### Symptom reviews and examples of self-report assessment scales and symptom-specific HRQoL measures

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Commonly used measures</th>
<th>No of items</th>
<th>Validity/reliability refs</th>
<th>Validity and Reliability in cancer</th>
<th>Examples of cancer clinical trials where scale identified a treatment effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>FACT-An (Anaemia/fatigue; includes the FACIT-F) ¹</td>
<td>20</td>
<td>² ⁴</td>
<td>+ +</td>
<td>Some Cronbach alphas &gt;0.9</td>
</tr>
<tr>
<td>Anorexia/Cachexia</td>
<td>FAACT (Anorexia/Cachexia)</td>
<td>12</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Constipation</td>
<td>Constipation Assessment Scale (CAS) (a paediatric version is also available)</td>
<td>8</td>
<td>¹¹ ¹²</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Patient Assessment of Constipation Quality of Life questionnaire (PAC-QOL) &amp; Patient Assessment of Constipation Symptoms (PAC-SYM)</td>
<td></td>
<td></td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>FACT-D (Diarrhoea)</td>
<td>11</td>
<td></td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Borg Scale (severity of breathlessness)</td>
<td>1</td>
<td>¹⁷ ¹⁹</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>Cancer Dyspnoea Scale (CDS) (quality of breathlessness)</td>
<td>12</td>
<td>¹⁰</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Chronic Respiratory (Disease) Questionnaire– dyspnea subscale (CRQ-D) (functional impairment caused by breathlessness)</td>
<td>19</td>
<td>¹²</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Brief Fatigue Inventory (BFI)</td>
<td>9</td>
<td>²³</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>FACIT-F (fatigue)</td>
<td>13</td>
<td>³ ²⁷</td>
<td>+</td>
<td>Some Cronbach alphas &gt;0.9</td>
</tr>
<tr>
<td>Hormonal (e.g., hot flushes)</td>
<td>FACT-ES³</td>
<td>18/19</td>
<td>²⁹</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lymphoedema</td>
<td>Arm symptom subscale in FACT-B+4³</td>
<td>4</td>
<td>³¹</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Mucositis</td>
<td>For a summary of oral mucositis scales, see Table 1 from Sonis et al. (2004),³³ reproduced below</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Domain</td>
<td>Tool/Scale</td>
<td>Cronbach Alpha</td>
<td>Validity</td>
<td>Reliability</td>
<td>Notes</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------------</td>
<td>----------------</td>
<td>----------</td>
<td>-------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>Functional Living Index – Emesis (FLIE)</td>
<td>18</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>Morrow Assessment of Nausea and Emesis (MANE)</td>
<td>17</td>
<td>+</td>
<td>?</td>
<td>?</td>
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<tr>
<td></td>
<td>Multinational Association of Supportive Care in Cancer (MASCC) Antiemesis Tool (MAT)</td>
<td>8</td>
<td>+</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Rhodes Index of Nausea and Vomiting – FORM 2 (INV-2)</td>
<td>8</td>
<td>+</td>
<td>+</td>
<td>Some Cronbach alphas &gt;0.9</td>
</tr>
<tr>
<td></td>
<td>Rhodes Index of Nausea, Vomiting, and Retching (INVR) (revised version of INV)</td>
<td>8</td>
<td>+</td>
<td>+</td>
<td></td>
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<tr>
<td>Neutropaenia</td>
<td>FACT-N</td>
<td>19</td>
<td>?</td>
<td>?</td>
<td></td>
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<tr>
<td>Pain</td>
<td>Unidimensional (e.g., pain intensity or relief) Standard visual analogue scale (VAS)</td>
<td>1 per dimension</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Categorical verbal scales (VRS)</td>
<td>1 per dimension</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Categorical numerical scales (NRS)</td>
<td>1 per dimension</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Brief Pain Inventory (BPI)</td>
<td>11</td>
<td>+</td>
<td>?</td>
<td>Some Cronbach alphas &gt;0.9</td>
</tr>
<tr>
<td></td>
<td>McGill Pain Questionnaire (MPQ)</td>
<td>20</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McGill Pain Questionnaire short form (SF-MPQ)</td>
<td>15</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Xerostomia</td>
<td>Xerostomia-specific Questionnaire</td>
<td>8</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

* Evaluations reported for validity and reliability are based on criteria adapted from Bot et al. (2004).
$ Symptom scale can be used in combination with the FACIT core measure, the FACT-G, and disease-specific modules to give a multi-dimensional assessment of HRQoL.
# All validation data for the Rhodes Index of Nausea and Vomiting- FORM 2 (INV-2) refer to the 5-item original version of the INV.
References

1. Schwartz RN. Anemia in patients with cancer: incidence, causes, impact, management, and use of treatment guidelines and protocols. *American Journal of Health-System Pharmacy*. Feb 1 2007;64(3 Suppl 2):S5-13; quiz S28-30 PURPOSE: The incidence, etiology, impact, and considerations in developing guidelines for treating anemia in patients with cancer are described. SUMMARY: Anemia is common in patients with cancer. The incidence and severity of anemia depend on the type and extent of the malignancy; the type, schedule, and intensity of cancer therapy; and patient age, gender, and comorbid conditions. Anemia may be the result of the malignancy itself, cancer treatment, blood losses, nutritional deficiencies, hemolysis, endocrine disorders, or inflammatory cytokines associated with chronic disease. Anemia can have a profound impact on physical and psychosocial function and quality of life. Guidelines and protocols for treating anemia should be evidence-based and take into consideration patient age, the type and extent of malignancy, comorbid conditions, and the etiology and impact of anemia. Patient-specific issues that guidelines should address include strategies for identifying patients with anemia, treating anemia, evaluating the response to treatment, and modifying treatment based on response. Erythropoietic agents are preferred over blood transfusions for patients whose anemia is chronic, although transfusions are indicated for acute, severe blood losses. Iron supplementation often is required in patients receiving erythropoietic therapy or with iron deficiency due to hemorrhage. CONCLUSION: The use of evidence-based guidelines and protocols that take into consideration the heterogeneity of patients with cancer can optimize anemia treatment. [References: 42].

2. Cella D. The Functional Assessment of Cancer Therapy-Anemia (FACT-An) Scale: a new tool for the assessment of outcomes in cancer anemia and fatigue. *Seminars in Hematology*. Jul 1997;34(3 Suppl 2):13-19 Anemia, frequently associated with cancer and cancer treatment, can use a variety of symptoms that diminish overall quality of life (QOL). Fatigue is the most commonly reported symptom among cancer patients and can significantly affect their daily lives. Using the Functional Assessment of Cancer Therapy-General (FACT-G) instrument, which measures general QOL, as a core questionnaire, 20 new questions related to the impact of fatigue and other anemia-related symptoms on patients with cancer were developed. Two new instruments were produced: the FACT-Fatigue (FACT-F), consisting of the FACT-G plus 13 fatigue items (the Fatigue Subscale), and the FACT-Anemia (FACT-An), consisting of the FACT-F plus seven items addressing other concerns related to anemia, but unrelated to fatigue. FACT-F and FACT-An demonstrated good stability (r = .87 for both) and strong internal consistency (alpha = .95 and .96, respectively). Test-retest reliability coefficients for the Fatigue Subscale and nonfatigue items also showed good stability (r = .84 to .90), and the Fatigue Subscale showed strong internal consistency (alpha = .93 to .95). Convergent and discriminant validity testing revealed a significantly positive relationship with other known measures of fatigue, a significant negative relationship with vigor, and an anticipated lack of relationship with social desirability. The FACT-An, FACT-F, and Fatigue Subscale were found to successfully discriminate patients based on hemoglobin (Hb) level and Eastern Cooperative Oncology Group (ECOG) performance status. When patients were divided into two groups by Hb levels, patients with Hb levels greater than 12 g/dL reported significantly less fatigue, fewer nonfatigue anemia symptoms, better physical well-being, better functional well-being, and higher general QOL. The FACT-An, the FACT-F, and the Fatigue Subscale are useful measures of QOL in cancer patients and add focus to the widespread clinical problems of anemia and fatigue.


4. Cella D, Eton DT, Lai J-S, Peterman AH, Merkel DE. Combining anchor and distribution-based methods to derive minimal clinically important differences on the Functional Assessment of Cancer Therapy (FACT) anemia and fatigue scales. *Journal of Pain & Symptom Management*. Dec 2002;24(6):547-561 Magnitude differences in scores on a measure of quality of life that correspond to differences in function or clinical course are called clinically important differences (CIDs). Anchor-based and distribution-based methods were used to provide ranges of CIDs for five targeted scale scores of the Functional Assessment of Cancer Therapy-Anemia (FACT-An) questionnaire. Three samples of cancer patients were used: Sample 1 included 50 patients participating in a validation study of the FACT-An; Sample 2 included 131 patients participating in a longitudinal study of chemotherapy-induced fatigue; sample 3 included 2,402 patients enrolled in a
A community-based clinical trial evaluating the effectiveness and safety of a treatment for anemia. Three clinical indicators (hemoglobin level; performance status; response to treatment) were used to determine anchor-based differences. One-half of the standard deviation and 1 standard error of measurement were used as distribution-based criteria. Analyses supported the following whole number estimates of a minimal CID for these five targeted scores: Fatigue Scale = 3.0; FACT-G total score = 4.0; FACT-An total score = 7.0; Trial Outcome Index–Fatigue = 5.0; and Trial Outcome Index–Anemia = 6.0. These estimates provide a basis for sample size estimation when planning for a clinical trial or other longitudinal study, when the purpose is to ensure detection of meaningful change over time. They can also be used in conjunction with more traditional clinical markers to assist investigators in determining treatment efficacy.

Fallowfield L, Gagnon D, Zagari M, et al. Multivariate regression analyses of data from a randomised, double-blind, placebo-controlled study confirm quality of life benefit of epoetin alfa in patients receiving non-platinum chemotherapy. British Journal of Cancer. Dec 2 2002;87(12):1341-1353 Cancer-related anaemia is associated with a wide spectrum of symptoms that can negatively affect quality of life. Because epoetin alfa has demonstrated efficacy in correcting cancer-related anaemia, the impact of this treatment on quality of life was evaluated in a multinational, randomised, double-blind, placebo-controlled trial in 375 anaemic cancer patients receiving non-platinum-based chemotherapy. The cancer-specific measures of quality of life included the general scale (FACT–G Total) and fatigue subscale (FACT–An Fatigue subscale) of the Functional Assessment of Cancer Therapy–Anaemia and the Cancer Linear Analogue Scales measuring energy, ability to do daily activities, and overall quality of life. These measures were also used to examine the relationship between haemoglobin levels and quality of life. Both univariate and multiple linear regression analyses of quality of life data were performed. Results of the univariate analysis have been reported previously. The a priori-planned multiple linear regression analysis, which accounted for the effects of disease progression and several other possibly confounding variables on quality of life, showed a significant advantage for epoetin alfa over placebo for the five scales (all, P<0.05), and confirmed the results of the univariate analysis. For cancer-specific measures, significant correlations were demonstrated between baseline haemoglobin and quality of life (r, range: 0.14-0.26, all P<0.05) and between change in haemoglobin and change in quality of life (r, range: 0.26-0.34, all P<0.01). These findings provide evidence that increasing haemoglobin levels by epoetin alfa administration can significantly improve cancer patients’ quality of life.

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Early intervention with epoetin alfa during platinum-based chemotherapy: an analysis of the results of a multicenter, randomized, controlled trial based on initial hemoglobin level. Oncologist. Feb 2006;11(2):206-216 OBJECTIVE: This analysis of the results of a randomized, controlled trial evaluating the effects of epoetin alfa (EPO) therapy on transfusion requirements, hemoglobin (Hb), and quality of life (QOL) in patients with cancer receiving platinum-based chemotherapy was conducted to evaluate the effect of initial Hb level on study outcomes. METHODS: Patients with Hb levels < or =12.1 g/dl were randomized 2:1 to receive EPO, 10,000 U three times weekly s.c. or best supportive care (BSC) until 4 weeks after their last chemotherapy cycle. For this analysis, patients were stratified by baseline Hb level (< or =9.7 g/dl, >9.7 g/dl to < or =10.5 g/dl, >10.5 g/dl to < or =11.3 g/dl, and >11.3 g/dl to < or =12.1 g/dl), and study results were reanalyzed. RESULTS: Significantly fewer EPO patients than BSC patients with initial Hb levels >9.7 g/dl to < or =12.1 g/dl required transfusions. EPO maintained Hb levels throughout the study for patients with Hb levels >11.3 g/dl to < or =12.1 g/dl, compared with a decrease with BSC. For patients with baseline Hb levels >10.5 g/dl, for whom the mean changes from baseline to last assessment were measured by the Cancer Linear Analogue Scale assessments of energy and overall QOL as well as by the Functional Assessment of Cancer Therapy (FACT)-Fatigue and FACT-An Anemia subscale, QOL scores were significantly greater with EPO than with BSC. QOL declined in patients receiving BSC, and the mean decreases in QOL scores were greater for BSC patients with baseline Hb levels >10.5 g/dl, compared with the overall BSC group. CONCLUSION: In patients with cancer receiving platinum-based chemotherapy and with baseline Hb levels >10.5 g/dl, early intervention with EPO reduces transfusions, maintains Hb level, and maintains or improves QOL. This study supports the positive effects of early intervention when analyzed according to initial Hb value.

BACKGROUND: Chemotherapy-related anemia is prevalent among patients with hematologic malignancies. A randomized, open-label, multicenter trial of early versus late epoetin alfa in this population was conducted, focusing on quality of life (QOL).

METHODS: Patients with non-Hodgkin lymphoma, Hodgkin lymphoma, chronic lymphocytic leukemia, or multiple myeloma and baseline hemoglobin of 10 to 12 g/dL who were scheduled for > or = 4 months of myelosuppressive chemotherapy were randomized to receive < or = 16 weeks of epoetin alfa at a dose of 40,000 U once weekly immediately (early) or to wait and only receive epoetin alfa if hemoglobin decreased to < 9 g/dL (late). Those patients with a hemoglobin level > 12 g/dL after 3 chemotherapy cycles were not randomized. The primary endpoint was a mean change in the Functional Assessment of Cancer Therapy-Anemia (FACT-An) total. RESULTS: In all, 269 patients with a hemoglobin level < or = 12 g/dL were randomized. The mean total FACT-An increased 3.84 (95% confidence interval [95% CI], 0.21-7.46) in early patients and decreased 4.37 (95% CI, -7.99 to -0.74) in late patients (P = .003). Early patients had significantly (P < .05) higher mean scores for total FACT-General; FACT-General physical and functional well-being subscales, total anemia scale, and fatigue subscale; and daily activity, energy, and important activity Linear Analog Scale Assessment scales, as well as reduced bedrest days and restricted activity days. The mean hemoglobin increased 1.2 g/dL (95% CI, 0.98-1.46) in early patients but decreased 0.2 g/dL (95% CI, -0.32-0.12) in late patients (P < .0001). Adverse events were similar between groups (with fatigue being the most prevalent); clinically relevant thromboembolic events were more common in early patients. CONCLUSIONS: Treating mild anemia immediately with epoetin alfa during chemotherapy for hematologic malignancy significantly improved QOL, productivity, and hemoglobin compared with delaying treatment until the hemoglobin level decreases to < 9.0 g/dL. 2006 American Cancer Society.

8. Ockenga J, Valentini L. Review article: anorexia and cachexia in gastrointestinal cancer.[see comment]. Alimentary Pharmacology & Therapeutics. Oct 1 2005;22(7):583-594 In patients with gastrointestinal malignancies, i.e. cancers of the stomach, colon, liver, biliary tract or pancreas, progressive undernutrition can be regularly observed during the course of illness. Undernutrition significantly affects the patients' quality of life, morbidity and survival. Pathogenetically, two different causes are relevant in the development of undernutrition in patients with gastrointestinal cancer. One cause is reduced nutritional intake. This condition is referred to as anorexia and can be worsened by the side effects of cancer therapy. The other cause is the release of endogenous transmitters and/or other products of the tumour leading to the cachexia syndrome, which is characterized by loss of body weight, negative nitrogen balance and fatigue. Cancer anorexia and cancer cachexia may have synergistic negative effects in affecting the patients' status. In this review, current nutritional support strategies with respect to different clinically relevant situations are described. An algorithm of the treatment strategies, including dietetic counselling, oral supplements, enteral and parenteral nutritional support is given. One focus is the approach of nutrition-focused patient care, which shows promising results. In addition, the possibilities of pharmacological intervention are discussed. [References: 57].

