# Screening for mental disorders in cancer patients – discriminant validity of HADS and GHQ-12 assessed by standardized clinical interview

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ABSTRACT The detection and classification of comorbid mental disorders has major implications in cancer care. Valid screening instruments for different diagnostic specifications are therefore needed. This study investigated the discriminant validity of the German versions of the Hospital Anxiety and Depression Scale (HADS) and the General Health Questionnaire (GHQ-12). A total of 188 cancer patients participated in the examination, consisting first of the assessment of psychological distress and, second, of the diagnosis of mental disorders according to DSM-IV by clinical standardized interview (CIDI). Discriminant validity of the two instruments regarding the diagnosis of any mental disorder, anxiety, depression and multiple mental disorders was compared using ROC analysis.

Overall, the total HADS scale shows a better screening performance than the GHQ-12, especially for the detection of depressive and anxiety disorders. Best results are achieved for depressive disorders with an area under the curve (AUC) of 0.80, a sensitivity of 79% and a specificity of 76% (cut-off point = 17). For the ability of the instruments to detect patients with mental disorders in general, the GHQ-12 (AUC: 0.68) shows a similar overall accuracy to the HADS (AUC: 0.70). The screening performance of both scales for comorbid mental disorders is comparable.

The HADS is a valid screening instrument for depressive and anxiety disorders in cancer care. The GHQ-12 can be considered as an alternative to the HADS when diagnostic specifications are less detailed and the goal of screening procedures is to detect patients with single or multiple mental disorders in general. Limitations of conventional screening instruments are given through the differing methodological approaches of screening tests (dimensional approach) and diagnosis according to DSM-IV (categorical approach).

Key words: cancer, screening, mental disorder, comorbidity, anxiety, depression

#### Introduction

In the past numerous studies have drawn attention to psychiatric distress that patients who are suffering from a tumour disease have to deal with. The majority of these patients can cope with the diagnosis, the necessary treatment and the resulting change in their lives. A significant number, however, develop clinically relevant psychiatric syndromes that must be classified by the current classification systems (DSM-IV and ICD-10) at least as an adjustment disorder, frequently as a manifest psychiatric disorder (Massie and Holland, 1989; Strain, 1998). Additionally, psychiatric disorders may appear that existed premorbidly, the symptoms either reappearing or being intensified by the tumour disease (Breitbart, 1995). The prevalence rates of mental disorders in patients with cancer were set at up to 53% depending on tumour type, treatment setting and methods (study design, diagnostic instruments etc.) (Massie and Popkin, 1998; Noyes et al., 1998; Van't Spijker et al., 1997). Depressive syndromes are the most frequent (up to 50%) often fulfilling the criteria of major depression (McDaniel et al., 1995). Although clinically relevant, comorbid mental disorders (such as anxiety and affective disorders) have received only little scientific attention up to now.

For the affected patients as well as for the attending teams, it is of great importance to recognize psychological symptoms early and to introduce psychological or psychiatric intervention in time, thus preventing the chronification of disorders (Zabora, 1998). Besides the considerable influence of mental impairment regarding the course of tumour disease and the reduction of life quality, undetected psychological disorders can lead to an extended hospital stay and additional costs (Payne et al., 1999; Zabora, 1998). On account of the specific problems involved in diagnosing psychiatric disorders in cancer patients (such as overlap of depression criteria with symptoms of disease and treatment), efficient instruments are necessary to reliably identify patients in urgent need of psychological and psychiatric measures (Payne et al., 1999). Screening instruments can therefore contribute to the effective use of scarce resources in health care. However, the available instruments must be compared regarding their validity and accuracy of detection (Hall et al., 1999; Ibbotson et al., 1994; Chochinov et al., 1997; Hopwood et al., 1991).

