

Evidence for Neuropathic Pain: A Quantitative Exploration and Trend Analysis of Articles in PubMed Database

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Abstract

Background: Neuropathic pain is defined as pain arising from dysfunction of somatosensory system according to Neuropathic pain special interest group of International association for the study of pain.

Objective of study: To quantitatively explore the existing evidence base for 'neuropathic pain' in PubMed through a review and analysis of current scientific literature.

Methods: Descriptive exploratory study through a literature search was done to identify nine time-points in the timeline from 1970-2010, with five-year intervals in order to identify the scientific trend. The number of obtained citations were classified and analyzed under the names of search filters of PubMed namely- text availability, publication date, species, article type, language, gender, subject areas, journal categories and age groups. The numbers for categories and subcategories of search filters were considered for comparison and analysis. Descriptive analysis using frequencies on Microsoft Excel 2010 worksheet was done.

Results: There was an exponential increase in number of articles on neuropathic pain over the 40 years. There was more number of 'abstract available' articles. Human studies were more than animal studies. There was more number of reviews, case reports and clinical trials among the article types. More articles were of English language, with nearly equal gender representation. There were more number of articles on cancer, and MEDLINE journals had more articles, with more in adult and middle-age.

Conclusion: The number of articles on 'neuropathic pain' is steadily increasing with more studies indexed in PubMed every year. The study findings are of importance to biomedical librarians and neuroscientists for neuropathic pain-related evidence retrieval.

Key words: Neuropathic pain evidence; PubMed analysis; Nerve pain; Research analysis; Reporting trend.

Introduction

Neuropathic pain is defined as pain arising from dysfunction of somatosensory system according to Neuropathic pain special interest

group of International association for the study of pain.[1] This replaced the originally known definition of neuropathic pain as pain arising from dysfunction of the nervous system and subsequently was then classified into central and peripheral neuropathic pain based upon dysfunction of central or peripheral nervous system respectively.[2]

The aetiological terms associated with neuropathic pain are many, and could be categorized under anatomical, physiological, pathological, clinical and mechanistic. The leading causes for neuropathic pain include diabetes mellitus, HIV/AIDS, chemotherapy, and other miscellaneous causes such as inflammatory disorders and drug/toxin-induced.[3] The global burden of neuropathic pain is well recognized by not only individual

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suffering in terms of chronic disabling pain and its associated psychosocial disturbances, but also in healthcare costs and economic burden on society as a whole.[4]

Emerging methods of evaluation of neuropathic pain include clinical, radiological, laboratory tests and self-report questionnaires.[5] The variety of treatment options range from medical-pharmacological,[6] and surgical methods[7] to complementary and alternative medicine and non-pharmacological methods such as physiotherapy[8] which include exercise therapy, electrical modalities and manual physical therapy.[9]

The existing clinical practice guidelines[10,11] emphasize a comprehensive multidisciplinary biopsychosocial approach[12] to evaluation and management of people with neuropathic pain along a continuum of aetiopathogenetic, symptomatic and/or palliative approach to care.[13]

The clinical decision making in neuropathic pain had evolved from a mono-disciplinary to a multi-disciplinary focus,[14] and is more evidence-based[15,16] or evidence-informed.[17] Access to evidence and availability of research evidence are two essential initial factors that contribute to EBP/EIP, and PubMed is the most widely searched and accessed database with more than 22 million indexed citations of biomedical literature. In an attempt to conceptualize evidence-based practice, evidence-informed practice and practice-based research, periodic analysis of evidence in terms of availability, accessibility and applicability would provide valuable clinically relevant information for practice.[18] Previous reports have analyzed the availability of evidence in PubMed,[19] and there is a need to know the evidence for neuropathic pain so that future practice, education, research and administration could be directed towards policy development and implementation.

The objective of this study was to quantitatively explore the existing evidence base for 'neuropathic pain' in PubMed through

a review and analysis of current scientific literature.

Methodology

Study design:

Descriptive exploratory study

Search methods:

The study methodology was a replication of previously used method as described by Kumar and Sisodia.[19] Two reviewers performed an independent blinded search of PubMed using specific search strategy and they independently extracted and synthesized the data from the selected studies using a structured checklist. At all stages of the review process, all disagreements were solved by mutual consensus before proceeding to the subsequent stages of the review.