9. Ribaudo JM, Cella D, Hahn EA, et al. Re-validation and shortening of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire. Quality of Life Research. 2000;9(10):1137-1146 PURPOSE: The original Functional Assessment of Anorexia/Cachexia Therapy (FAACT) was designed to measure general aspects of quality of life (QOL) as well as specific anorexia/cachexia-related concerns. Our primary purpose was to reduce the number of anorexia/cachexia subscale items in a manner that either retains or improves reliability, validity and precision. METHODS: The FAACT was administered using an interactive computer program that allowed immediate entry of the data. A total of 213 patients were recruited. RESULTS: A combined empirical and conceptual approach led to the reduction of the anorexia/cachexia subscale (A/CS) from 18 to 12 items. A 26-item trial outcome index (TOI) combining physical well-being (PWB), functional well-being (FWB), and the A/CS-12 was highly reliable and sensitive to change in performance status rating (PSR). We found that PWB, FWB, and A/CS-12 subscales performed differently. Specifically, PWB and FWB scores decreased in patients whose (PSR) worsened. However, although A/CS-12 scores were responsive to change in PSR over time, average A/CS-12 scores of all patients, even those whose PSR worsened, improved over the course of treatment. CONCLUSIONS: Elimination of six items from the anorexia/cachexia subscale of the FAACT was accomplished without loss of internal consistency or sensitivity to change in performance status. The A/CS-12 subscale provides unique, important information not captured by a generic chronic illness questionnaire.
10. Solomon R, Cherny NI. Constipation and diarrhea in patients with cancer. Cancer Journal. Sep-Oct 2006;12(5):355-364 Constipation and diarrhea are both common problems in patients with advanced cancer. They are source of major morbidity and distress. Constipation is, overall, more common that diarrhea. Diarrhea may be severe and, in some cases, associated with life-threatening dehydration and electrolyte abnormalities. Indeed, with some of the newer chemotherapy agents, this is a problem seen with increasing frequency. Oncologists must be familiar with the common causes of constipation and diarrhea in cancer patients and the strategies to evaluate and manage these common and distressing symptoms. Both with constipation and diarrhea, there is a differential diagnosis. In many cases, management can be complex and challenging. Approaches to diagnosis, evaluation, and management are reviewed. [References: 71].

11. McMillan SC, Williams FA. Validity and reliability of the Constipation Assessment Scale. Cancer Nursing. Jun 1989;12(3):183-188 Constipation is a significant problem in patients receiving neurotoxic chemotherapeutic agents, narcotic analgesics, antidepressants, tranquilizers, and muscle relaxants. Increasingly, as acute care moves into the community, nurses will need valid and reliable methods of assessing constipation in individuals with cancer. The purpose of this project was to study the validity and reliability of the Constipation Assessment Scale, a new tool designed to assess the presence and severity of constipation. The sample consisted of two groups: a control group of 32 working adults and a patient group of 32 adults at risk for constipation because of treatment with Vinca alkaloids or morphine. Consenting subjects were asked to complete the eight-item Constipation Assessment Scale (CAS). A significant difference in intensity of symptoms between the two groups (t = 6.32, p less than 0.0001) demonstrates the ability of the CAS to differentiate between subjects with and without constipation and thus provides evidence of construct validity of the scale. Further analysis of scores of the two subgroups in the patient group (subjects receiving morphine vs. Vinca alkaloids) revealed a significant difference (t = 2.54, p less than 0.01) in symptom intensity. This latter finding supports the ability of the CAS to differentiate between moderate and severe symptom intensity. Subjects completed the CAS in approximately 2 min. To study the test-retest reliability of the scale, a group of 16 apparently healthy working adults were asked to fill out the CAS twice with a 1-h delay. The two sets of scores were correlated (r = 0.98). (ABSTRACT TRUNCATED AT 250 WORDS).

12. Woolery M, Carroll E, Fenn E, et al. A constipation assessment scale for use in pediatric oncology. Journal of Pediatric Oncology Nursing. Mar-Apr 2006;23(2):65-74 Constipation is prevalent in pediatric oncology patients because of treatment with vinca alkaloids and/or narcotics and lifestyle changes secondary to disease process. Sequelae of constipation include anorexia, nausea, vomiting, abdominal pain, emergency department visits, and a decrease in quality of life. There are no reliable instruments to measure constipation in children. A pilot study (N = 21) evaluating the presence and severity of constipation and the reliability and validity of a modified version of the adult Constipation Assessment Scale (CAS) in children with cancer was conducted. Patients receiving weekly vinca alkaloids and/or narcotics = 2 times per day were recruited. Initial bowel function assessments included standardized nursing and nutrition assessments, history/physical review, and baseline CAS score repeated at 1 hour to assess test-retest reliability. Subsequent assessments included CAS administered 3 times per week and daily patient bowel diaries. Test-retest reliability was evident (r = .93; P = .000). Acceptable construct validity was indicated by a difference in mean CAS scores (t = 4.4, P <.001). Patients reported difficulty with CAS questions and response selections. Symptoms asked on CAS were often not viewed as a problem.

13. Marquis P, De La Loge C, Dubois D, McDermott A, Chassany O. Development and validation of the Patient Assessment of Constipation Quality of Life questionnaire. Scandinavian Journal of Gastroenterology. May 2005;40(5):540-551 OBJECTIVE: Chronic constipation is characterized by difficult, infrequent, or seemingly incomplete bowel movements. The Patient Assessment of Constipation Quality of Life (PAC-QOL) questionnaire was developed to address the need for a standardized, patient-reported outcomes measure to evaluate constipation over time. MATERIAL AND METHODS: Items for the PAC-QOL were generated from the literature, clinical experts, and patients. Following principal components and multi-trait analyses, 28 items were retained forming four subscales (worries and concerns, physical discomfort, psychosocial discomfort, and satisfaction) and an overall scale. Validation studies were conducted in the United States, Europe, Canada, and Australia, to evaluate the internal consistency reliability (Cronbach’s alpha), reproducibility (Intraclass Correlation Coefficients (ICCs)), validity (analysis of variance models), and responsiveness (effect size) of the PAC-QOL scales. RESULTS: The
PAC-QOL scales were internally consistent (Cronbach’s alpha >0.80) and reproducible (ICCs >0.70, except for the satisfaction subscale ICC=0.66). PAC-QOL scale scores were significantly associated with abdominal pain (p<0.001) and constipation severity (p<0.05). Effect sizes in patients reporting improvements in constipation over a 6-week period were moderate to large, with subscale effect sizes ranging from 0.76 to 3.41 and the overall scale effect size=1.77. Similar findings were observed in validation studies conducted in Europe, Canada, and Australia. CONCLUSIONS: The PAC-QOL is a brief but comprehensive assessment of the burden of constipation on patients’ everyday functioning and well-being. Multinational studies demonstrate that the PAC-QOL is internally consistent, reproducible, valid, and responsive to improvements over time.

14. Frank L, Kleinman L, Farup C, Taylor L, Miner P, Jr. Psychometric validation of a constipation symptom assessment questionnaire. *Scandinavian Journal of Gastroenterology.* Sep 1999;34(9):870-877 BACKGROUND: Clinical management of constipation is complicated by the lack of a gold standard for evaluation of symptoms. A constipation symptom assessment instrument, the PAC-SYM, was developed to address the patient perspective on the disorder. Instrument content was based on literature review and results of focus groups. METHODS: Two hundred and sixteen patients at nine sites participated in a 6-week psychometric evaluation of the PAC-SYM. The final instrument contained 12 items assigned to 3 subscales: stool symptoms, rectal symptoms, and abdominal symptoms. The psychometric properties of this final instrument were assessed. RESULTS: Internal consistency and test-retest reliability of the final instrument was high (Cronbach’s alpha = 0.89; intraclass correlation = 0.75). Concurrent validity was supported by the correlation with both subject and investigator constipation severity ratings (r= 0.68 and 0.72, respectively; P < 0.0001). Scores were moderately correlated with instruments measuring quality of life. Comparison of treatment responders with nonresponders showed the ability of the instrument to differentiate between groups on the basis of clinical severity (t = -6.12, P < 0.0001 ). Scores changed significantly over time among responders, indicating instrument responsiveness. CONCLUSIONS: The PAC-SYM is internally consistent, reproducible under stable conditions, valid, and responsive to change and provides a comprehensive means to assess the effectiveness of treatment for constipation.

15. O’Brien BE, Kaklamani VG, Benson AB, 3rd. The assessment and management of cancer treatment-related diarrhea. *Clinical Colorectal Cancer.* Mar 2005;4(6):375-381; discussion 382-373 Cancer treatment-induced diarrhea affects a high percentage of patients with cancer that receive chemotherapy or radiation treatment. Widely used criteria for measuring treatment-induced diarrhea, such as the National Cancer Institute Common Toxicity Criteria, do not account for important characteristics of treatment-induced diarrhea. These characteristics include the assessment of the duration of the diarrhea, coexisting symptoms, abdominal cramping, or the presence of nocturnal diarrhea. Until recently, there were no universally accepted guidelines for the management of diarrhea. An expert panel developed guidelines with recommendations regarding assessment of the patient and treatment. These guidelines stress the importance of a thorough assessment of the patient, and treatment based upon severity of symptoms. By employing these guidelines, the aggressive management of diarrhea may impact the overall morbidity of this symptom. Education regarding the importance of diarrhea is essential. Patients who are informed will better understand their role in managing this side effect and when to contact their health care provider with emergent symptoms. Early recognition and management of diarrhea will be essential to improve control of diarrhea, and in turn will positively impact patients' quality of life. [References: 24].

16. Dorman S, Byrne A, Edwards A. Which measurement scales should we use to measure breathlessness in palliative care? A systematic review. *Palliative Medicine.* Apr 2007;21(3):177-191 INTRODUCTION: There is no universally accepted measurement scale to assess breathlessness in adult palliative care patients. This significantly hampers clinical practice and research into effective interventions. The aim is to systematically identify and appraise breathlessness measurement scales, which are validated for use in palliative care or which show potential for use. METHODS: We undertook systematic searches of electronic databases (Cochrane databases 2005, MEDLINE 1966-2005, OLDMEDLINE 1950-1965, EMBASE 1980-2005, PsycINFO 1872-2005, AMED 1985-2005, CINAHL 1982-2005, SIGLE 1980-2005) with follow-up searches (reference lists of included papers, hand-searches of relevant journals). The basic search strategy was 'breathlessness (etc.) AND measurement (scales, validation etc.) AND palliative care/cardiac failure/respiratory disease/ neoplasm etc.', modified for each database, without language restriction. Patient-based scales with evaluations of at least two psychometric characteristics were included.
Exercise-based tests were excluded. Scales were appraised with particular emphasis on construct validity and responsiveness. RESULTS: We identified 29 scales: six to measure breathlessness severity, four to assess breathlessness descriptions, and 19 to measure functional impact of breathlessness. SEVERITY: The Numeric Rating Scale (NRS) and modified Borg Scale have been evaluated in COPD (the NRS has also been evaluated in cancer). Both require further assessment of responsiveness and test-retest reliability over time intervals relevant to palliative care. Visual Analogue Scales have also been evaluated, but require larger sample sizes than NRS for evidence of intervention effectiveness. DESCRIPTIONS: The Japanese Cancer Dyspnoea Scale (CDS) has been evaluated in patients with cancer, but requires further assessment of construct validity and responsiveness. FUNCTIONAL IMPACT: The Chronic Respiratory Questionnaire dyspnoea subscale (CRQ-D) has been evaluated in chronic lung diseases and heart failure; the MND Respiratory Scale is similar. CRQ-D has face and construct validity, test-retest reliability and responsiveness, and shows promise for palliative care. CONCLUSION: The NRS, modified Borg, CRQ-D and CDS appear most suitable for use in palliative care, but further evaluation is required before adopting any scale as standard. This review has been registered with the Cochrane collaboration and will be published and updated as a Cochrane review. [References: 114].

17. Borg GA. Psychophysical bases of perceived exertion. Medicine & Science in Sports & Exercise. 1982;14(5):377-381 There is a great demand for perceptual effort ratings in order to better understand man at work. Such ratings are important complements to behavioral and physiological measurements of physical performance and work capacity. This is true for both theoretical analysis and application in medicine, human factors, and sports. Perceptual estimates, obtained by psychophysical ratio-scaling methods, are valid when describing general perceptual variation, but category methods are more useful in several applied situations when differences between individuals are described. A presentation is made of ratio-scaling methods, category methods, especially the Borg Scale for ratings of perceived exertion, and a new method that combines the category method with ratio properties. Some of the advantages and disadvantages of the different methods are discussed in both theoretical-psychophysical and psychophysiological frames of reference.

18. Mador MJ, Rodis A, Magalang UJ. Reproducibility of Borg scale measurements of dyspnea during exercise in patients with COPD. Chest. Jun 1995;107(6):1590-1597 The purpose of this study was to evaluate the moderate term (5 weeks) reproducibility of Borg scale ratings of the effort to breathe (Borge) and the degree of discomfort evoked by breathing (Borgd) in patients with COPD during exercise. Six subjects with moderately severe COPD (FEV1, 1.42 +/- 0.50 L) underwent progressive incremental exercise (15 W/min) on a cycle ergometer to a symptom-limited maximum every week for 6 weeks (first week used as practice session). Minute ventilation (VE), oxygen consumption (VO2), and Borg ratings were obtained every minute during exercise. Borge and Borgd were highly correlated in each subject (r = 0.99 +/- 0.01). Borg scores were not significantly different across study days during both maximal and submaximal exercise. The within-subject coefficient of variation (CV) for Borge during maximal exercise was 13.9 +/- 9.0% (range, 6 to 31%) which was not significantly different from that observed for the physiological indices: 8.2 +/- 4.1% (range, 4 to 15%) for VE and 5.2 +/- 3.4% (range, 1 to 10%) for VO2. In contrast, at 66% of the maximum workload, the within-subject CV for Borge was 25.0 +/- 8.0% (range, 12 to 32%). In conclusion, during incremental exercise Borg ratings of dyspnea are not as reproducible as physiologic indices in patients with COPD.

19. Ries AL. Minimally clinically important difference for the UCSD Shortness of Breath Questionnaire, Borg Scale, and Visual Analog Scale. Copd: Journal of Chronic Obstructive Pulmonary Disease. Mar 2005;2(1):105-110 Dyspnea is a primary symptom of chronic lung disease and an important outcome measure for clinical trials. Several standardized measures have been developed to evaluate this important symptom and are being used increasingly in clinical trials. The minimally clinically important difference (MCID) is not well defined for these measures but is important in interpreting the clinical meaning of results of studies in this area. The purpose of this paper is to evaluate the MCID for three commonly used measures to assess dyspnea in chronic lung disease: UCSD Shortness of Breath Questionnaire (SOBQ), Borg Scale (Borg), and Visual Analog Scale (VAS). The
analysis is based on a retrospective review of published trials evaluating the response to a pulmonary rehabilitation or exercise intervention that is known to produce modest, but clinically meaningful changes for such patients. Using a distribution-based approach based primarily on effect size, the recommended MCID for these measures are: 5-units for the SOBQ, 1-unit for the Borg scale, and approximately 10 to 20 units for the VAS.

[References: 31].

20. Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y. Development and validation of the Cancer Dyspnoea Scale: a multidimensional, brief, self-rating scale. British Journal of Cancer. Feb 2000;82(4):800-805 Dyspnoea is one of the most frequent and refractory symptoms in cancer patients. Lack of an appropriate assessment tool for dyspnoea seems to disturb establishment of management strategy. The purpose of this study was to develop and validate a brief self-rating scale to assess the multidimensional nature of dyspnoea in cancer patients. We developed a 12-item scale, the Cancer Dyspnoea Scale (CDS), composed of three factors (sense of effort/sense of anxiety/sense of discomfort), by using factor analysis. One hundred and sixty-six patients with advanced or recurrent lung cancer participated in the validation phase. The CDS showed good feasibility (average time required to complete it was 140 s). Construct validity, confirmed by repeating factor analysis, was good. Convergent validity, confirmed by a relation to Visual Analogue Scale of dyspnoea and modified Borg's scale, was also good (average: \( r=0.57 \) and 0.52, respectively, and both \( P<0.001 \)). The CDS had good internal consistency (average Cronbach's alpha = 0.86) and stability (average test-retest reliability \( r=0.66, P<0.005 \)). The present study demonstrated that the CDS is a brief, valid and feasible scale for assessing the multidimensional nature of dyspnoea in cancer patients.

21. Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. Thorax. Oct 1987;42(10):773-778 Since the relationships between pulmonary function, exercise capacity, and functional state or quality of life are generally weak, a self-report questionnaire has been developed to determine the effect of treatment on quality of life in clinical trials. One hundred patients with chronic airflow limitation were asked how their quality of life was affected by their illness, and how important their symptoms and limitations were. The most frequent and important items were used to construct a questionnaire evaluating four dimensions: dyspnoea, fatigue, emotional function, and the patient's feeling of control over the disease (mastery). Reproducibility, tested by repeated administration to patients in a stable condition, was excellent: the coefficient of variation was less than 12% for all four dimensions. Responsiveness (sensitivity to change) was tested by administering the questionnaire to 13 patients before and after optimisation of their drug treatment and to another 28 before and after participation in a respiratory rehabilitation programme. In both cases large, statistically significant improvements in all four dimensions were noted. Changes in questionnaire score were correlated with changes in spirometric values, exercise capacity, and patients' and physicians' global ratings. Thus it has been shown that the questionnaire is precise, valid, and responsive. It can therefore serve as a useful disease specific measure of quality of life for clinical trials.

22. Jean-Pierre P, Figueroa-Moseley CD, Kohli S, Fiscella K, Palesh OG, Morrow GR. Assessment of cancer-related fatigue: implications for clinical diagnosis and treatment. Oncologist. 2007;12 Suppl 1:11-21 Cancer-related fatigue (CRF) is a highly prevalent and debilitating symptom experienced by most cancer patients during, and often for considerable periods after, treatment. The recognition of the importance of CRF to patients' psychosocial and cognitive functioning, as well as to their quality of life, has driven the development of a wide range of assessment tools for screening and diagnosis of CRF. Over 20 different measures have been used to assess CRF from either a unidimensional or multi-dimensional perspective. Unidimensional measures are often single-question scales that generally focus on identifying the occurrence and severity of CRF, whereas multidimensional measures may also examine the effect of CRF across several domains of physical, socio-emotional, and cognitive functioning. This paper provides an overview and critique of measures commonly used to assess CRF. Single-question assessment is the most commonly used and the most useful methodology. Strategies to facilitate reliable assessment of CRF are also discussed. Disclosure of potential conflicts of interest is found at the end of this article. [References: 76].

23. Mendoza TR, Wang XS, Cleeland CS, et al. The rapid assessment of fatigue severity in cancer patients: use of the Brief Fatigue Inventory. Cancer. Mar 1 1999;85(5):1186-1196 BACKGROUND: Fatigue is a major disease and treatment burden for cancer patients. Several scales have been created to measure fatigue, but many are long and difficult for very ill patients to complete, or they are not easy to translate for non-English speaking
patients. The Brief Fatigue Inventory was developed for the rapid assessment of fatigue severity for use in both clinical screening and clinical trials. METHODS: The study enrolled 305 consecutive, consenting adult inpatients and outpatients with cancer who could understand and complete the self-report measures used in the study. The same instruments also were administered to 290 community-dwelling adults to obtain a comparison sample. Research staff completed a form that indicated the primary site and stage of the cancer, rated the Eastern Cooperative Oncology Group performance status of the patient, described the characteristics of the pain, and described the current pain treatment being provided to the patients. RESULTS: The BFI was shown to be an internally stable (reliable) measure that tapped a single dimension, best interpreted as severity of fatigue. It correlated highly with similar fatigue measures. Greater than 98% of patients were able to complete it. A range of scores defining severe fatigue was identified. CONCLUSIONS: The BFI is a reliable instrument that allows for the rapid assessment of fatigue level in cancer patients and identifies those patients with severe fatigue.

24. Hanna A, Sledge G, Mayer ML, et al. A phase II study of methylphenidate for the treatment of fatigue. Supportive Care in Cancer. Mar 2006;14(3):210-215 BACKGROUND: Cancer-related fatigue (CRF) is one of the most distressing symptoms patients experience and is seen well after the completion of treatment. Methylphenidate (Ritalin) use includes the treatment of opiate-induced somnolence, depression, and reduced cognition. This phase II study was performed to evaluate the effects of methylphenidate on CRF. PATIENTS AND METHODS: The criteria for the eligibility of patients included the following: a history of breast cancer, absence of disease for greater than 6 months but less than 5 years, a hemoglobin level of >12 g%, less than moderate depression on the Brief Zung Self-Assessment of Change (CGI-C) to determine improvement in clinical condition, the Epworth Sleepiness Scale (ESS) to determine patient-estimated wakefulness, and electrocardiography. RESULTS: A total of 395 patients were enrolled in the study (armodafinil 150 mg/d, 133; armodafinil 250 mg/d, 131; placebo, 131); 392 received >or=1 dose of study drug (armodafinil 150 mg/d, 131; armodafinil 250 mg/d, 131; placebo, 130). The armodafinil and placebo groups were well matched with regard to age (mean [SD], 49.2 [8.9] vs 50.1 [9.4] years), sex (71% vs 69% men), race (84% vs 87% white), and body weight (mean [SD], 110.3 [24.9] vs 111.9 [24.0] kg). At the final visit, the mean (SD) change from baseline in MWT sleep latency across the morning and afternoon was significantly greater in the armodafinil combined group compared with the...
placebo group (+1.9 [7.3] vs 1.7 [8.6] minutes; \( P < 0.001 \)). Also at the final visit, the proportions of patients who showed at least minimal improvement on the CGI-C, and the mean (SD) changes from baseline in ESS and BFI scores, were significantly greater in the armodafinil group compared with those in the placebo group (72% vs 37%, -5.5 [5.0] vs -3.3 [4.7], and -1.2 [2.2] vs -0.6 [2.0], respectively; \( P < 0.001 \), \( P < 0.001 \), and \( P < 0.01 \), respectively). No significant effects on nighttime sleep, as assessed using polysomnography, were found with armodafinil. AEs reported in the armodafinil combined and placebo groups were headache, nausea, insomnia, anxiety, and dizziness. Serious AEs (ulcerative colitis, migraine, worsening of Axis II and mood disorder, and duodenal ulcer) were reported in 4 (1.5%) patients receiving armodafinil and were considered by the investigator not or unlikely to be drug related. CONCLUSIONS: In this selected population of patients with OSA/HS and residual ES despite effective treatment with nCPAP, armodafinil QD used as an adjunct to nCPAP treatment was associated with improved wakefulness and overall clinical condition. Clinical benefit was shown at the first assessment and maintained for the 12-week duration of the study. Armodafinil was also associated with significantly reduced interference of ES with daily activities and global fatigue. Armodafinil was well tolerated, with no adverse effect on nighttime sleep or nCPAP use.

26. Cruciani RA, Dvorkin E, Homel P, et al. Safety, tolerability and symptom outcomes associated with L-carnitine supplementation in patients with cancer, fatigue, and carnitine deficiency: a phase I/II study. Journal of Pain & Symptom Management. Dec 2006;32(6):551-559 Carnitine deficiency is among the many metabolic disturbances that may contribute to fatigue in patients with cancer. Administration of exogenous L-carnitine may hold promise as a treatment for this common symptom. Little is known about L-carnitine safety, tolerability, and dose-response in patients with cancer. We conducted a Phase I/II open-label trial to assess the safety and tolerability of exogenous L-carnitine and clarify the safe dose range associated with symptom effects for future controlled trials. Adult patients with advanced cancer, carnitine deficiency (free carnitine <35 for males or <25 microM/L for females, or acyl/free carnitine ratio >0.4), moderate to severe fatigue, and a Karnofsky Performance Status (KPS) score \( > \) or \( = \) 50 were entered by groups of at least three into a standard maximum tolerated dose design. Each successive group received a higher dose of L-carnitine (250, 750, 1250, 1750, 2250, 2750, 3000 mg/day, respectively), administered in two daily doses for 7 days. To compare symptom outcomes before and after supplementation, patients completed validated measures of fatigue (Brief Fatigue Inventory [BFI]), depressed mood (Center for Epidemiologic Studies Depression Scale [CES-D]), quality of sleep (Epworth Sleeplessness Scale [ESS]), and KPS at baseline and 1 week later. Of the 38 patients screened for carnitine levels, 29 were deficient (76%). Twenty-seven patients participated ("intention to treat, ITT") (17 males, 10 females), and 21 completed the study ("completers"); 17 of these patients ("responders," mean +/-[SD] age=57.9+/-15) had increased carnitine levels at the end of the supplementation period. The highest dose achieved was 3000 mg/day. No patient experienced significant side effects and no toxicities were noted. Analysis of all the patients accrued (ITT, n=27) showed a total carnitine increase from 32.8+/-10 to 54.3+/-23 microM/L (\( P<0.001 \)) and free carnitine increase from 26.8+/-8 to 44.1+/-17 microM/L (\( P<0.001 \)). BFI decreased significantly, from 66+/-12 to 39.7+/-26 (\( P<0.001 \)); ESS decreased from 12.9+/-12 to 9+/-6 (\( P=0.001 \)); and CES-D decreased from 29.2+/-12 to 19+/-12 (\( P<0.001 \)). A separate analysis of the 17 "responders" showed a dose-response relationship for total- \( (r=0.54, P=0.03) \), free-carnitine \( (r=0.56, P=0.02) \) levels, and fatigue (BFI) scores \( (r=-0.61, P=0.01) \). These findings suggest that L-carnitine may be safely administered at doses up to 3000 mg/day and that positive effects may be more likely at relatively higher doses in this range. This study provides the basis for the design of future placebo-controlled studies of L-carnitine supplementation for cancer-related fatigue.

27. Reddy S, Bruera E, Pace E, Zhang K, Reyes-Gibby CC. Clinically important improvement in the intensity of fatigue in patients with advanced cancer. Journal of Palliative Medicine. Oct 2007;10(5):1068-1075 Cancer-related fatigue (CRF) is the most common symptom experienced by patients with cancer. Clinically important improvement in the intensity of fatigue in palliative care patients has not been well established. We reviewed the data from 3 clinical trials of fatigue in 194 patients receiving palliative care treatment. Patients completed the Functional Assessment for Chronic Illness Therapy Fatigue (FACIT-F) and Edmonton Symptom Assessment System (ESAS) at baseline and day 8 and their global perception of fatigue improvement (Global benefit score [GBS]: 1 = not beneficial, 7 = greatly important) during day 8. A GBS of 4 or more (moderate improvement, consistently beneficial) was considered a clinically significant improvement. Change scores in the ESAS
and FACIT-F from baseline to day 8 were compared to the GBS greater than 4. Receiver-operating characteristic curves were also derived for ESAS and FACIT-F change scores for a GBS greater than 4, greater than 5, and greater than 6. Results showed the mean patient age was 56 (+/-12) years, and 37% were men. A reduction of approximately 10 points in FACIT-F (sensitivity = 73%, specificity = 78%, area under the curve = 0.82) and 4 points in ESAS fatigue (sensitivity = 66%, specificity = 72%, area under the curve = 0.78) score was best able to predict a clinically important improvement (GBS >/= 4). We were able to characterize the relationship between FACIT-F and ESAS scores and patients' global perception of improvement but further studies are needed to validate our findings.

28. Headley JA, Ownby KK, John LD. The effect of seated exercise on fatigue and quality of life in women with advanced breast cancer. Oncology Nursing Forum Online. Sep 2004;31(5):977-983 PURPOSE/OBJECTIVES: To examine the effects of a seated exercise program on fatigue and quality of life (QOL) in women with metastatic breast cancer. DESIGN: Randomized, controlled, longitudinal trial. SETTING: Outpatient clinic of a comprehensive cancer center. SAMPLE: Convenience sample of 38 women who were beginning outpatient chemotherapy. METHODS: Subjects were randomized to a control or intervention group; the intervention was performance of a seated exercise program using home videotape three times per week for four cycles of chemotherapy. All subjects completed the Functional Assessment of Chronic Illness Therapy Fatigue Version IV (FACIT F) at baseline and at the time of the next three cycles. Subjects were asked to document the frequency, duration, and intensity of all exercise participation on monthly calendars. MAIN RESEARCH VARIABLES: Exercise, fatigue, and QOL. FINDINGS: 32 subjects, 16 per group, completed the study follow-up. With a mixed modeling approach, total FACIT F scores for the entire sample declined at a significant rate (p = 0.003) beginning with cycle 3 but at a slower rate for the experimental group (p = 0.02). Fatigue scores indicated less increase and physical well-being subscale scores showed less decline for the experimental group (p = 0.008 and p = 0.02, respectively). CONCLUSIONS: Women with advanced breast cancer randomized to the seated exercise intervention had a slower decline in total and physical well-being and less increase in fatigue scores starting with the third cycle of chemotherapy. IMPLICATIONS FOR NURSING: Seated exercise may be a feasible exercise program for women with advanced cancer for controlling fatigue and improving physical well-being.

29. Fallowfield LJ, Leaty SK, Howell A, Benson S, Cella D. Assessment of quality of life in women undergoing hormonal therapy for breast cancer: validation of an endocrine symptom subscale for the FACT-B. Breast Cancer Research & Treatment. May 1999;55(2):189-199 Existing quality of life instruments do not include adequate items to measure the side effects and putative benefits of hormonal treatments given in breast cancer. We report the development and validation of an 18 item endocrine subscale (ES) to accompany a standardised breast cancer quality of life measure, the Functional Assessment of Cancer Therapy (FACT-B). The FACT-ES (FACT-B plus ES) was tested initially on 268 women with breast cancer receiving endocrine treatments. Alpha coefficients for all subscales demonstrated good internal consistency (range alpha = 0.65-0.87). Test-retest reliability of the ES indicated good stability (r = 0.93, p < 0.001). Advanced breast cancer patients' quality of life was high, showing the efficacy of endocrine therapy, but women with primary disease reported better physical, social, and functional well-being and fewer breast cancer concerns. Most frequently reported symptoms were loss of sexual interest (31%), weight gain (25%), and hot flushes (24%). Significant differences were found between treatment groups for hot flushes and vaginal dryness. Two assessments of the instrument's responsiveness to change were made; 32 women in a clinical trial of endocrine therapy and 18 women without breast cancer taking HRT completed the FACT-ES at baseline, 4, 8, and 12 weeks. Trial patients reported significantly more symptoms at 8 and 12 weeks than at baseline. Women taking HRT reported significantly fewer or less severe symptoms than at baseline. In conclusion the FACT-ES has acceptable validity and reliability and is sensitive to clinically significant change, making it suitable for clinical trials of endocrine therapy.