Today the Hospital Anxiety and Depression Scale (HADS) is the most frequently used self-report questionnaire for psychological distress in cancer care (Carroll et al., 1993; Herrmann, 1997; Zigmond and Snaith, 1983). As the original English version has been translated into and validated in many languages, good psychometric properties have been demonstrated repeatedly (Chaturvedi et al., 1994; Costantini et al., 1999; Herrmann, 1997; Kugaya et al., 1998; Malasi et al., 1991; Razavi, 1990). The HADS was specifically designed for patients with physical illness; therefore, the items do not include somatic symptoms of psychological distress. The bidimensional structure of the inventory, containing both an anxiety and a depression subscale, has been confirmed by most studies (Costantini et al., 1999; Herrmann, 1997; Moorey et al., 1991; Spinhoven et al., 1997). Nevertheless, some authors failed to recognize the two dimensions. It seems unclear, whether the subscales really measure two distinct mood states (anxiety/depression), which often coexist, as shown in epidemiological general population studies (Angst et al. 1997; Kendler et al. 1993; Magee et al. 1996; Merikangas 1990) and by clinical experience (Costantini et al., 1999; Dunbar et al., 2000; Le Fevre et al., 1999). To that end, several authors decided to use the 14-item total score as a global measure of emotional distress, sustaining the original theoretical framework of the HADS, which was conceived for the evaluation of milder and mixed features of mood disorders (Costantini et al., 1999; Hopwood et al., 1991; Ibbotson et al., 1994; Kugaya et al., 2000; Razavi et al., 1990; Van't Spijker et al., 1997).

Likewise, the General Health Questionnaire in its 12-item version is a short self-report questionnaire, excluding somatic items and assessing global burden of disease (Goldberg and Williams, 1988). Conceived for the detection of psychiatric 'cases' in epidemiological studies, up to now it has mainly been used in large mental health studies in the community and in primary care (Goldberg et al., 1998; Jacob et al., 1997; Schmitz et al., 1999; Üstün and Sartorius, 1995). Earlier versions of the GHQ in its 30- and 28-item versions have been implemented with the HADS among cancer patients (Ford et al., 1995; Ibbotson et al., 1994). Le Fevre and colleagues (1999) compared the screening ability of the GHQ-12 and the HADS for patients in palliative care. All the studies investigating the discriminant validity of self-report questionnaires in cancer care used either the diagnostic results from clinical or structured clinical interviews (such as SKID) as criteria (Costantini et al., 1999; Ibbotson et al., 1994; Razavi et al., 1990; Kugaya et al., 1998; Le Fevre et al., 1999). The CIDI has been implemented as diagnostic measure in cancer care twice up to now (Grassi et al., 1997; Jenkins et al., 1991) but so far no study has carried out a validation of two short screening instruments using standardized clinical interview diagnoses as the 'gold standard' for validity.

The aim of this study was to implement both screening instruments in the same sample of patients to compare their accuracy of detection and utility for cancer care. The instruments were compared regarding:

- the ability to detect mental disorders in general;
- the ability to detect depressive disorders; and
- anxiety disorders; as well as
- the ability to identify mental illness in patients with comorbid psychiatric disorders.

#### Methods

#### Sample

The study was carried out within the first German clinical epidemiological study on the prevalence of mental disorders and associated factors in outpatient and inpatient cancer care (Härter et al., 2000; Härter et al., in press). Between May 1998 and June 2000 patient samples were recruited from four different inpatient clinics, one outpatient clinic and two specialized practices for oncology and haematology in southern Germany. During a specific period of time, all patients

were included consecutively, thus minimizing selection biases. The survey was based on a two-stage procedure. First, patients were administered the HADS (Herrmann et al., 1995), the GHQ-12 (Linden, 1990) and the SF-36 Health Survey (Bullinger and Kirchberger, 1998) for life quality. To record mental disorders every second patient was asked to participate in a clinical interview using the German version of the CIDI (Wittchen and Pfister, 1997), a standardized interview, which is well established in epidemiological research (Wittchen et al., 1994, 1998). This assessment system enables the diagnosis of mental disorders reliably and efficiently for specific periods of time (for example, four-weeks, prevalence, lifetime prevalence) using the scientific DSM-IV-criteria. The evaluation is computerized and for that reason objective regarding the evaluator. The main advantage of this procedure is the high inter-rater reliability. All the interviewers were psychologists or medical doctors with basic clinical experience and had been trained in this method. In all patients entering the second stage and being interviewed within two to five days after the screening procedure the CIDI led to psychiatric diagnosis according the criteria of DSM-IV or to an absence of diagnosis. The subsample of 188 patients (113 inpatients, 75 outpatients) having completed the questionnaires and the CIDI represented the database for this validation study. Their mean age is 54 years (SD 12.1). Because an important part of the study was conducted in oncological wards of a gynaecological department, the percentage of women (73%) is nearly three times higher than that of men (27%). The cancer sites are breast cancer (42%), gastrointestinal (15%), gynaecological (14%), haematological (12%), urological (4%) and other tumours (13%). Of the 188 patients, 64% have metastases and the mean time since first diagnosis is 2.7 years (SD 4.1).