Search strategy

A combination of using search filters in PubMed was used for this study. "(Neuropraxia [Title/Abstract] OR Neuropraxic [Title/Abstract] OR Neurotmesis [Title/Abstract] OR Neurolysis [Title/Abstract] OR neuronal [Title/Abstract] OR neural [Title/Abstract] OR neuritis [Title/Abstract] OR neuritic [Title/Abstract] OR neurologic [Title/Abstract] OR neurological [Title/Abstract] OR nervous [Title/Abstract] OR neuralgic [Title/Abstract] OR neuropathy [Title/Abstract] OR neuropathic [Title/Abstract] OR neurolytic [Title/Abstract] OR neurogenic [Title/Abstract] OR nerve [Title/Abstract] OR neuroma [Title/Abstract]) AND (pain [Title/Abstract] OR painful [Title/Abstract])" was entered through advanced search option of PubMed. A thorough literature search was done to identify nine time-points in the timeline from 1970-2010 in a 40-year period, with five-year intervals in order to identify the scientific trend. The search was performed in the month of November 2012, and retrieved numbers of citations were then used as data for extraction and synthesis.

Data extraction and synthesis

The number of obtained citations were classified and analyzed under the names of search filters of PubMed namely-text availability, publication date, species, article type, language, gender, subject areas, journal categories and ages. The numbers for categories and subcategories of search filters were considered for comparison and analysis.

Data analysis

All data were entered in Microsoft Excel 2010 worksheet and computed descriptively using their respective frequencies- numbers and percentiles. All comparisons were done visually in order to obtain an overall appearance and trend.

Figure 1: 40-year trend for number of 'neuropathic pain' articles based upon year of publication

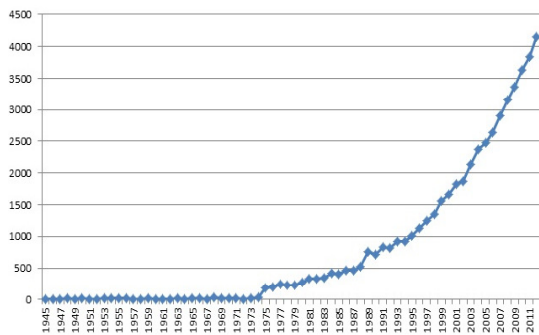


Figure 2: Relative prevalence of sub-categories for text availability among 'neuropathic pain' articles

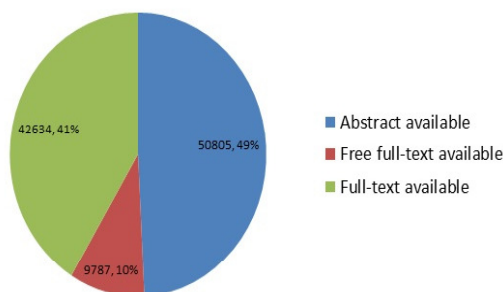


Figure 3: Comparison of 40-year trend between the three subcategories of text availability among 'neuropathic pain' articles

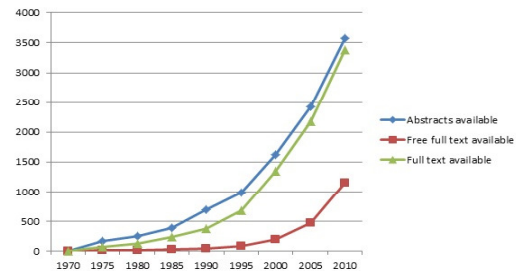


Figure 4: Relative prevalence of sub-categories for species among 'neuropathic pain' articles

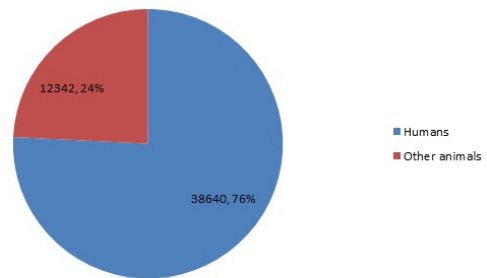


Figure 5: Comparison of 40-year trend between the two subcategories of species among 'neuropathic pain' articles