30. Fallowfield LJ, Bliss JM, Porter LS, et al. Quality of life in the intergroup exemestane study: a randomized trial of exemestane versus continued tamoxifen after 2 to 3 years of tamoxifen in postmenopausal women with primary breast cancer. Journal of Clinical Oncology. Feb 20 2006;24(6):910-917 PURPOSE: To compare and describe the quality of life (QOL) of women allocated to tamoxifen or exemestane within the Intergroup Exemestane Study (IES). PATIENTS AND METHODS: Postmenopausal women with primary breast cancer who were disease free after 2 to 3 years were randomly assigned to switch from tamoxifen to exemestane or continue with tamoxifen until 5 years of treatment were
Coster S, Poole K, Fallowfield LJ. The validation of a quality of life scale to assess the impact of arm morbidity in breast cancer patients post-operatively. Breast Cancer Research & Treatment, Aug 2001;68(3):273-282. This paper documents the validation of a quality of life scale (QOL) designed to assess the impact of arm morbidity on patients following breast cancer surgery. A four item arm subscale was developed to supplement a multi-dimensional, validated breast cancer QOL tool, the functional assessment of cancer therapy (FACT-B). The new questionnaire, the FACT-B + 4, was validated on 279 women participating in a trial of sentinel node guided axillary therapy and 29 women attending a lymphoedema clinic. The subscale demonstrated good internal consistency (alpha coefficient = 0.62 to 0.88) and stability (test-retest reliability = 0.97). Lymphoedema patients reported significantly greater arm problems than a matched sample of pre-operative trial participants. The lymphoedema group also scored lower than trial patients on the FACT-B + 4 indicating a poorer quality of life (p < 0.05). A subset of 66 trial patients who had completed three consecutive assessments was used to evaluate the sensitivity of the questionnaire to change over time. Scores on the FACT-B + 4 were found to decline significantly between the pre-operative assessment and post-operative assessment at 1 month. Arm problems significantly increased during this period. FACT-B + 4 score increased again from 1 month to 12 weeks post-surgery and symptoms reduced, as the extent of arm morbidity resolved. The FACT-B + 4 appears to be psychometrically robust and sensitive to patient rehabilitation, making it suitable for use in longitudinal surgical trials. Given the dearth of existing scales available to measure arm morbidity, we hope this new tool will prove useful to researchers.

Fleissig A, Fallowfield LJ, Langridge CI, et al. Post-operative arm morbidity and quality of life. Results of the ALMANAC randomised trial comparing sentinel node biopsy with standard axillary treatment in the management of patients with early breast cancer. Breast Cancer Research & Treatment, Feb 2006;95(3):279-293. This study is the first large prospective RCT of sentinel node biopsy (SNB) compared with standard axillary treatment (level I-III axillary lymph node dissection or four node sampling), which includes comprehensive and repeated quality of life (QOL) assessments over 18 months. Patients (n = 829) completed the Functional Assessment of Cancer Therapy - Breast (FACT-B+4) and the Spielberger State/Trait Anxiety Inventory (STAI) at baseline (pre-surgery) and at 1, 3, 6, 12, and 18 months post-surgery. There were significant differences between treatment groups favouring the SNB group throughout the 18 months assessment. Patients in the standard treatment group showed a greater decline in Trial Outcome Index (TOI) scores (physical well-being, functional well-being and breast cancer concerns subscales in FACT-B+4) and recovered more slowly than patients in the SNB group (p < 0.01). The change in total FACT-B+4 scores (measuring global QOL) closely resembled the TOI results. 18 months post-surgery approximately twice as many patients in the standard group compared with the SNB group reported substantial arm swelling (14% versus 7%) (p = 0.002) or numbness (19% versus 8.7%) (p < 0.001). Despite the uncertainty about undergoing a relatively new procedure and the possible need for further surgery, there was no evidence of increased anxiety amongst patients randomised to SNB (p > 0.05). For 6 months post-surgery younger patients reported less favourable QOL scores (p < 0.001) and greater levels of anxiety (p < 0.01). In view of the benefits regarding arm functioning and quality of life, the data from this randomised study support the use of SNB in patients with clinically node negative breast cancer.

BACKGROUND: A frequent complication of anticancer treatment, oral and gastrointestinal (GI) mucositis, threatens the effectiveness of therapy because it leads to dose reductions, increases healthcare costs, and impairs patients’ quality of life. The Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology assembled an international multidisciplinary panel of experts to create clinical practice guidelines for the prevention, evaluation, and treatment of mucositis. METHODS: The panelists examined medical literature published from January 1966 through May 2002, presented their findings at two separate conferences, and then created a writing committee that produced two articles: the current study and another that codifies the clinical implications of the panel’s findings in practice guidelines. RESULTS: New evidence supports the view that oral mucositis is a complex process involving all the tissues and cellular elements of the mucosa. Other findings suggest that some aspects of mucositis risk may be determined genetically. GI proapoptotic and antiapoptotic gene levels change along the GI tract, perhaps explaining differences in the frequency with which mucositis occurs at different sites. Studies of mucositis incidence in clinical trials by quality and using meta-analysis techniques produced estimates of incidence that are presented herein for what to our knowledge may be a broader range of cancers than ever presented before. CONCLUSIONS: Understanding the pathobiology of mucositis, its incidence, and scoring are essential for progress in research and care directed at this common side-effect of anticancer therapies. Copyright 2004 American Cancer Society. [References: 404].


OBJECTIVES: To systematically review studies of antiemetics used in the treatment of nausea in patients with far-advanced cancer. DATA SOURCES: Randomized controlled trials (RCT) and uncontrolled studies identified by electronic and hand searching. REVIEW METHODS: Identified studies were appraised for quality and effect size. RESULTS: Of 21 studies included, 2 were systematic reviews, 7 were RCT and 12 were uncontrolled studies or case series. Differences in interventions and outcomes amongst the RCT precluded any quantitative data synthesis and all seven studies were prone to bias. Whereas uncontrolled studies indicated a high response rate to standard regimens (75-93% for both nausea and vomiting), RCT showed much lower response rates to these agents (23-36% for nausea, 18-52% for vomiting). The two methods of antiemetic choice (choice based either on the inferred mechanism or empirical) were equally effective. There is reasonably strong evidence for the use of metoclopramide in cancer-associated dyspepsia and steroids in malignant bowel obstruction. There was conflicting evidence about the efficacy of serotonin antagonists compared with standard treatments (e.g. metoclopramide, dopamine antagonists and dexamethasone). There was little or no evidence of the efficacy of some commonly used and seemingly effective drugs such as haloperidol, cyclizine, and methotrimeprazine. CONCLUSION: Evidence supporting the existing consensus-based guidelines for management of nausea and vomiting in advanced cancer is sparse. Current approaches to treatment based on the neuropharmacology of the emetic pathway may be inappropriate in this setting. Well-designed studies of the impact of "standard" management and novel agents on nausea and vomiting in palliative populations are needed. [References: 49].


Lower hemibody radiotherapy is an effective palliative treatment for patients with wide-spread bone metastases, but is frequently associated with the unpleasant side effects of nausea and vomiting. Patients often require admission to hospital for at least an overnight stay, with its inevitable costs. This study has investigated the clinical efficacy and safety profile of ondansetron, a SHT3 receptor antagonist, and compared it to a standard antiemetic combination, chlorpromazine and dexamethasone. Sixty-six patients were randomised to receive antiemetic prophylaxis with either oral ondansetron or a combination of chlorpromazine and dexamethasone (33 patients in each arm): 60 were treated with lower abdominal radiotherapy (8 Gy mid-plane dose) and 6 with radiotherapy to the upper
lumbar spine (12.5 Gy incident dose). Patients were assessed for severity of nausea and vomiting and for whether they would use the same antiemetic again. Quality of life was assessed using the Functional Living Index Cancer (FLIC) and Functional Living Index Emesis (FLIE) quality-of-life questionnaires. A detailed cost-benefit analysis was also performed. Ondansetron scored highly as an antiemetic, being significantly better at controlling emesis on all four study days (P < 0.001) and significantly better at controlling nausea on day 1 (P < 0.001) than the standard combination of chlorpromazine and dexamethasone. Quality of life was better in the ondansetron-treated group, and ondansetron was found to be safe with no significant adverse effects. As a result, 98% of patients and investigators would use ondansetron again. Cost-benefit analysis revealed that, when complete control of emesis is the aim, ondansetron is not unduly expensive compared to the standard antiemetic regimen. As ondansetron was clearly effective in patients receiving hemibody irradiation it seems it would be prudent to adopt it for use in such patients routinely. The use of ondansetron would allow them to be treated as outpatients, with the attendant financial and psychosocial benefits of such an approach.


38. Razavi D, Delvaux N, Farvacques C, et al. Prevention of adjustment disorders and anticipatory nausea secondary to adjuvant chemotherapy: a double-blind, placebo-controlled study assessing the usefulness of alprazolam. *Journal of Clinical Oncology*. Jul 1993;11(7):1384-1390 PURPOSE AND METHODS: Although a high prevalence of adjustment disorders and anticipatory nausea secondary to adjuvant chemotherapy (CT) has been reported, little has been done to develop strategies to prevent these problems. A double-blind, placebo-controlled study was therefore designed to assess the usefulness of adding low-dose alprazolam (0.5 mg to 2 mg per day) to a psychologic support program including progressive relaxation training designed to prevent the aforementioned conditions. Fifty-seven women undergoing adjuvant CT for stage II primary breast cancer agreed to participate in the assessment, which was conducted at four time points: before starting CT, 6 weeks after CT, before the fourth CT, and after the fourth CT. The Hospital Anxiety and Depression Scale (HADS), Montgomery and Asberg Depression Rating Scale (MADRS), Hamilton Anxiety Scale (HAS), Revised Symptom Checklist (SCL-90-R), Morrow Assessment of Nausea and Emesis (MANE), and World Health Organization (WHO) grading of acute and subacute toxicities were used to compare the alprazolam (AA) and placebo (PA) arms of the study. RESULTS: At the second evaluation, the results showed a higher rate of anticipatory nausea (18% v 0%) in the PA compared with the AA arm (P = .038). These differences were no more significant at each of the further assessments. Significant differences were found for the intake of hypnotics at each assessment visit, with the rate of hypnotic users being significantly higher in the PA (19%) compared with the AA (0%) arm at the fourth assessment (P < .05). Anxiety and depression scores of self- and observer-report were similar in the two arms. A significant relationship was found between the development of anticipatory nausea and the self-report of anxiety and depression score measured by HADS at baseline. The average HADS total score at baseline was 15.33 (SD = 6.56) for patients who developed anticipatory nausea and 11.23 (SD = 6.67) for other patients. CONCLUSION: The adjunct of alprazolam to a psychologic support program delays the occurrence of anticipatory nausea and controls sleeping problems secondary to adjunct CT. Although studies are needed to improve the efficacy reported here, physicians may already consider the use of alprazolam for cancer patients undergoing CT.

40. Molassiotis A, Yung HP, Yam BMC, Chan FYS, Mok TSK. The effectiveness of progressive muscle relaxation training in managing chemotherapy-induced nausea and vomiting in Chinese breast cancer patients: a randomised controlled trial. *Supportive Care in Cancer*. Apr 2002;10(3):237-246 This study was a randomised controlled trial designed to assess the effectiveness of progressive muscle relaxation training (PMRT) in the clinical management of chemotherapy-related nausea and vomiting as an adjuvant intervention to
accompany pharmacological antiemetic treatment (metoclopramide and dexamethasone i.v.). Seventy-one chemotherapy-naïve breast cancer patients of an outpatient oncology unit of a university hospital in Hong Kong participated, with 38 subjects randomised to the experimental group and 33 to the control group. The intervention included the use of PMRT 1 h before chemotherapy was administered and daily thereafter for another 5 days (for a total of six PMRT sessions). Each session lasted for 25 min and was followed by 5 min of imagery techniques. The instruments used for data collection included the Chinese versions of the Profile of Mood States and the State-Trait Anxiety Inventory (measured before chemotherapy and then at day 7 and day 14 after chemotherapy), and the Morrow Assessment of Nausea and Vomiting Scale, which was used daily for the first 7 post-chemotherapy days. The use of PMRT considerably decreased the duration of nausea and vomiting in the experimental group compared with the control group (P < 0.05), whereas there were trends toward a lower frequency of nausea and vomiting (P = 0.07 and P = 0.08 respectively). Neither nausea nor vomiting differed in intensity between the two groups. The significant effects were mainly evident on the first 4 post-chemotherapy days, when differences were statistically significant. Although there was a significantly less severe overall mood disturbance in the experimental group over time (P < 0.05), this did not apply in the case of anxiety. Such findings suggest that PMRT is a useful adjuvant technique to complement antiemetics for chemotherapy-induced nausea and vomiting and that incorporation of such interventions in the care plan can enhance the standards of care of cancer patients who experience side effects of chemotherapy.

41. Hickok JT, Roscoe JA, Morrow GR, King DK, Atkins JN, Fitch TR. Nausea and emesis remain significant problems of chemotherapy despite prophylaxis with 5-hydroxytryptamine-3 antiemetics: a University of Rochester James P. Wilmot Cancer Center Community Clinical Oncology Program Study of 360 cancer patients treated in the community. Cancer. Jun 1 2003;97(11):2880-2886 BACKGROUND: Clinical reports suggest that nausea remains a side effect of chemotherapy despite widespread use of serotonin receptor antagonists. This study summarized the frequency, timing, and intensity of postchemotherapy nausea for patients receiving doxorubicin, cisplatin, or carboplatin. METHODS: Three hundred sixty chemotherapy-naïve patients (73% female) were enrolled in a study testing the ability of an information intervention to reduce nausea. Of these, 322 subjects completed the Morrow Assessment of Nausea and Emesis (MANE), as well as a 5-day self-report diary, at Cycle 1 (300 subjects completed the MANE and self-report diary at Cycle 2). All patients received a 5-hydroxytryptamine-3 receptor antagonist (ondansetron) with dexamethasone on the day of treatment. RESULTS: Seventy-six percent of the patients developed nausea during the 5-day period, beginning with the Cycle 1 infusion, and 73% of patients reported delayed nausea (DN) during Days 2-5. The proportions were similar during Cycle 2. Fifty-five percent of patients described their DN as being of moderate or greater intensity compared with 28% of patients who described acute nausea. Carboplatin was less likely to cause DN than either of the other agents (56% of 106 patients compared with 75% of 47 receiving cisplatin and 83% of 169 taking doxorubicin). The mean peak DN severity was 4.34 (range, 1-7) for doxorubicin, which was significantly higher than the mean peak value for carboplatin (3.66) but was not significantly different from the mean peak value for cisplatin (4.26). Eighteen percent of patients did not experience nausea until Day 3 or later. CONCLUSIONS: Despite prophylaxis with ondansetron, the majority of patients receiving one of these common chemotherapy agents experienced nausea. The frequency of DN was nearly twice that of acute nausea. Results show the need for continued development of antiemetics that are effective against DN. Copyright 2003 American Cancer Society.

42. Molassiotis A, Coventry PA, Stricker CT, et al. Validation and psychometric assessment of a short clinical scale to measure chemotherapy-induced nausea and vomiting: the MASCC antiemesis tool. J Pain Symptom Manage. 2007;34(2):148-159 There is a lack of clinical tools to facilitate communication between clinicians and patients about chemotherapy-induced nausea and vomiting (CINV). The Multinational Association of Supportive Care in Cancer (MASCC) has developed such a tool, which is an eight-item scale for the assessment of acute and delayed nausea and vomiting, and is completed once per cycle of chemotherapy. The aim of the current study was to assess its psychometric properties, specifically reliability and validity, cultural transferability and equivalence, and congruence with proxy assessments, as well as to determine if accuracy of recall of CINV events using the MASCC Antiemesis Tool (MAT) differed over time from chemotherapy. A prospective study was carried out with adult cancer patients and their informal carers from two hospitals, one each in the United Kingdom (UK) and United States of America (U.S.). Patients completed the Rhodes Index for nausea, vomiting and retching (INVR) daily for
the first five days after chemotherapy and were then asked to complete the MAT at one week, two weeks, or three weeks after chemotherapy. Carers completed an adapted MAT concurrently with patients. The sample consisted of 87 patients and 22 informal carers. The internal consistency reliability of the scale was high, with Cronbach alphas of 0.77 (patient sample) and 0.82 (carer sample). Responses were similar between the UK and U.S. samples in terms of nausea and vomiting, and both samples found the scale easy to use. Contrasted-groups validity (using age as a grouping variable) and concurrent validity (MAT compared with INVR) suggested that the scale is sensitive to detect the different dimensions of CINV and performed well against a daily assessment of nausea/vomiting (total score correlation r=0.86, P<0.001). Recall of events was high even three weeks after chemotherapy (correlations with INVR of 0.44-0.99, all P<0.01). Factor analysis clearly identified three factors, namely vomiting, acute nausea, and delayed nausea. Proxy assessments by carers were congruent with the patients' responses, especially in relation to vomiting. The MAT is a reliable, valid, clear, and easy-to-use clinical tool that could facilitate discussion between clinicians and patients about their nausea and vomiting experience, thereby potentially aiding treatment decisions. Regular assessment of nausea and vomiting after chemotherapy has the potential to significantly improve CINV management.