### Data analysis

In order to compare the discriminant validity of the screening instruments, four analyses were performed. In the first analysis all patients with a current psychiatric diagnosis (four-weeks' prevalence) were selected as cases. For the following analysis this group of patients was divided into subgroups. The second analysis entered all patients with a current depressive disorder only (such as major depression and dysthymia). Patients with exclusively anxiety disorders (panic disorder, simple phobias and so forth) were referred to as cases in the third analysis. Because phobias do not necessarily impair patients' daily lives only those phobias with a reported degree of severity that indicated a need of treatment were included. Patients with more than one psychiatric diagnosis from different diagnostic categories (such as major depression and panic disorder) entered the fourth analysis.

According to recent findings that question the two subscales as separate measures of anxiety and depression (Costantini et al., 1999; Hopwood et al., 1991; Ibbotson et al., 1994; Kugaya et al., 2000; Razavi et al., 1990; Van't Spijker et al., 1997), the global score (0-42) of the HADS was used. The differences in mean scores of HADS and GHQ-12 between the patients with current mental disorders and no diagnosis were analysed with t-test. An ANOVA was performed for the detection of differences in mean scores between the patients without diagnosis and the patients with depressive disorders, anxiety disorders and comorbid mental disorders. Normality of variances had been explored with the Kolmogorov-Smirnov test and the equality of variances had been tested with the Levene-test adjusting the p-values for the comparison of mean scores according to its result.

Receiver operating characteristics (ROC) analysis (Murphy et al., 1987; Zweig and Campbell, 1993) was used to evaluate the diagnostic accuracy of the HADS and the GHQ-12 (score 0-12) to detect the cases in each of the four diagnostic categories. The results of the CIDI-procedure concerning current (four-week prevalence) psychiatric diagnosis were used as criteria. The ROC-curve expresses the sensitivity and specificity for each score and represents an index of the overall ability of the instrument to discriminate between cases and non-cases (Zweig and Campbell, 1993). The estimation of the area under the curve (AUC) quantifies this accuracy. The values range between 0.5 (no discriminatory ability) and 1.0 (perfect discrimination). Furthermore it expresses an estimated probability that a randomly selected case scores higher on the screening instrument than a randomly selected non-case (Dunn, 2000). For each diagnostic group the ROC curves and the corresponding AUCs for both screening instruments were compared. The cut-off points that minimize false positive and false negative test results for each diagnostic category are reported, as well as the corresponding sensitivity, specificity and the predictive values (PPV and NPV).

#### Results

#### Patients

More than half of the 188 patients have a lifetime diagnosis of mental disorder (Table 1). There are 21% who fulfil the criteria for a current DSM-IV diagnosis (four-weeks' prevalence). Affective disorders are present in 10%, and anxiety disorders in 7% of the patients. For affective disorders due to medical condition and anxiety disorders not otherwise specified the symptomatology is related to the cancer disease and does not fulfil the criteria for major depression or generalized anxiety disorder. The diagnostic procedures of the CIDI do not include adjustment disorders as a diagnosis. The prevalence rate of anxiety disorders includes only those phobias with need of treatment operationalized through the reported degree of severity. Another 7% of the patients have other mental disorders either exclusively or additionally.