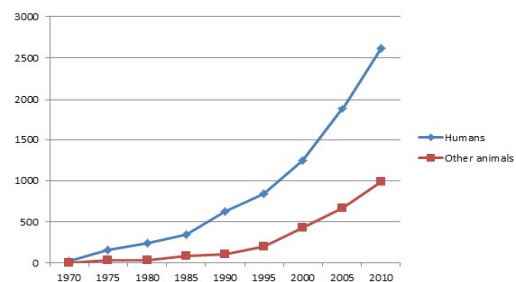


Figure 6: Relative prevalence of sub-categories for article types among 'neuropathic pain' articles

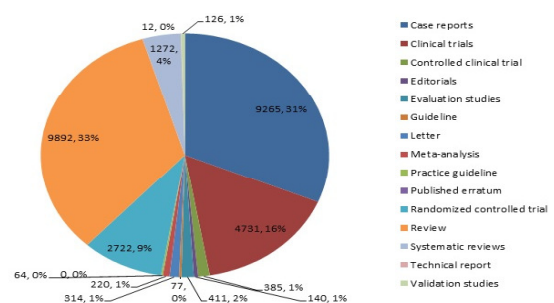


Figure 7: 40-year trend for number of articles based upon article types among 'neuropathic pain' articles

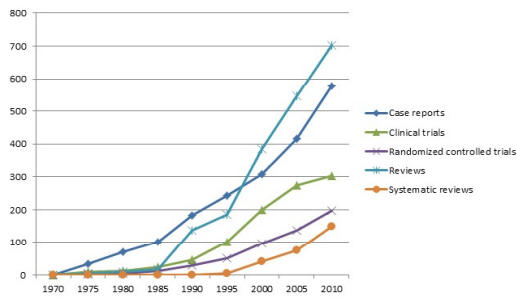
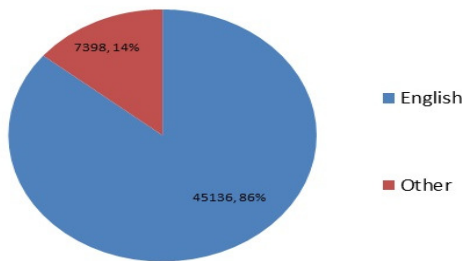


Figure 8: Relative prevalence of sub-categories for language among 'neuropathic pain' articles



Results

The total number of "neuropathic pain" articles was 52,354 (on 25th November 2012) and 44,528 articles indexed during the search period (1970-2010) were identified by searching through publication dates in search filters of PubMed.

Trend for number of 'neuropathic pain' articles

The number of 'neuropathic pain' articles per year increased gradually from 1945 to 1990,

Figure 9: 40-year trend for number of English language articles among 'neuropathic pain' articles

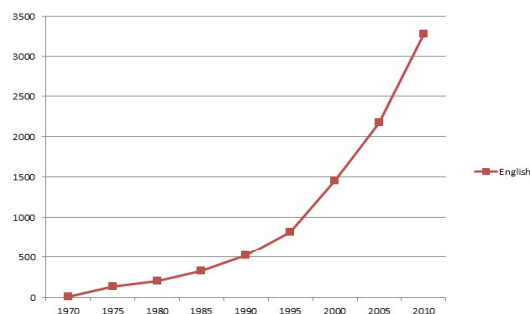
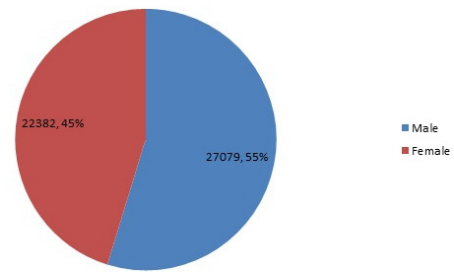


Figure 10: Relative prevalence of sub-categories for gender among 'neuropathic pain' articles



and sharply afterwards until 2011 (Figure 1).

Text availability of 'neuropathic pain' articles

There was greater number of 'abstract available' articles than 'full text available' and 'free full text available' articles (Figure 2). The increase in number of 'full text available' and 'abstract available' articles were more rapid after 1995, and was more than that of 'abstract available' articles (Figure 3).