BACKGROUND: Despite widespread application of Rhodes Index of Nausea and Vomiting--Form 2 (INV2) in practice and research, empirical analyses have not been consistently performed to verify the a priori factors that guided the subclass construction of the symptoms. OBJECTIVES: To examine the dimensional structure of Rhodes INV in a sample of pregnant women. METHOD: Data were collected from 152 pregnant women who were experiencing some degree of nausea and vomiting during early pregnancy and analyzed using structural equation modeling techniques. Five competing measurement structures were tested and compared. The structure (model) that provided the closest fit to the data was selected and relationships (factor loadings) between the constructs and indicators were established. RESULTS: The model fitting the data the closest was a three-factor structure measuring nausea, vomiting, and retching as three separate, but correlated dimensions. The factor loadings were high (0.73-0.96) and significant (p < .001). The model treating nausea and vomiting as a one-factor concept as well as the model including two factors named symptom occurrence and symptom distress did not fit the data. CONCLUSION: Rhodes INV2 is a valid measurement tool if subscales are formed to reflect the multidimensional structure of nausea and vomiting in pregnancy.


BACKGROUND: Highly emetogenic combination alkylator therapy is routinely used in autologous bone marrow transplantation for treatment of eligible patients with solid tumors. Antiemetic therapy remains less than optimal in this setting. METHODS. One hundred twenty-six patients with cancer receiving high dose cisplatin, cyclophosphamide, and carmustine with autologous bone marrow support were randomized to receive one of four double-blinded antiemetic regimens: 4-day continuous infusion prochlorperazine (6 mg/m2 intravenous [i.v.] loading dose followed by 1.5 mg/m2/hour) or metoclopramide (80 mg/m2 iv loading dose followed by 20 mg/m2/hr) each with either dronabinol 5 mg/m2 or placebo capsules for two doses before carmustine on the last day of chemotherapy. All subjects received scheduled lorazepam and diphenhydramine throughout the 4-day study period. Efficacy was measured by the Emetic Process Rating Scale and the Rhodes Index of Nausea and Vomiting (INV) Form 2. RESULTS. One hundred six patients completed the study and were fully evaluable. The median number of emetic episodes on the metoclopramide study arm were: 1 (0-7, day -6), 1 (0-6, day -5), 2 (0-9, day -4), and 2 (0-10, with dronabinol day -3) or 2 (0-7, no dronabinol day -3) and on the prochlorperazine study arm were: 4 (0-12, day -6), 0 (0-8, day -5), 0 (0-12, day -4) and 2.5 (0-9, with dronabinol day -3) or 2 (0-12, no dronabinol day -3). Metoclopramide was significantly better on the first day of therapy (day -6, P < .002) and prochlorperazine was significantly better on the third day of therapy (day -4, P < 0.002). There was no significant difference among any of the four arms on the last day of chemotherapy (day -3), or when the median number of emetic episodes over the total study period were compared. The patients' assessment of nausea, vomiting, and retching on the INV Form 2
was consistent with the observer ratings. Toxicities requiring dose reduction or discontinuation of antiemetic drugs included diarrhea, cardiac arrhythmias, sedation, anxiety, and akathisia. CONCLUSIONS. Both metoclopramide and prochlorperazine in combination with lorazepam and diphenhydramine offer good control of nausea and vomiting although the sedation and low risk for cardiac toxicity limit the regimen to an inpatient setting with close monitoring. No regimen was clearly superior during the entire treatment period but prochlorperazine offered more consistent control after the first day.


PURPOSE/OBJECTIVES: To determine the reliability of the Index of Nausea, Vomiting, and Retching (INV), a new format of the Rhodes Index of Nausea and Vomiting Form 2 (INV-2). DESIGN AND SETTING: A parallel form study was conducted at a large, Midwestern teaching hospital and a cancer center. SAMPLE: Convenience sample of 159 subjects: 40 obstetrical, 60 oncological, 59 medical/surgical. METHODS: Two instruments, the INV and the INV-2, were administered approximately 30-60 minutes apart. One-half of the subjects completed the INV first, and the other half completed the INV-2 first. MAIN OUTCOME MEASURES: Equivalency measures of reliability correlation coefficients for both instruments. FINDINGS: A high rate of agreement was found in the responses between the two forms. In cases of clear disagreement, the responses to the INV were more frequently consistent than the responses to the original form. CONCLUSIONS: INV has tested reliability and is more user friendly for the patient and the healthcare provider. IMPLICATIONS FOR NURSING PRACTICE: Nurses have a focal role in managing symptoms. Managing nausea, vomiting, and retching requires excellent assessment skills of the patient’s personal symptom experience and knowledge of pharmacology. Efficient, cost-saving assessments require accurate self-report instruments that permit patients to quantify their symptom experiences. The INV can provide a scientific base from which to prescribe and teach patients and may improve their quality of life. Reliable and valid self-reporting instruments are essential for managing these adverse symptoms.


BACKGROUND: The Index of Nausea and Vomiting (INV), developed by Rhodes and others in 1984, measures three dimensions of upper gastrointestinal distress: nausea, vomiting and retching (NVR). While the revised version has been tested with a variety of high-risk populations, there are no data suggesting that it can be used to assess upper gastrointestinal distress among the growing numbers of ambulatory or day surgery patients. AIM: The aim of this study was to evaluate a modified version of the INV for use with ambulatory surgery patients. METHODS: A secondary analysis was conducted using data obtained from a descriptive study designed to identify risk factors for postdischarge nausea and vomiting (PDNV) among adult ambulatory surgery patients. Patients who reported PDNV (n = 190) participated via phone interview 24 hours after discharge by completing a modified Rhodes INV. FINDINGS: Reliability analysis (alpha = 0.897) indicated that the modified Rhodes INV measured upper gastrointestinal distress as a single concept in the postdischarge ambulatory surgical sample. One item of the 8-item scale was dropped. Principal component analysis extracted one factor that accounted for 67% of the variance with all items loading. CONCLUSIONS: Upper gastrointestinal distress following ambulatory surgery discharge comprises a different symptom mix than during other high-risk events such as pregnancy or chemotherapy. Further research on the differences in assessing NVR among different populations is indicated.


Despite the development of effective antiemetic drugs, nausea and vomiting remain the main side effects associated with cancer chemotherapy. The purpose of this study was to examine the effect of acupressure on emesis control in postoperative gastric cancer patients undergoing chemotherapy. Forty postoperative gastric cancer patients receiving the first cycle of chemotherapy with cisplatin and 5-Fluorouracil were divided into control and intervention groups (n = 20 each). Both groups received regular antiemesis medication; however, the intervention group received acupressure training and was instructed to perform the finger acupressure maneuver for 5 minutes on P6 (Nei-Guan) point located at 3-finger widths up from the first palmar crease, between palmaris longus and flexor carpi radialis tendons point, at least 3 times a day before chemotherapy and mealtimes or based on their needs. Both groups received equally frequent nursing visits and consultations, and reported nausea and vomiting using Rhode's Index of Nausea, Vomiting and Retching. We found significant differences between
49. Padilla G, Ropka ME. Quality of life and chemotherapy-induced neutropenia. Cancer Nursing. May-Jun 2005;28(3):167-171 This report summarizes recent data on neutropenia-related quality of life (QOL), including measures and interventions. Neutropenia is a common adverse effect of cytotoxic chemotherapy. The clinical significance of QOL in patients with chemotherapy-induced neutropenia (CIN) remains largely unexplored, although recent studies have shown a correlation between severe CIN and impaired QOL. Neutropenia typically occurs at the same time as other adverse effects. Data indicate that other toxicities are worse in the presence of febrile neutropenia and that these concurrent events may have a greater effect on QOL. Precautions that are taken to minimize the incidence of infection in patients with neutropenia may also affect their QOL. Future research should focus on accurately defining and measuring QOL in patients with CIN as well as on assessing ways to manage CIN more effectively and thus improve QOL. A number of interventions may have a positive influence on QOL in patients with cancer and neutropenia. Hematopoietic growth factor support, for example, reduces the incidence and sequelae of neutropenia and may provide a QOL benefit. To assess the effect of such interventions, neutropenia-specific QOL instruments, such as the Functional Assessment of Cancer Therapy-Neutropenia (FACT-N), may be valuable tools. [References: 36].

50. Ropka ME, Padilla G. Assessment of neutropenia-related quality of life in a clinical setting. Oncology Nursing Forum Online. Mar 2007;34(2):403-409 PURPOSE/OBJECTIVES: To examine how neutropenia affects quality of life (QOL) and explore strategies to assess neutropenia-related QOL in clinical practice. DATA SOURCES: Published articles, abstracts, conference proceedings, and clinical practice guidelines. DATA SYNTHESIS: Neutropenia can have a detrimental effect on the QOL of patients receiving chemotherapy. A neutropenia-related QOL questionnaire can help nurses better identify patients at risk for developing neutropenia and monitor patients who already have it. In some cases, the questionnaire may be the first step in the initiation of interventions to improve patient care. Ideally, the QOL questionnaire should be easy to use, provide clinically meaningful information, and be easily adapted from existing QOL measurement tools. CONCLUSIONS: Effective implementation of QOL assessments into clinical practice can lead to the initiation of interventions that may improve neutropenia-related QOL in patients with cancer receiving chemotherapy. IMPLICATIONS FOR NURSING: Nurses can enhance their clinical judgment and affect patient treatment by implementing a questionnaire that assesses patients' neutropenia-related QOL. [References: 54].


52. Caraceni A. Evaluation and assessment of cancer pain and cancer pain treatment. Acta Anaesthesiologica Scandinavica. Oct 2001;45(9):1067-1075 Evaluation and assessment are the first steps of any strategy for the management of cancer pain, and are fundamental for any clinical research project in this field. Different clinical systems for evaluation and classification of cancer pain syndromes are available and their clinical usefulness should be tested. The measurement of pain intensity is necessary to document and assess the outcome of established and new treatments. Visual analogue scales, verbal and numerical rating scales and some multidimensional tools such as the Brief Pain Inventory and the McGill Pain Questionnaire are helpful in the assessment of cancer pain provided the limitations of their validity are considered. Specific questions arise when these tools are used in long-term repeated assessments of cancer patients. Assessment and measuring techniques deserve more investigations to optimize standard valid procedures and to enable us to exchange clinical information and produce comparable data in research. [References: 84].

53. Caraceni A, Cherny N, Fainsinger R, et al. Pain measurement tools and methods in clinical research in palliative care: recommendations of an Expert Working Group of the European Association of Palliative Care. Journal of Pain & Symptom Management. Mar 2002;23(3):239-255 An Expert Working Group was convened under the auspices of the Steering Committee of the Research Network of the European Association of Palliative Care to review the status of the use of pain measurement tools (PMTs) in palliative care research conducted in a multilingual-multicenter setting. Based on a literature review and on the experts' opinion, the present work recommends that standardized methods should be applied for the use of PMTs in research in palliative care. Visual analogue scales, numerical rating scales, and verbal rating scales are considered valid to assess pain...
intensity in clinical trials and in other types of studies. Among the multidimensional questionnaires designed to assess pain, the McGill Pain Questionnaire and Brief Pain Inventory are valid in many multilingual versions. Specific recommendations for PMT use and administration, depending on the study type and aim, are reviewed. Special population requirements specific of clinical situations encountered in palliative care (elderly, terminal, cognitively impaired patients, pediatric patients) are also considered. [References: 90].

54. De Conno F, Caraceni A, Gamba A, et al. Pain measurement in cancer patients: a comparison of six methods. Pain. May 1994;57(2):161-166 A consecutive sample of 53 chronic cancer pain patients were administered 5 different pain intensity scales: a visual analogue scale (VAS), a numerical rating scale from 0 to 10 (NRS), a verbal rating scale (VRS), the Italian Pain Questionnaire (Italian version of the McGill Pain Questionnaire) (PRI), and the Integrated Pain Score (IPS) which is an instrument designed at the Pain Therapy and Palliative Care Division of the National Cancer Institute of Milan to integrate pain intensity and duration in a single measure. These scales were administered before and after a definite therapy change. At the time of the second evaluation the patients were also administered a pain relief scale (IRS). A factor analysis of the scoring properties of these instruments revealed a high degree of association between the variables. A single factor clearly emerged explaining most of the different scales variability. A logistic regression analysis showed that VAS, NRS, VRS were more strongly associated with IRS than PRI and IPS.

55. Jensen MP. The validity and reliability of cancer pain measures. Journal of Pain. 2003;4(1):2-21 Abstract: To be most useful, clinical trials of cancer pain treatments should use pain measures that are both reliable and valid. A great variety of measures are now available that may be used to assess cancer pain. However, there are not yet any clear guidelines for selecting one or more measures over the others. The purpose of this article is to summarize the evidence concerning the validity and reliability of cancer pain measures. One hundred sixty-four articles were identified that provided psychometric data of pain measures among patients with cancer. The results indicate that commonly used single-item ratings of pain intensity are all valid and adequately reliable as measures of pain intensity, although some scales appear to be easier for patients with cancer to understand and to use than others. Multiple-item measures of pain intensity are reliable, but evidence concerning their validity is lacking. There is a paucity of research examining the psychometric properties of measures of cancer pain interference, pain relief, pain site, the temporal aspects of pain, and pain quality. This lack of evidence limits the conclusions that may be drawn concerning the reliability and validity of these other pain measures. Composite measures that combine ratings of pain intensity and pain interference into a single score appear to be both valid and reliable for describing patient populations, although their usefulness in clinical trials may be limited because they can obscure the contributions of intensity and interference to the total score. Proxy measures of cancer pain (pain ratings made by someone other than the patient) may be useful when patients are not able to provide pain ratings, but they should not be used as replacements for patient ratings when patient self-report measures are available. The discussion includes specific recommendations for selecting from among the available pain measures, as well as recommendations for future research into the assessment of cancer pain.

56. Jensen MP. Review of Measures of Neuropathic Pain. Current Pain and Headache Reports. 2006;10:159-166 Eight measures of neuropathic pain exist that have been designed to discriminate neuropathic from non-neuropathic pain and detect treatment effects. The current paper describes these measures and summarizes the evidence supporting their validity. Based on the available evidence, the Leeds Assessment of Neuropathic Signs and Symptoms appears to have the most empirical support as a measure that distinguishes patients with and without neuropathic pain in patient samples presenting with mixed chronic pain problems. However, given the lack of overlap in measures designed for this purpose, it is likely that the validity of any one measure could be improved by incorporating items from the others. The Neuropathic Pain Scale (NPS) has the most empirical support as a measure of treatment outcome, although a new measure that includes the NPS items (the Pain Quality Assessment Scale) will likely prove to be even more useful, because it includes pain descriptors common to people with neuropathic and other chronic pain conditions not included on the NPS.


OBJECTIVE: To compare the responsiveness of six questionnaires using three hypotheses of change: (i) change due to supportive-expressive group therapy (SEGT), (ii) improved mood defined as a small effect size (.2) on Profile of Mood States (POMS) Total Mood Disturbance score and (iii) progression of disease.

METHOD: Data from the "Breast Expressive-Supportive Therapy" study, a multicentre randomized controlled trial of change due to SEGT versus standard of care in women with metastatic breast cancer were used. Questionnaires studied were: POMS, Impact of Event Scale, Psychosocial Adjustment to Illness Scale (PAIS), EORTC QLQ-C30, Mental Adjustment to Cancer and a Pain visual analog scale (VAS). Responsiveness to change was evaluated using the standardized response mean. POMS was used as the standard.

RESULTS: POMS was the most responsive questionnaire to change due to SEGT. Questionnaires measuring psychosocial attributes were responsive to improvement in mood. EORTC QLQ-C30, PAIS, PAIN VAS and MAC were the most responsive to disease progression. More responsive questionnaires were associated with the smallest sample size required to detect an effect. CONCLUSIONS: Responsiveness to change is context specific. The POMS was the most responsive questionnaire to psychosocial therapy.

