The purpose of this study was to investigate psychosocial stress in a large sample of cancer patients using an expert rating scale. Specific aims were to analyse the relevance of setting variables (type of clinic, contact initiative, therapy) and gender. A total of 6365 patients were assessed in 105 institutions. Univariate and multivariate statistical analysis of setting variables indicated that patients treated in palliative care settings showed highest distress scores compared to patients recruited from hospitals and outpatient clinics (P<0.001). Significant differences were also found for contact initiative (P<0.001); lowest distress was found in patients who were recruited by routine contact. Patients who asked for psychosocial support or who were recruited by the medical staff showed the highest distress scores. The analysis of therapy groups showed that patients receiving radiotherapy or surgery were not more distressed than patients without therapy. The most distressing treatment was chemotherapy. Gender had differential effects on clinic type (P<0.001) and contact initiative (P<0.001) but not on treatment and diagnosis. Expert rating scales are an important complement for self-assessment questionnaires to evaluate psychological distress of cancer patients in psychosocial studies as well as in routine medical care.