Figure 11: Comparison of 40-year trend between the subcategories of gender among 'neuropathic pain' articles

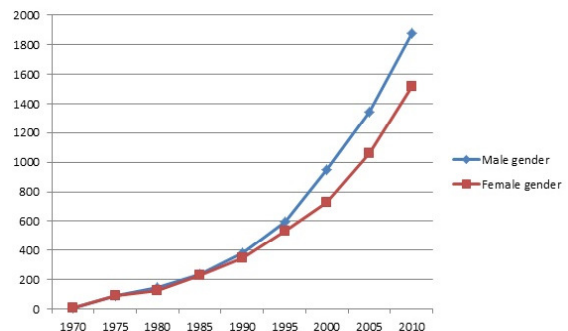


Figure 12: Relative prevalence of sub-categories for subject areas among 'neuropathic pain' articles

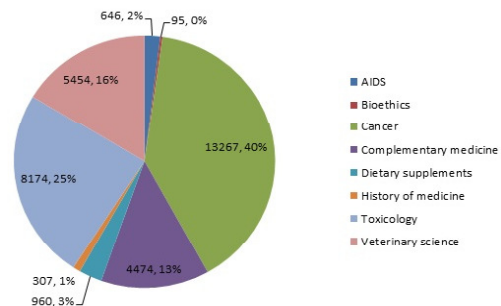


Figure 13: 40-year trend for number of articles under subject category among 'neuropathic pain' articles

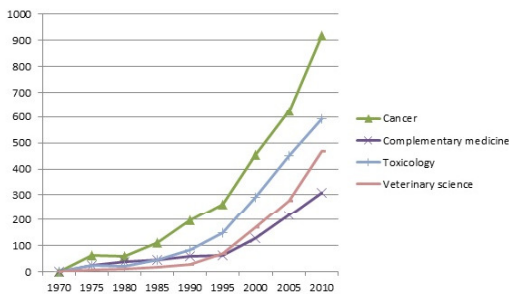
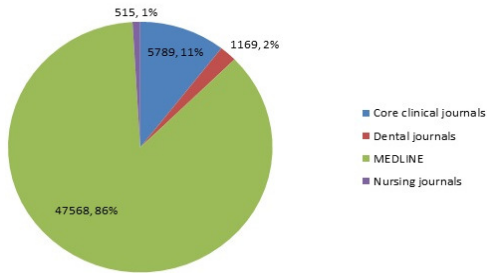


Figure 14: Relative prevalence of sub-categories for journals among 'neuropathic pain' articles



Species studied in 'neuropathic pain' articles

The number of articles and the trend of increase were more in human studies than on other animals' studies (Figure 4, Figure 5).

Types of 'neuropathic pain' articles

Reviews, case reports and clinical trials were more in number than other article types (Figure 6). The rapid increase in number of reviews, case reports and clinical trials on 'neuropathic pain' occurred from 1995 onwards (Figure 7).

Language of 'neuropathic pain' articles

The number of articles and the trend of increase was more for studies on English language than on other languages (Figures 8 and 9).

Gender studied in 'neuropathic pain' articles

The relative prevalence of number of articles and the corresponding trend was marginally

Figure 15: Comparison of 40-year trend for number of 'neuropathic pain' articles in MEDLINE journals

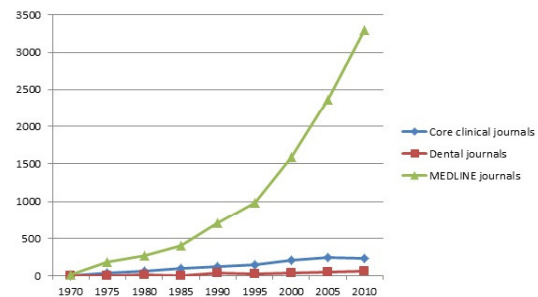
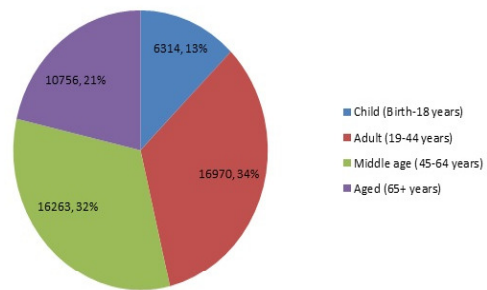


Figure 16: Relative prevalence of sub-categories for ages among 'neuropathic pain' articles



more for 'male' gender' than 'female gender' amongst the 'neuropathic pain' articles (Figures 10 and 11).