59. Wallenstein SL, Heidrich G, 3rd, Kaiko R, Houde RW. Clinical evaluation of mild analgesics: the measurement of clinical pain. British Journal of Clinical Pharmacology. Oct 1980;10 Suppl 2:319S-327S Two 10 cm visual analogue scales were compared with a 0–10 point numerical rating scale and a four-point verbal descriptive scale, in assessing pain severity in twelve patients with post-operative pain following removal of an impacted lower third molar. High correlations were shown between the pain scores from the two visual analogue scales and the numerical scale, but a lower correlation was obtained when the four-point scale was compared with the other scales. Analgesic efficacy was found to be dependent on the type of scale used. The 10 cm visual analogue scale was more sensitive than other pain scales and could discriminate between small changes in pain intensity.

60. Bostrom B, Sandh M, Lundberg D, Fridlund B. A comparison of pain and health-related quality of life between two groups of cancer patients with differing average levels of pain. Journal of Clinical Nursing. Sep 2003;12(5):726-735 A study was performed to describe and compare pain and Health-Related Quality of Life (HRQOL) in two groups of cancer patients in palliative care as well as to describe the correlation between pain and HRQOL. Forty-seven patients with mild average pain [Visual Analogue Scale (VAS) \( \leq 3 \)] and 28 patients with moderate to severe average pain (VAS > 3) were included. Medical Outcomes Study Short Form (SF-36) was used to evaluate HRQOL, pain intensity levels were measured with the VAS on Pain-O-Meter. Compared to patients with mild pain, patients with moderate to severe pain had statistically significant, higher pain intensity for the items 'pain at time of interview', 'worst pain in the past 24 hours' and 'pain interrupting sleep.' They also had the lowest scores of the SF-36 dimensions: physical functioning, role-physical, and bodily pain. Patients with moderate to severe pain had statistically significant, fewer months of survival. There were statistically significant positive correlations between pain items and negative correlation between pain and SF-36 dimensions. The conclusion is that pain has a negative impact on HRQOL, especially on physical health and that pain increases towards the final stages of life. Even if patients have to endure symptoms such as fatigue and anxiety during their short survival time, dealing with pain is an unnecessary burden, which can be prevented.

61. Wittekindt C, Liu W-C, Preuss SF, Guntinas-Lichius O. Botulinum toxin A for neuropathic pain after neck dissection: a dose-finding study. Laryngoscope. Jul 2006;116(7):1168-1171 OBJECTIVES: Botulinum toxin type A (BtxA) has been reported to be feasible in chronic neuropathic pain after neck dissection. The impact of the dose on the outcome has not been investigated yet. STUDY DESIGN: Twenty-three patients with neuropathic pain after neck dissection were selected for an open and prospective phase II trial. METHODS: In the low-dose group (n=13), a concentration of 10 mouse units (MU)/0.1 mL saline and in the high-dose-group (n=10), a concentration of 20 MU/0.1 mL saline were injected subcutaneously. Pain and quality of life were assessed at day 0 and day 28, respectively, by visual analog scales (VAS) and European Organization for Research and Treatment of Cancer (EORTC) quality-of-life core and EORTC quality-of-life head and neck module questionnaires. RESULTS: Patients in the low-dose group showed a significant pain reduction (VAS) from 4.3 at day 0 to 3.0 at day 28 (P<.05). The mean pain VAS values in the high-dose group did not improve significantly. No serious adverse events were observed. There were trends toward improvement in quality of life in the low-dose group. CONCLUSIONS: BtxA in a low concentration seems to be a useful therapeutic option in chronic neuropathic pain of the neck and shoulder after neck dissection.
62. Marinangeli F, Ciccozzi A, Aloisio L, et al. Improved cancer pain treatment using combined fentanyl-TTS and tramadol. *Pain Practice.* Dec 2007;7(4):307-312 The aim of the study was to facilitate dose escalation of strong opioids. In this randomized open-label study the influence of tramadol on dose adjustment of transdermal fentanyl in advanced cancer pain control was prospectively evaluated. Seventy patients affected by intractable cancer disease with visual analog scale (VAS) score >3 were enrolled. Thirty-five patients were treated conventionally with increasing transdermal fentanyl dosage as required (group F) and 35 patients received oral tramadol added to their transdermal fentanyl before each increment of the transdermal opioid dosage (group T). Pain control was equally satisfactory in the two groups. VAS scores at baseline (T: 4.36 +/- 1.53; F: 4.51 +/- 1.36; n.s.) and at the end of the study (T: 1.8 +/- 1.6; F: 1.6 +/- 1.5; n.s.) did not differ. However, in the tramadol group this level of pain control was achieved with much slower dose escalation of fentanyl. The mean application time of the fentanyl-Transdermal Therapeutic System patch for each dosage (25, 50, 75 microg/hour) was significantly greater in patients receiving tramadol. No patient in group T escalated to the 100 microg/hour patch, while in 12 patients of group F the 100 microg/hour patch was applied after a 75 microg/hour patch mean application period of 18.6 +/- 4.7 days. The number of fentanyl-TTS dosage changes was significantly lower in group T (1.2 +/- 0.4 vs. 2.3 +/- 0.5; P < 0.05). The mean total duration of treatment in group T, was 37.1 +/- 11.6 days. The amount of fentanyl used at study end was 56.6 +/- 11.2 microg/hour plus 141.1 +/- 151.9 mg tramadol per day (median: 200 mg/day) in group T patients compared with 84.1 +/- 12.2 microg/hour in group F patients (P < 0.05). The combination of a strong opioid with a weak opioid to treat severe cancer pain allowed a more gradual increase of analgesic delivery than was possible using fentanyl-TTS alone, minimizing periods of under- and overdosing. In addition, it considerably slowed the pace of fentanyl dose escalation. In conclusion, this TTS fentanyl-tramadol analgesic protocol provides a useful alternative to the usual treatment of cancer pain with fentanyl-TTS alone, especially in case of quick progression of disease and pain.

63. Alimi D, Rubino C, Pichard-Leandri E, Fermand-Brule S, Dubreuil-Lemaire M-L, Hill C. Analgesic effect of auricular acupuncture for cancer pain: a randomized, blinded, controlled trial. *Journal of Clinical Oncology.* Nov 15 2003;21(22):4120-4126 PURPOSE: During the last 30 years, auricular acupuncture has been used as complementary treatment of cancer pain when analgesic drugs do not suffice. The purpose of this study is to examine the efficacy of auricular acupuncture in decreasing pain intensity in cancer patients. PATIENTS AND METHODS: Ninety patients were randomly divided in three groups; one group received two courses of auricular acupuncture at points where an electrodermal signal had been detected, and two placebo groups received auricular acupuncture at points with no electrodermal signal (placebo points) and one with auricular seeds fixed at placebo points. Patients had to be in pain, attaining a visual analog score (VAS) of 30 mm or more after having received analgesic treatment adapted to both intensity and type of pain, for at least 1 month of therapy. Treatment efficacy was based on the absolute decrease in pain intensity measured 2 months after randomization using the VAS. RESULTS: The main outcome was pain assessed at 2 months, with the assessment at 1 month carried over to 2 months for the eight patients who interrupted treatment after 1 month. For three patients, no data were available because they withdrew from the study during the first month. Pain intensity decreased by 36% at 2 months from baseline in the group receiving acupuncture; there was little change for patients receiving placebo (2%). The difference between groups was statistically significant (P <.0001). CONCLUSION: The observed reduction in pain intensity measured on the VAS represents a clear benefit from auricular acupuncture for these cancer patients who are in pain, despite stable analgesic treatment.

64. Gracely RH, McGrath P, Dubner R. Validity and sensitivity of ratio scales of sensory and affective verbal pain descriptors: manipulation of affect by diazepam. *Pain.* Jun 1978;5(1):19-29 The results of two experiments suggest that sensory and affective verbal descriptors provide a valid scaling method which discriminates between the sensory intensity and the affect, or unpleasantness, of electrocutaneous stimuli. Twenty-four subjects judged the sensory intensity and affect of noxious electrocutaneous stimuli by choosing verbal descriptors from randomized lists and by cross-modality matching to time duration and to handgrip force. The psychophysical functions for sensory intensity generated by the descriptor and the cross-modality functions for sensory intensity generated by the descriptor and the cross-modality methods are the same. Psychophysical functions for affect generated by the descriptor and the cross-modality methods are different. However, only the descriptor method produces psychophysical functions for affect that are significantly different from all the sensory functions. This result suggests that


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only the descriptor method distinguishes between sensory intensity and affect. The discriminative power of the descriptor method is demonstrated further in an experiment in which 32 subjects rated either the sensory intensity or the affect of the electrocutaneous stimuli immediately before and after an i.v. administration of 5 mg diazepam. This common minor tranquilizer significantly lowered affective descriptor responses (P less than 0.005) without altering sensory descriptor and sensory and affective handgrip responses. These experiments indicate that sensory and affective verbal pain descriptors may be used as a valid and sensitive tool for the evaluation of pain and pain control methods.
patients who participated, 59 received C/A and 62 received H/A. Of the total number of cases, 59% were aged 60 to 89 years, and 55% were men. At baseline, 88% of the patients described their pain intensity as moderate; 12%, severe. Of the patients who received C/A, 58% responded to the initial dosage of 150/2500 mg/d, and 8% of the patients responded to the double dosage; 34% did not experience any pain relief. In patients with H/A, pain was reported as absent or mild in 56% of patients at the starting dosage of 25/2500 mg/d; an additional 15% of the patients responded to the double dosage; the remaining 29% of patients did not experience any pain relief. None of the between-group differences in response rates were significant. The most common AEs in the C/A and H/A groups were constipation (36% and 29%, respectively), dizziness (24% and 19%), vomiting (24% and 16%), and dry mouth (15% and 18%), with no significant differences between groups. CONCLUSION: In this study, efficacy and tolerability were comparable between C/A and H/A over 23 days of treatment in these patients with moderate or severe, chronic, cancer-related pain.

67. Schoeneich G, Palmedo H, Dierke-Dzierzon C, Muller SC, Biersack HJ. Rhenium-186 HEDP: palliative radionuclide therapy of painful bone metastases. Preliminary results. Scandinavian Journal of Urology & Nephrology. Oct 1997;31(5):445-448 The aim of this study was to evaluate the efficacy of rhenium-186 hydroxyethyledine diphosphonate (Re-186 HEDP) for pain relief in patients with disseminated bone metastases primarily from prostate or breast cancer. Up to now, 44 patients taking analgesics were entered in this study and received one or more injections of 1295 MBq of Re-186 HEDP. An analgesic effect of more than 20%, evaluated by using a verbal rating scale (VRS) and a visual analoguous scale (VAS), was defined as significant and could be achieved in 60% of these patients. Duration of clinical response averaged 1-4 months (median 5.5 weeks). Side effects such as a moderate decrease of platelets or an increase of pain for 1-2 days (flare-up effect) were observed. Radioactive treatment with Re-186 HEDP appears to be a useful compound for the palliation of painful skeletal metastases and improvement of the remaining quality of life.

68. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain. Oct 1986;27(1):117-126 The measurement of subjective pain intensity continues to be important to both researchers and clinicians. Although several scales are currently used to assess the intensity construct, it remains unclear which of these provides the most precise, replicable, and predictively valid measure. Five criteria for judging intensity scales have been considered in previous research: ease of administration of scoring; relative rates of incorrect responding; sensitivity as defined by the number of available response categories; sensitivity as defined by statistical power; and the magnitude of the relationship between each scale and a linear combination of pain intensity indices. In order to judge commonly used pain intensity measures, 75 chronic pain patients were asked to rate 4 kinds of pain (present, least, most, and average) using 6 scales. The utility and validity of the scales was judged using the criteria listed above. The results indicate that, for the present sample, the scales yield similar results in terms of the number of subjects who respond correctly to them and their predictive validity. However, when considering the remaining 3 criteria, the 101-point numerical rating scale appears to be the most practical index.

69. Jensen MP, Turner JA, Romano JM. What is the maximum number of levels needed in pain intensity measurement? Pain. Sep 1994;58(3):387-392 An important issue that has yet to be resolved in pain measurement literature concerns the number of levels needed to assess self-reported pain intensity. An examination of treatment outcome literature shows a large variation in the number of levels used, from as few as 4 (e.g., 4-point Verbal Rating scales (VRS)) to as many as 101 (e.g., 101-point Numerical Rating scales (NRS)). The purpose of this study was to provide an empirically derived guideline for determining the number of levels needed. Chronic pain patients (n = 124) provided pre- and post-treatment measures of pain intensity using 101-point NRS for least, most, current, and average pain. The patients’ responses to the measures were examined closely to determine the actual number of levels used. In addition, their responses to the 101-point scales were recorded to form 7 scales of varying levels (2- to 101-point scales). The sensitivity of the 7 recorded scales was examined. The results indicated that little information is lost if 101-point scales are coded as 11- or 21-point scales. Moreover, examination of the actual responses to the 101-point measure showed that almost all patients treated it as a 21-point scale by providing responses in multiples of 5 or 10, while a substantial number of patients treated it as an 11-point scale, providing responses in multiples of 10 only. The results suggest that 10- and 21-point scales provide sufficient levels of discrimination, in general, for chronic pain patients to describe pain intensity.
70. Paice JA, Cohen FL. Validity of a verbally administered numeric rating scale to measure cancer pain intensity. *Cancer Nursing*. Apr 1997;20(2):88-93 The ability to quantify pain intensity is essential when caring for individuals in pain in order to monitor patient progress and analgesic effectiveness. Three scales are commonly employed: the simple descriptor scale (SDS), the visual analog scale (VAS), and the numeric (pain intensity) rating scale (NRS). Patients with English as a second language may not be able to complete the SDS without translation, and visually, cognitively, or physically impaired patients may have difficulty using the VAS. The NRS has been found to be a simple and valid alternative in some disease states; however, the validity of this scale administered verbally, without visual cues, to oncology patients has not yet been established. The present study examined validity of a verbally administered 0-10 NRS using convergence methods. The correlation between the VAS and the NRS was strong and statistically significant (r = 0.847, p < 0.001), supporting the validity of the verbally administered NRS. Although all subjects were able to complete the NRS and SDS without apparent difficulty, 11 subjects (20%) were unable to complete the VAS. The mean opioid intake was significantly higher for the group that was unable to complete the VAS (mean 170.8 mg, median 120.0 mg, SD = 135.8) compared to the group that had no difficulty with the scale (mean 65.6 mg, 33.0 mg, SD = 99.7) (Mann-Whitney test, p = 0.0065). The verbally administered 0-10 NRS provides a useful alternative to the VAS, particularly as more contact with patients is established via telephone and patients within the hospital are more acutely ill.

71. Crul BJP, Blok LM, van Egmond J, van Dongen RTM. The present role of percutaneous cervical cordotomy for the treatment of cancer pain. *Journal of Headache & Pain*. Feb 2005;6(1):24-29 The results obtained by percutaneous cervical cordotomy (PCC) were analysed in 43 terminally ill cancer patients treated in our institution from 1998 to 2001. We wished to determine whether there is still a place for PCC in the actual clinical situation with its wide choice of pain therapies. All patients had severe unilateral pain due to cancer, resistant to opioids and co-analgesics. Following PCC, mean pain intensity was reduced from Numeric Rating Scale (NRS) 7.2 to 1.1. At the end of life, pain had increased to NRS 2.9. Initially following PCC a good result (NRS<3) was obtained in 95% of patients. At the end of life, a good result was still present in 69% of patients. Mean duration of survival after the intervention was 118 days (2-1460). In general, complications were mild and mostly subsided within 3-4 days. There was one case of partial paresis of the ipsilateral leg. PCC remains a valuable treatment in patients with treatment-resistant cancer pain and still deserves a place in the treatment of terminal cancer patients with severe unilateral neuropathic or incidence pain.

