, Verma S. Comorbidities in chronic neuropathic pain. *Pain Med.* 2004;5(suppl 1):S9-S27.

19. Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch Intern Med.* 2005;165:863-867.

20. McCarberg B. Managing the comorbidities of postherpetic neuralgia. *J Am Acad Nurse Pract.* 2003;15(12 suppl):16-21.

21. Goldstein DJ, Lu Y, Detke MJ, Lee TC, Iyengar S. Duloxetine vs placebo in patients with painful diabetic neuropathy. *Pain.* 2005;116:109-118.

22. Rice AS, Maton S, Postherpetic Neuralgia Study Group. Gabapentin in postherpetic neuralgia: a randomised, double blind, placebo controlled study. *Pain.* 2001;94:215-224.

23. Lesser H, Sharma U, LaMoreaux L, Poole RM. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology.* 2004;63:2104-2110.