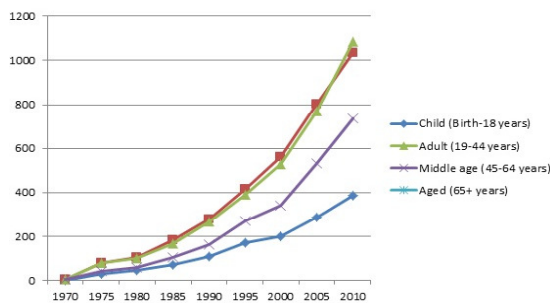
Subject categories of 'neuropathic pain' articles

A prominently large number of 'neuropathic pain' articles were indexed under the subject category of 'cancer' followed by 'toxicology' and 'veterinary science' (Figure 12). The trend analysis for 'neuropathic pain' articles indexed under subject category of 'cancer' and 'toxicology' showed a rapid increase in number of articles from the year 1995 onwards (Figure 13).

Journals publishing 'neuropathic pain' articles

Maximum articles on 'neuropathic pain' were indexed in MEDLINE journals, and some articles in core clinical journals, dental and nursing journals (Figure 14). The trend analysis for 'neuropathic pain' articles indexed in MEDLINE showed a rapid increase in number of articles from the year 1995 onwards (Figure

Figure 17: Comparison of 40-year trend between the subcategories of ages among 'neuropathic pain' articles



15).

Age of study population in 'neuropathic pain' articles

The relative prevalence of number of articles and the corresponding trend was more for 'neuropathic pain' articles indexed under 'adult age' and 'middle age' than 'child' and 'old age' (Figures 16 and 17).

Discussion

This study aimed to evaluate the existing evidence base for neuropathic pain and it was found that large number of articles was found that increased in number per year after 1995. The number of articles indexed in PubMed per year provided an overall picture of extent to which research evidence was available for retrieval over the years. The future studies on contribution of pain journals, anesthesiology journals and neurology journals to the existing evidence base for neuropathic pain could be done using advanced search features of PubMed to identify journal-specific reporting trends.[20] Also, this study analyzed PubMed database since it is freely accessible and commonly used, and future analyses of other databases such as AMED, CENTRAL, Google scholar, EMBASE, Scopus, CINAHL, PsycINFO and Cochrane library would provide more valuable information.[21-3]

One of the acceptable limitation of searching evidence through PubMed is that non-Medline-

indexed journals and journals included in PubMed central would be included into PubMed, which might presumably endanger the quality of the search retrieval.[24] Journal quality and article quality are two inter-related indicators for appraisal of evidence from the source of dissemination to the disseminated evidence per se.

There was more number of 'abstract available' articles on neuropathic pain. Availability of abstracts is essential when compared to linked full text articles that are available upon payment and/or subscription. The availability of information in abstracts although is limited but does provide an overview of the study. Quality and reporting standards of abstracts could be analyzed in future reviews.[25,26]

More number of human studies than animal studies implicates an effective shift from bench to bedside, with more clinical and patient-based studies reported compared to basic laboratory studies on experimental neuropathic pain.[27]

There were more reviews, case reports and clinical trials among the article types. This however poses a concern since reviews and case reports are indicative of first-level research on extension of knowledge into practice in terms of perspectives,[28] clinical commentaries and case situations. Reviews also may generate and explain new hypotheses both tested and untested, using a non-systematic or a narrative approach, with a focused theoretical basis.[29]

More articles were of English language, with nearly equal gender representation. This may be due to greater number of journals in pain, anesthesiology and neurology which were published in English. The equal gender representation reflected the nearly equal gender-related prevalence and characteristics amongst patients with neuropathic pain.[30]