72. Wirz S, Wartenberg HC, Elsen C, Wittmann M, Diederichs M, Nadstawek J. Managing cancer pain and symptoms of outpatients by rotation to sustained-release hydromorphone: a prospective clinical trial. *Clinical Journal of Pain*. Nov-Dec 2006;22(9):770-775 PURPOSE: In this prospective clinical trial we examined the technique of opioid rotation to oral sustained-release hydromorphone for controlling pain and symptoms in outpatients with cancer pain. METHODS: Before and after rotation, 50 patients were assessed by Numerical Analog Scales [Numerical Rating Scales (NRS)], or as categorical parameters, and analyzed by descriptive and confirmatory statistics (ANOVA, Wilcoxon, chi). RESULTS: Rotation was successful in 64% of patients experiencing pain (60%), and gastrointestinal (32%) and central (26%) symptoms under oral morphine (38%), transdermal fentanyl (22%), tramadol (20%), oxycodone (12%), or sublingual buprenorphine (8%). NRS of pain (4.1 to 3.2; P=0.015), gastrointestinal symptoms, especially defecation rates (P=0.04), and incidence of insomnia improved after an increase in morphine-equivalent doses from 108.9 to 137.6 mg/d without modifying concomitant analgesics or coanalgesics. CONCLUSIONS: Switching the opioid to oral hydromorphone may be a helpful technique to alleviate pain and several symptoms, but it is still not clear to what extent the underlying mechanisms, such as the technique of rotation itself, better dose adjustment, or using a different opioid have an impact.

73. Yu S-y, Qiu H, Ma Z-s, et al. [Effects of sustained release morphine hydrochloride tablets in management of cancer pain: a survey of 567 patients]. *Chung-Hua i Hsueh Tsa Chih [Chinese Medical Journal]*. Mar 17 2004;84(6):450-455 OBJECTIVE: To evaluate the effect and adverse effects of morphine hydrochloric sustained release for patients with cancer pain. METHODS: A total of 567 patients, 369 males (65.1%) and 198 females (34.9%), aged 65 - 90 with a mean age of 72.6, with cancer pain, 67.4% with severe pain, 28.2% with moderate pain, a and 4.4% with mild pain, that were treated in 25 hospitals from 13 provinces received oral morphine hydrochloric sustained release. The recommended initial dosage was 30 mg every 12 hours, and then the dosage was regulated according to the
effects until the ideal anesthesia was achieved. All patients were asked to record the attacks of pain, quality of life, and any side effect of the treatment. 

RESULTS: The baseline mean pain intensity (NRS) was 7.0 +/- 1.8. On the day 1, 5, 10, 15, 20, 25 and 30, the mean pain scores were decreased to 4.6 +/- 2.6, 2.8 +/- 1.8, 2.7 +/- 1.8, 2.6 +/- 1.7, 2.5 +/- 1.6, 2.3 +/- 1.4, and 2.2 +/- 1.4 respectively (all P = 0.000). The general effective rate on day 30 was 89.8%. The mean dosages were 66 +/- 56 mg/d initially, 84 +/- 64 mg/d (10 - 800 mg/d) on day 15, and 92 +/- 67 mg/d (10 - 800 mg/d) on day 30. On the day 30, 55.1% of the patients received a dosage <or= 60 mg/d, 35.1% of them received a dosage of 61 - 120 mg/day, 7.6% of them received a dosage of 121 - 240 mg/day, and 2.2% of them received a dosage >or= 241 mg/d. Ninety-one point six percent (89.4% - 95.8%) of the patients took morphine orally twice daily. The poor quality of life rate in the patients was 90.5% before treatment, and were 56.8% and 49.6% respectively on the day 15 and day 30 (P = 0.0000 and P = 0.0009). The incidence of side effects was 35.6% on day 1, and 15.1% on day 30. The common side effects were constipation (14.3%), nausea (13.4%), dizziness (3.4%), vomiting (2.8%), drowsiness (0.7%), dysuria (0.4%), mental symptoms (0.2%), and respiratory depression (0.2%). Sixty-eight point four percent of the patients preferred continuation of sustained release morphine hydrochloride treatment.

CONCLUSION: Oral treatment with sustained release morphine hydrochloride for patients with cancer pain is effective, safe, and convenient, and can improve the quality of life.

Sustained release morphine hydrochloride is worth recommending as a first-line drug for the treatment of patients with moderate to severe cancer pain, and the usually dosage is 120 mg or less per day.


75. Daut RL, Cleeland CS, Flanery RC. Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases. Pain. Oct 1983;17(2):197-210 This paper reports the development of a self-report instrument designed to assess pain in cancer and other diseases. It is argued that issues of reliability and validity should be considered for every pain questionnaire. Most research on measures of pain examine reliability to the relative neglect of validity concerns. The Wisconsin Brief Pain Questionnaire (BPQ) is evaluated with regard to both reliability and validity. Data from patients with cancer at 4 primary sites and from patients with rheumatoid arthritis suggest that the BPQ is sufficiently reliable and valid for research purposes. Additional methodological and theoretical issues related to validity are discussed, and the need for continuing evaluation of the BPQ and other measures of clinical pain is stressed.

76. Serlin RC, Mendoza TR, Nakamura Y, Edwards KR, Cleeland CS. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. Pain. May 1995;61(2):277-284 As a way of delineating different levels of cancer pain severity, we explored the relationship between numerical ratings of pain severity and ratings of pain's interference with such functions as activity, mood, and sleep. Interference measures were used as critical variable to grade pain severity. We explored the possibility that pain severity could be classified into groupings roughly comparable to mild, moderate, and severe. Our hypothesis was that mild, moderate, and severe pain would differentially impair cancer patients' function. We were able to identify boundaries among these categories of pain severity in terms of their interference with function. We also examined the extent to which cancer patients from different language and cultural groups differ in their self-reported interference as a function of pain severity level. We found optimal cutpoints that form 3 distinct levels of pain severity that can be defined on a 0-10-point numerical scale. We determined that, based on the degree of interference with cancer patients' function, ratings of 1-4 correspond to mild pain, 5-6 to moderate pain, and 7-10 to severe pain. Our analysis illustrates that the pain severity-interference relationship is non-linear. These cutpoints were the same for each of the national samples in our analysis, although there were slight differences in the specific interference items affected by pain. These cutpoints might be useful in clinical evaluation, epidemiology, and clinical trials.

77. Twycross R, Harcourt J, Bergl S. A survey of pain in patients with advanced cancer. Journal of Pain & Symptom Management. Nov 1996;12(5):273-282 One hundred eleven patients with advanced cancer and pain newly referred to a palliative care center completed the Brief Pain Inventory (BPI) weekly for up to 4 weeks. The aims were (a) to review the numbers and causes of pain, (b) to consider the usefulness of the BPI in the evaluation of pain in cancer patients, and (c) to determine the impact of treatment. A total of 370 pains were recorded initially, a median of 3 per patient; 85% had more than 1 pain and more than 40% had 4 or more pains. Causes of pain were cancer (46%), debility (29%), treatment (5%), concurrent disorder (8%), and no stated cause (12%). The top 10
individual causes accounted for 73% of the pains. Seventy-six (68%) of the patients completed two BRIs, but only 46 (41%) completed 5. After 4 weeks, the median number of pains had fallen to 1.5; 78% still had more than 1 pain, but only 20% had 4 or more pains. Intensity of pain also declined, particularly in the first 2 weeks. With their last BPI, 23% had become completely pain free and a further 27% achieved acceptable relief (worst pain scores 1-4), compared with none and 24% initially. Of those who completed all five BPIs, the final respective figures were 22% and 29%. In contrast, 23% of patients still had unacceptable severe pain noted on their last BPI (worst pain scores 8-10), compared with none and 24% initially. Of those who completed five BPIs, the final figure was 20%. Highly significant correlations were observed between all seven interference factors and present, worst, and average pain intensities. After 4 weeks, the pattern was more variable, particularly in relation to present pain, suggesting that interference factors may have a limited utility as a measure of satisfactory pain management. Many patients did not answer all the questions in the BPI. It was concluded that the BPI is not brief enough for routine clinical use, and that the short form of the BPI (BPI-SF) is too short. A pain diary card will be developed comprising mainly pain scores, a pain relief score and a satisfaction with pain management score.

78. Callstrom MR, Atwell TD, Charboneau JW, et al. Painful metastases involving bone: percutaneous image-guided cryoablation--prospective trial interim analysis. Radiology. Nov 2006;241(2):572-580 PURPOSE: To prospectively determine the safety and effectiveness of percutaneous cryoablation for the reduction of pain, improvement in the activities of daily life, and reduction in the use of analgesic medications for patients with painful metastatic lesions involving bone. MATERIALS AND METHODS: This study was compliant with HIPAA and was approved by the institutional review board. Written informed consent was obtained. During 18 months, 14 patients (eight men, six women; age range, 21-72 years; mean age, 54 years) with one or two painful metastatic lesions involving bone, with a score of 4 or greater out of 10 for worst pain in a 24-hour period, and who did not respond to or refused conventional radiation treatment or chemotherapy were treated with percutaneous cryoablation. Patient response was measured with the Brief Pain Inventory, and analgesic use was recorded before and after the procedure at days 1 and 4, weekly for 4 weeks, and then every other week for a total of 6 months. Complications were monitored. Analysis of the primary end points was undertaken with paired comparison procedures by using paired t tests across individual time points supplemented with repeated measures analysis of variance. RESULTS: Treated lesions were 1-11 cm in diameter. Before cryoablation, the mean score for worst pain in a 24-hour period was 6.7 of 10; the score decreased to 3.8 (P = .003) 4 weeks after treatment. Mean pain interference with activities of daily living was 5.5 of 10 before treatment and decreased to 3.2 (P = .004) 4 weeks after treatment. All eight (100%) patients (exact 95% binomial confidence interval: 63%, 100%) for whom narcotics were prescribed prior to the procedure reported a reduction in these medications after cryoablation. No serious complications were observed. CONCLUSION: Percutaneous cryoablation is a safe and effective method for palliation of pain due to metastatic disease involving bone.

79. Nishio M, Sano M, Tamaki Y, et al. [A multicenter study to determine the efficacy and safety of strontium (89Sr) chloride for palliation of painful bony metastases in cancer patients]. Nippon Igaku Hoshasen Gakkai Zasshi - Nippon Acta Radiologica. Oct 2005;65(4):399-410 PURPOSE: A multicenter study was conducted to evaluate the efficacy of strontium chloride (89SrCl2) for palliation of painful bony metastases using the Visual Analogue Scale (VAS), Brief Pain Inventory (BPI) and Functional Assessment for Cancer Therapy-General (FACT-G). METHODS: Ninety patients received a single injection of 2.0 MBq/kg and were classified as responders if VAS scores decreased without increased use of analgesics or if analgesic consumption decreased without an increase in the VAS. RESULTS: In the 69 subjects that could be evaluated, mean VAS values decreased significantly from 48.0 +/- 20.8 mm at baseline to 24.1 +/- 22.3 mm at last visit(Week 12) (p < 0.0001). VAS decreased more than 10 mm in 58.0% of these subjects, and analgesic consumption was reduced more than 10% in 39.1% of subjects. The response rates were 46.4% (95% confidence interval (CI) 34.3-58.8%) in the 69 subjects that could be evaluated and 43.3% (95% CI 32.9-54.2%) in all subjects. The scoring in BPI for interference in daily life improved together with improvement in its pain scores. Total FACT-G score showed significant improvement, as did its score in the subsection of physical well-being. Both platelets and leucocytes decreased by 22% at nadir (week 8), and such profiles of myelosuppression by 89SrCl2 were similar to those in the previous clinical studies. CONCLUSION: These results suggest the clinical utility of 89SrCl2 for pain
palliation, which leads to QOL improvement in patients with painful generalized bone metastases.

80. Wardley A, Davidson N, Barrett-Lee P, et al. Zoledronic acid significantly improves pain scores and quality of life in breast cancer patients with bone metastases: a randomised, crossover study of community vs hospital bisphosphonate administration. British Journal of Cancer. May 23 2005;92(10):1869-1876 Patients with bone metastases from breast cancer often experience substantial skeletal complications -- including debilitating bone pain -- which negatively affect quality of life. Zoledronic acid (4 mg) has been demonstrated to reduce significantly the risk of skeletal complications in these patients and is administered via a short, 15-min infusion every 3 weeks, allowing the possibility for home administration. This study compared the efficacy and safety of zoledronic acid administered in the community setting vs the hospital setting in breast cancer patients with > or =1 bone metastasis receiving hormonal therapy. After a lead-in phase of three infusions of 4 mg zoledronic acid in the hospital setting, 101 patients were randomized to receive three open-label infusions in the community or hospital setting, followed by three infusions in the opposite venue (a total of nine infusions). The Brief Pain Inventory (BPI) and the European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire 30 (EORTC QLQ-C30) were used to assess potential benefits of zoledronic acid therapy. At study end, analysis of the BPI showed significant reductions in worst pain (P=0.008) and average pain in the last 7 days (P=0.039), and interference with general activity (P=0.012). In each case, there were significantly greater improvements in pain scores after treatment in the community setting compared with the hospital crossover setting for worst pain (P=0.021), average pain (P=0.003), and interference with general activity (P=0.001). Overall global health status showed a significant median improvement of 8.3% (P=0.013) at study end. Physical, emotional, and social functioning also showed significant overall improvement (P=0.013, 0.005, and 0.043, respectively). Furthermore, physical, role, and social functioning showed significantly greater improvements after treatment in the community setting compared with the hospital crossover setting (P=0.018, 0.001, and 0.026, respectively). There was no difference between hospital and community administration in renal or other toxicity, with zoledronic acid being well tolerated in both treatment settings. These data confirm the safety and quality-of-life benefits of zoledronic acid in breast cancer patients with bone metastases, particularly when administered in the community setting.

81. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. Pain. Sep 1975;1(3):277-299 The McGill Pain Questionnaire consists primarily of 3 major classes of word descriptors--sensory, affective and evaluative--that are used by patients to specify subjective pain experience. It also contains an intensity scale and other items to determine the properties of pain experience. The questionnaire was designed to provide quantitative measures of clinical pain that can be treated statistically. This paper describes the procedures for administration of the questionnaire and the various measures that can be derived from it. The 3 major measures are: (1) the pain rating index, based on two types of numerical values that can be assigned to each word descriptor, (2) the number of words chosen; and (3) the present pain intensity based on a 1-5 intensity scale. Correlation coefficients among these measures, based on data obtained with 297 patients suffering several kinds of pain, are presented. In addition, an experimental study which utilized the questionnaire is analyzed in order to describe the nature of the information that is obtained. The data, taken together, indicate that the McGill Pain Questionnaire provides quantitative information that can be treated statistically, and is sufficiently sensitive to detect differences among different methods to relieve pain.

82. Graham C, Bond SS, Gerkovich MM, Cook MR. Use of the McGill pain questionnaire in the assessment of cancer pain: replicability and consistency. Pain. Jun 1980;8(3):377-387 The McGill Pain Questionnaire (MPQ) is a recent empirically derived instrument designed to provide quantitative information on major dimensions of pain. Although widely used as an outcome measure in clinical research, little attention has been directed specifically at the instrument itself. The present study addressed this need. Detailed findings were obtained for both single and multiple administrations of the MPQ in two subject samples, each composed of 18 cancer outpatients in pain. These data were compared to similar, but less extensive, data reported by Melzack [6]. MPQ indices proved highly replicable over the two subject samples tested and were remarkably similar to the findings reported by Melzack for a different cancer pain patient sample. No differences were found between the written form of MPQ administration used in the present study and the oral procedure followed by Melzack. The consistency of pain descriptor subclass choice in the present samples was high, ranging from 66% to 80.4% over 4 administrations, and these values compare well
with the value of 70.3% reported earlier by Melzack. However, the present subjects selected a larger set of pain descriptor words compared to the word set reported to be characteristic of cancer pain by Dubuisson and Melzack [2]. Both individual and group analyses indicated the MPQ is best used as a measure of immediate pain, and not as a summary measure of past pain over a defined period of time. These findings support the use of the MPQ as a reliable, multi-dimensional measure of immediate pain, and suggest the potential value of future research aimed at refining the psychometric properties of the instrument.