There was more number of articles on subject category of cancer, which is best understood in terms of greater body of knowledge in all conditions of cancer and nerve such as neuroma, neurofibroma, neurilemmoma,

neuroblastoma, all of which cause pain.[31] Also, many other situations such as chemotherapy and other cancer treatments may lead to neuropathy and pain.[32]

MEDLINE journals had more articles on neuropathic pain which could only be assumed due to the higher quality of indexing status among Journals,[33] which has to be further explored according to journal-specific reporting trends. There were more number of articles in age groups adult and middle-age, which again could be due to increased prevalence of neuropathic pain in this population[34] and age-specific behavioral responses for neuropathic pain was also demonstrated in experimental models.[35]

The study findings are of significance to educators, clinicians, researchers and policy makers dealing with neuropathic pain patients, since the evidence base is essentially important for understanding neurological diseases and their rehabilitation in the field of neurosciences.

Conclusion

The number of articles on 'neuropathic pain' is steadily increasing with more studies indexed in PubMed every year. The study findings are of importance to biomedical librarians and neuroscientists for neuropathic pain-related evidence retrieval.

References

1. Geber C, Baumgärtner U, Schwab R, Müller H, Stoeter P, Dieterich M, et al. Revised definition of neuropathic pain and its grading system: an open case series illustrating its use in clinical practice. *Am J Med.* 2009; 122(10 Suppl): S3-12.
2. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology.* 2008; 70: 1630-5.
3. Boulton A. What causes neuropathic pain? *J Diabetes Complications.* 1992; 6: 58-63.
4. Doth AH, Hansson PT, Jensen MP, Taylor RS. The burden of neuropathic pain: a systematic review and meta-analysis of health utilities. *Pain.* 2010; 149: 338-44.
5. Haanpää M, Attal N, Backonja M, Baron R, Bennett M, Bouhassira D, et al. NeuPSIG guidelines on neuropathic pain assessment. *Pain.* 2011; 152: 14-27.
6. Kumar SP, Adhikari P, Jeganathan PS, D'Souza SC. Medical management of diabetic peripheral neuropathic pain: a focused review of literature. *Int J Neurol Neurosurg.* 2010; 2(1): 29-46.
7. Kumar SP, Adhikari PA, Jeganathan PS, Misri ZK. Surgical management of painful diabetic peripheral neuropathy-a focused review. *Int J Neurol Neurosurg.* 2012; 4(1): 21-5.
8. Kumar SP, Adhikari P, Jeganathan PS, D'Souza SC. Physiotherapy management of painful diabetic peripheral neuropathy: a current concepts review of treatment methods for clinical decision-making in practice and research. *Int J Curr Res Rev.* 2010; 2(9): 29-39.
9. Kumar SP, Adhikari P, Jeganathan PS, Kumar V. Neurodynamic mobilization for neuropathic pain- a review of current evidence. *Journal of Indian Association of Physiotherapists.* 2011; 9: 32-9.
10. Yang CM, Chen NC, Shen HC, Chou CH, Yeh PS, Lin HJ, et al. Guideline of neuropathic pain treatment and dilemma from neurological point of view. *Acta Neurol Taiwan.* 2012; 21: 136-44.
11. Mailis A, Taenzer P. Evidence-based guideline for neuropathic pain interventional treatments: spinal cord stimulation, intravenous infusions, epidural injections and nerve blocks. *Pain Res Manag.* 2012; 17: 150-8.
12. Turk DC, Audette J, Levy RM, Mackey SC, Stanos S. Assessment and treatment of psychosocial comorbidities in patients with neuropathic pain. *Mayo Clin Proc.* 2010; 85(3 Suppl): S42-50.
13. Chetty S, Baalbergen E, Bhigjee AI, Kamerman P, Ouma J, Raath R, et al. Clinical practice guidelines for management of neuropathic pain: expert panel recommendations for South Africa. *S Afr Med J.* 2012; 102(5): 312-25.
14. Garven A, Brady S, Wood S, Hatfield M, Bestard J, Korngut L, et al. The impact of enrollment in a specialized interdisciplinary neuropathic pain clinic. *Pain Res Manag.* 2011;

- 16(3): 159-68.
15. Finnerup NB, Otto M, Jensen TS, Sindrup SH. An evidence-based algorithm for the treatment of neuropathic pain. *Med Gen Med.* 2007; 9(2): 36.
 16. Finnerup NB, Otto M, McQuay HJ, Jensen TS, Sindrup SH. Algorithm for neuropathic pain treatment: an evidence based proposal. *Pain.* 2005; 118: 289-305..
 17. Rycroft-Malone J. Evidence-informed practice: from individual to context. *J Nurs Manag.* 2008; 16(4): 404-8.
 18. Epstein I. Reconciling evidence-based practice, evidence-informed practice, and practice-based research: the role of clinical data-mining. *Soc Work.* 2011; 56: 284-8.
 19. Kumar SP, Sisodia V. PubMed as an altar of science-an exploratory synthesis and quantitative analysis of published articles. *Journal of Academy of Medical Sciences.* 2012; under review.
 20. Sood A, Erwin PJ, Ebbert JO. Using advanced search tools on PubMed for citation retrieval. *Mayo Clin Proc.* 2004; 79: 1295-9.
 21. Falagas ME, Pitsouni EI, Malietzis GA, Pappas G. Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. *FASEB J.* 2008; 22: 338-42.
 22. Moseley AM, Sherrington C, Elkins MR, Herbert RD, Maher CG. Indexing of randomised controlled trials of physiotherapy interventions: a comparison of AMED, CENTRAL, CINAHL, EMBASE, hooked on evidence, PEDro, PsycINFO and PubMed. *Physiotherapy.* 2009; 95: 151-6.
 23. Michaleff ZA, Costa LO, Moseley AM, Maher CG, Elkins MR, Herbert RD, et al. CENTRAL, PEDro, PubMed, and EMBASE are the most comprehensive databases indexing randomized controlled trials of physical therapy interventions. *PhysTher.* 2011; 91: 190-7.
 24. Cornell A, Bushman B, Womack K. Analysis of journals that did not meet selection criteria for inclusion in the National Library of Medicine collection but have manuscripts in PubMed Central. *J Med Libr Assoc.* 2011; 99: 168-70.
 25. Sharma S, Harrison JE. Structured abstracts: do they improve the quality of information in abstracts? *Am J Orthod Dentofacial Orthop.* 2006; 130: 523-30.
 26. Timmer A, Sutherland LR, Hilsden RJ. Development and evaluation of a quality score for abstracts. *BMC Med Res Methodol.* 2003; 3: 2.
 27. Taneja A, Di Iorio VL, Danhof M, Della Pasqua O. Translation of drug effects from experimental models of neuropathic pain and analgesia to humans. *Drug Discov Today.* 2012; 17: 837-49.
 28. Baron R. Neuropathic pain: a clinical perspective. *Handb Exp Pharmacol.* 2009; (194): 3-30.
 29. Ashton JC. Neuropathic pain: an evolutionary hypothesis. *Med Hypotheses.* 2012; 78: 641-3.
 30. Tall JM, Stuesse SL, Cruce WL, Crisp T. Gender and the behavioral manifestations of neuropathic pain. *Pharmacol Biochem Behav.* 2001; 68: 99-104.
 31. Bennett MI, Rayment C, Hjermstad M, Aass N, Caraceni A, Kaasa S. Prevalence and aetiology of neuropathic pain in cancer patients: a systematic review. *Pain.* 2012; 153: 359-65.
 32. Farquhar-Smith P. Chemotherapy-induced neuropathic pain. *Curr Opin Support Palliat Care.* 2011; 5(1): 1-7.
 33. Jain NC. Medline indexes more journals than Index Medicus. *Natl Med J India.* 2003; 16: 177.
 34. Novak JC, Lovell JA, Stuesse SL, Cruce WL, McBurney DL, Crisp T. Aging and neuropathic pain. *Brain Res.* 1999; 833: 308-10.
 35. Pickering G, Jourdan D, Millecamps M, Chapuy E, Alliot J, Eschalier A. Age-related impact of neuropathic pain on animal behaviour. *Eur J Pain.* 2006; 10: 749-55.