83. Majani G, Tiengo M, Giardini A, Calori G, De Micheli P, Battaglia A. Relationship between MPQ and VAS in 962 patients. A rationale for their use. Minerva Anestesiologica. Jan-Feb 2003;69(1-2):67-73 BACKGROUND: 1) To analyse the information provided both by the Visual Analogue Scale (VAS) and by the McGill Pain Questionnaire (MPQ) in a cross-sectional study with patients affected by different kinds of pain and to study the relationship between VAS and MPQ scores in the same patient sample. METHODS: 962 patients affected by different kinds of pain (i.e. neuropathic pain, acute post-traumatic pain, chronic musculo-skeletal pain, headache, and cancer pain) were enrolled into the study during the first visit for pain management. The horizontal 10cm VAS and the Italian version of the MPQ were administered. RESULTS: VAS scores proved to be significantly lower in acute post traumatic and in chronic musculo-skeletal pain compared to headache and neuropathic pain. VAS scores were significantly higher in neuropathic pain compared to cancer pain. MPQ total score (Pain Rating Index, PRI) related to neuropathic pain was significantly higher than scores reported in the other pain groups, with the exception of cancer pain. Cancer pain MPQ total score was higher than acute post-traumatic and chronic musculo-skeletal PRI pain scores. Different patterns of MPQ dimensions emerged within each pain group. The association between VAS and PRI, analysed by means of stepwise multiple regression analyses was significantly different among the groups (p<0.0001). The percentage of VAS variance explained by MPQ PRI score ranged from 6% (headache) to 32% (neuropathic pain). CONCLUSIONS: Several differences emerged among the pain groups. VAS and MPQ resulted to address pain aspects only partially overlapping. In some clinical conditions (headache and cancer) the MPQ can provide more detailed and clinically useful information about patients' pain experience.

84. Wilkie DJ, Huang HY, Reilly N, Cain KC. Nociceptive and neuropathic pain in patients with lung cancer: a comparison of pain quality descriptors. Journal of Pain & Symptom Management. Nov 2001;22(5):899-910 Predictive validity of each word from the McGill Pain Questionnaire (MPQ) has not been investigated in relation to pain etiology. The purpose of this study was to explore differences in the words used to describe nociceptive and neuropathic pain. Patients with lung cancer (N = 123) selected words from the 78 MPQ pain quality descriptors and indicated the corresponding pain site for each word. Using only the MPQ pain location, and the cancer and treatment data abstracted from medical records, each pain site was classified as nociceptive or neuropathic (etiology). Pain etiology and quality descriptors were tested for proportional differences with sensitivity, specificity, and predictive value calculated for statistically significant descriptors. Of the 457 pain sites, 343 were classified as nociceptive (75%), 114 as neuropathic (25%). Lacerating, stinging, heavy, and suffocating were selected for a significantly larger proportion of nociceptive sites whereas throbbing, aching, numb, tender, punishing, pulling, tugging, pricking, penetrating, punishing, miserable, and nagging were selected for a larger proportion of neuropathic sites. Ten words correctly predicted 78% of the sites with 81% sensitivity to nociceptive pain and 59% sensitivity to neuropathic pain. Interestingly, several pain quality descriptors (burning, shooting, flashing, tingling, itching, and cold) previously associated with neuropathic pain did not distinguish between neuropathic and nociceptive pain. Infrequent selection of many MPQ words and lack of neurological exam data in the medical records are possible explanations for inconsistency with previous literature. Prospective studies are needed to validate pain quality descriptors for nociceptive and neuropathic types of lung cancer pain.

85. Dudgeon D, Raubertas RF, Rosenthal SN. The short-form McGill Pain Questionnaire in chronic cancer pain. Journal of Pain & Symptom Management. May 1993;8(4):191-195 A short form of the McGill Pain Questionnaire (SF-MPQ) was previously developed. It was found to correlate highly with and demonstrate differences due to treatment in a manner similar to the long form of the McGill Pain Questionnaire (LF-MPQ). The LF-MPQ was previously found to be a valid measurement of pain in the cancer population. The present study demonstrated that the sensory, affective, and total scores of the SF-MPQ correlated highly with the LF-MPQ on three administrations, each 3-4 wk apart in 24 patients with chronic pain due to cancer. Both the long and short total scores correlated highly with the
visual analogue scale (VAS) and present pain intensity (PPI) scale. The SF-MPQ demonstrated changes over time in a manner similar to the LF-MPQ in this patient group. These observations support the value of the SF-MPQ as a tool for studying interventions in patients with chronic pain due to cancer.

86. Beck SL. The therapeutic use of music for cancer-related pain. *Oncology Nursing Forum.* Nov-Dec 1991;18(8):1327-1337 The purpose of this experimental crossover study was to evaluate to what extent the therapeutic use of music would decrease pain in patients with cancer who were receiving scheduled analgesics. Baseline data were collected for three days. Subjects then were assigned randomly to listen to their preference of seven types of relaxing music or a control (a 60-cycle hum) twice daily for three days. Then they crossed over into the alternate group for the next three days. Finally, each subject returned to a follow-up baseline period. Pain, the dependent variable, and mood, which was proposed as an intervening variable, were measured by visual analogue scales. The convenience sample included 15 outpatients with cancer, 12 female and 3 male, ages 20 through 87. Results of the McGill Pain Questionnaire (MPQ), a reliable and valid multidimensional instrument administered upon entry into the study, indicated that the study sample was comparable to other samples of patients with cancer who were in pain. There was an inconsistent relation between pain and mood. The effect of the music on pain varied by individual; 75% had at least some response and 47% had a moderate or great response. Multivariate Analysis of Variance (MANOVA) indicated a statistically significant decrease in pain from using either the music or sound, but there was no effect on mood. Although the mean percentage of change in pain for music was twice that for sound, the results did not differ statistically. The findings support the use of music as an independent nursing intervention to relieve pain.

87. Melzack R. The short-form McGill Pain Questionnaire. *Pain.* Aug 1987;30(2):191-197 A short form of the McGill Pain Questionnaire (SF-MPQ) has been developed. The main component of the SF-MPQ consists of 15 descriptors (11 sensory; 4 affective) which are rated on an intensity scale as 0 = none, 1 = mild, 2 = moderate or 3 = severe. Three pain scores are derived from the sum of the intensity rank values of the words chosen for sensory, affective and total descriptors. The SF-MPQ also includes the Present Pain Intensity (PPI) index of the standard MPQ and a visual analogue scale (VAS). The SF-MPQ scores obtained from patients in post-surgical and obstetrical wards and physiotherapy and dental departments were compared to the scores obtained with the standard MPQ. The correlations were consistently high and significant. The SF-MPQ was also shown to be sufficiently sensitive to demonstrate differences due to treatment at statistical levels comparable to those obtained with the standard form. The SF-MPQ shows promise as a useful tool in situations in which the standard MPQ takes too long to administer, yet qualitative information is desired and the PPI and VAS are inadequate.

88. Eisbruch A, Rhodus N, Rosenthal D, et al. How should we measure and report radiotherapy-induced xerostomia? *Seminars in Radiation Oncology.* Jul 2003;13(3):226-234 Xerostomia is commonly measured and graded using objective measures of major salivary gland output and observer-rated toxicity grading. The separation between the different grades is somewhat ambiguous in the current toxicity grading systems. We propose a new grading system based primarily on the functional deficits associated with xerostomia. Salivary flow rates have been added as a criterion to the grading system, notwithstanding the weak correlation reported in most studies between the symptoms and objective functional measures. In addition to the observer-rated toxicity grading, recording of patient-reported quality of life, using validated instruments, is encouraged. [References: 66].

89. Eisbruch A, Kim HM, Terrell JE, Marsh LH, Dawson LA, Ship JA. Xerostomia and its predictors following parotid-sparing irradiation of head-and-neck cancer. *International Journal of Radiation Oncology, Biology, Physics.* Jul 1 2001;50(3):695-704 PURPOSE: To assess long-term xerostomia in patients receiving parotid-sparing radiation therapy (RT) for head-and-neck cancer, and to find the patient and therapy-related factors that affect its severity. PATIENTS AND METHODS: From March 1994 through January 2000, 84 patients received comprehensive bilateral neck RT using conformal and multisegmental intensity-modulated RT (IMRT) aiming to spare the major salivary glands. Before RT and periodically through 2 years after the completion of RT, salivary flow rates from each of the major salivary glands were selectively measured. At the same time intervals, each patient completed an 8-item self-reported xerostomia-specific questionnaire (XQ). To gain a relative measure of the effect of RT on the minor salivary glands, whose output could not be measured, the surfaces of the oral cavity (extending to include the surface of the base of tongue) were outlined in the planning CT scans. The mean doses to the new organ
("oral cavity") were recorded. Forty-eight patients receiving unilateral neck RT were similarly studied and served as a benchmark for comparison. Factors predicting the XQ scores were analyzed using a random-effects model. RESULTS: The XQ was found to be reliable and valid in measuring patient-reported xerostomia. The spared salivary glands which had received moderate doses in the bilateral RT group recovered to their baseline salivary flow rates during the second year after RT, and the spared glands in the unilateral RT group, which had received very low doses, demonstrated increased salivary production beyond their pre-RT levels. The increase in the salivary flow rates during the second year after RT paralleled an improvement in xerostomia in both patient groups. The improvement in xerostomia was faster in the unilateral compared with the bilateral RT group, but the difference narrowed at 2 years. The major salivary gland flow rates had only a weak correlation with the xerostomia scores. Factors found to be independently associated with the xerostomia scores were the pre-RT baseline scores, the time since RT, and the mean doses to the major salivary glands (notably to the submandibular glands) and to the oral cavity. CONCLUSION: An improvement over time in xerostomia, occurring in tandem with rising salivary production from the spared major salivary glands, suggests a long-term clinical benefit from their sparing. The oral cavity mean dose, representing RT effect on the minor salivary glands, was found to be a significant, independent predictor of xerostomia. Thus, in addition to the major salivary glands, sparing the uninvolved oral cavity should be considered as a planning objective to further reduce xerostomia.


### Measurement of Oral Mucositis

<table>
<thead>
<tr>
<th>Scale title</th>
<th>Source</th>
<th>Elements measured</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple, validated/mutable mucositis scoring scales</td>
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<tr>
<td>NCI-CTC (clinical and research)</td>
<td>Trott et al., 2000[48]; see also <a href="http://cancer.gov/nci-ctc/">website 1</a></td>
<td>Combined elements symptom (pain, signs erythema, ulceration); function type of dys trophy/intake</td>
<td>Used widely in research and clinical care settings; specific scales for mucositis in patients undergoing head and neck radiation, chemotherapy, or HSCT</td>
<td>Research assessment potentially confounded by combination of symptoms, signs, and functional changes</td>
</tr>
<tr>
<td>WHO (clinical and research)</td>
<td><a href="http://www.who.int">WHO, 1979</a></td>
<td>Combined elements symptom (pain, signs erythema, ulceration); function type of dys trophy/intake</td>
<td>Used widely in research and clinical care settings; specific scales for mucositis in patients undergoing head and neck radiation, chemotherapy, or HSCT</td>
<td>Research assessment potentially confounded by combination of symptoms, signs, and functional changes</td>
</tr>
<tr>
<td>ITDG (clinical and research)</td>
<td><a href="http://www.itdg.org/members/vitalityonline.htm">ITDG free</a></td>
<td>Combined elements symptom (pain, signs unspecified); function unspecified</td>
<td>Used widely in research and clinical care settings; specific scales for mucositis in patients undergoing head and neck radiation, chemotherapy, or HSCT</td>
<td>Research assessment potentially confounded by combination of symptoms, signs, and functional changes</td>
</tr>
<tr>
<td>Detailed, objective mucositis scoring scales</td>
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<tr>
<td>OMS for HSCT (research)</td>
<td>Schubert et al., 1994[41]</td>
<td>Thirty-eight mucosal changes: signs (erythema, ulceration/pseudomembrane, edema, and selected sites); pain scores (range 0-10)</td>
<td>Specific to 15 oral anatomic sites; thereby permitting subanalysis of changes across the oral mucosa; eliminates confounders of symptoms and functional disturbances; scores consistent with NCI and WHO scores</td>
<td>Requires more examiner experience and time than NCI-CTC and WHO scales; only tested in patients undergoing HSCT</td>
</tr>
<tr>
<td>Twenty-item OMS for HSCT (research)</td>
<td>McGuire et al., 2002[45]</td>
<td>Twenty mucosal changes: signs (erythema, ulceration/pseudomembrane edema, and selected sites)</td>
<td>Specific to nine oral anatomic sites; clinical objective changes scored as in full OMS</td>
<td>Requires less expertise than OMS</td>
</tr>
<tr>
<td>OMIS for chemotherapy, radiation, and HSCT (research)</td>
<td>Sonis et al., 1994[46]</td>
<td>Signs (erythema, ulceration)</td>
<td>Same advantages as OMS with fewer oral anatomic sites scored</td>
<td>Requires more examiner experience and time than NCI-CTC and WHO scales; less than OMS</td>
</tr>
<tr>
<td>Spillman Radiation Mucositis Scale (research)</td>
<td>Spillman, 1989[47]</td>
<td>White discoloration, erythema, pseudomembrane ulceration</td>
<td>White objective measure of tissue injury of tissue injury</td>
<td>Requires further validation in multicenter setting</td>
</tr>
<tr>
<td>Combined objective-functional/ symptom scales</td>
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<tr>
<td>Oral Assessment Guide (clinical)</td>
<td>Ellis et al., 1988[47]</td>
<td>Signs (erythema, symptoms, pain, mucus changes); functional disturbances (swallowing voice)</td>
<td>Global scale that can reflect clinical status outcomes; suitable for randomization in clinical settings</td>
<td>Not all variables necessarily linked with clinical status; some variables not continuous</td>
</tr>
<tr>
<td>Western Consortium for Cancer Nursing Scale (clinical)</td>
<td>Western Consortium for Cancer Nursing Research, 1987[48]</td>
<td>Lesions, color, bleeding, subjective variables</td>
<td>Global scale that can reflect clinical status outcomes; refined in 1998, based on elimination of two measures other than lesions, color, or bleeding</td>
<td>Mixed objective, subjective, and functional variables; difficult to score precisely</td>
</tr>
<tr>
<td>Waldl Quantitative Scoring System for Oral Mucositis (clinical and research)</td>
<td>Waldl et al., 1996[46]</td>
<td>Mucosal changes, functional changes, sublingual, pain</td>
<td>Conceptual elements of NCI or WHO scale applied to specific anatomic sites; moderate training</td>
<td>Not validated; only tested in HSCT patients</td>
</tr>
<tr>
<td>Tandem Quantitative Scale of Oral Mucositis for HSCT (research)</td>
<td>Tandem et al., 1996[47]</td>
<td>Mucosal changes, functional changes, function (voice, swallow), pain</td>
<td>Includes four anatomic sites, range of severity</td>
<td>Not validated (pilot study only); only tested in HSCT patients; requires more significant training</td>
</tr>
<tr>
<td>Daily Mucositis Scale for HSCT (research and clinic)</td>
<td>Donnelly et al., 1992[47]</td>
<td>Erythema, oral edema, pain, dysphagia</td>
<td>Global scale that can reflect clinical status outcomes; less detailed than most</td>
<td>Validation in multicenter study needed</td>
</tr>
<tr>
<td>MacPherson Mouth Assessment (research and clinic)</td>
<td>Hambly et al., 1996[50]</td>
<td>Patient symptoms, ulceration, erythema/ulceration, pharyngeal/upper airway edema, swallowing difficulty</td>
<td>Ease of administration; generalizability (not site-specific)</td>
<td>Only reported for radiations mucositis; not validated (pilot study only)</td>
</tr>
<tr>
<td>In vivo measurement</td>
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<tr>
<td>Epithelial Viability Scale (research)</td>
<td>Wynnery et al., 1997[51]</td>
<td>Trypan blue-based exclusion, based on epithelial lesions</td>
<td>Early administered; in vitro objective measure, studied with both chemotherapy induced and radiation-induced mucositis</td>
<td>Early in development; requires additional validation</td>
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</tbody>
</table>