#### Screening performance

For the comparison of the instruments' ability to detect mental disorders in general, depressive and anxiety disorders in specific and comorbid mental disorders, the patients with a current psychiatric diagnosis (N = 40) were divided into three groups: a group of patients with only depressive disorders (N = 14), patients with only

**Table 1:** Psychiatric Diagnoses According to DSMAV, N= 188 Cancer Patients (in %)

Lifetime prevalence	52	
Current prevalence (four-week)	23	
Affective disorder	10	
Major depression	5	
Dysthymia	3	
Affective disorder due to medical condition	2	
Anxiety disorder	7	
Phobia and social phobia	3	
Panic disorder with/without agoraphobia	2	
PTSD	1	
Anxiety disorder not otherwise specified	1	
Obsessive compulsive disorder	1	
Substance dependence (alcohol, tobacco)	3	
Pain disorder		
Eating disorder	1	

one or more anxiety disorder (N = 11), and patients with more than one mental disorder from different diagnostic categories (N = 8). Seven patients fulfilled exclusively the criteria for substance dependence, somatoform or eating disorder and therefore entered only the first analysis. The patients of each group entered as cases the corresponding analysis. All other patients were used as non-cases for each analysis.

The mean scores of HADS and GHQ-12 are significantly higher in patients with a current psychiatric diagnosis than in patients with no mental disorder. In addition, the patients with depressive disorders and with comorbid mental disorders differ significantly from the patients without mental disorders. The patients with anxiety disorders also have a higher mean score than patients without a diagnosis even though this difference is not significant. The differences in mean scores between the three diagnostic groups are not significant.

The ability to identify patients with mental disorders from the corresponding diagnostic groups are reported in Figures 1 to 4. The overall accuracy of the two scales in detecting patients with mental disorders does not differ significantly (p = 0.61, test for equalities of area). Performing an ROC-analysis for the detection of depressive disorders in specific, the AUCs of both scales are higher. The AUC of the HADS surpasses the AUC of the GHQ-12 even though the difference is not significant (p = 0.50, test for equalities of area). Similarly, the analysis shows a better result for the HADS than the GHQ-12 in identifying anxiety disorders (p = 0.26, test for equalities of area). The fourth ROC-analysis tested the ability of both instruments to identify cases with different comorbid mental disorders. In this analysis, the AUCs of HADS and GHQ-12 are equally good (p = 0.82, test for equalities of area).

For three of the four diagnostic groups (mental disorder in general, depressive disorder, comorbid mental disorder) the best cut-off point is 16/17 for the HADS-score (table 2). For anxiety disorders the cut-off point has to be lowered for sufficient sensitivity. The most balanced values for sensitivity and specificity (79%, 76%) as well as the best positive predictive value (69%) are found for depressive disorders. For mental disorders in general and comorbid mental disorders, a sensitivity of 60% and 87% respectively and a specificity of 79% and 67% respectively, are found. The low positive predictive value for comorbid mental disorders

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#### Table 2: Mean scores of HADS and GHQ-12

	HADS mean score	SD	GHQ-12 mean score	SD
a) No diagnosis N 148	12*ª	6.8	3.6*a	3.6
b) Any mental disorder N=40	17.6*	8.5	6.1*	4.2
c) Depressive disorders N= 14	20.9ª	6.9	7.1ª	3.6
d) Anxiety disorders N = 11	17	8.2	5.8	4.4
e) Comorbid mental disorders N=8	21ª	7.3	7.6ª	3.6

\* t-test, p<.000; T=4; df--6 1, 1; a < b

<sup>a</sup> ANOVA, F=1 1.8; df--3; p <.000; c, e > a

\* t-test, p<.000; T=33; df--64; a < b

<sup>a</sup> ANOVA, F=8. 1; df=3; p<.007; c,e > a





**Figure 1:** Receiver Operating Characteristics (ROC) Curves for the Detection of Mental Disorders. The areas under the curve (AUC) (95% CI) are 0.70 (0.63-0.77) for the HADS, 0.68 (0.61-0.75) for the GHQ-12; p = 0.61 (test for equality of areas).

**Figure 2:** Receiver Operating Characteristics (ROC) Curves for the Detection of Depressive Disorders. The areas under the curve (AUC) (95% CI) are 0.80 (0.73-0.85) for the HADS, 0.75 (0.67-0.81) for the GHQ-12; p = 0.53 (test for equality of areas).





**Figure 3:** Receiver Operating Characteristics (ROC) Curves for the Detection of Anxiety Disorders. The areas under the curve (AUC) (95% CI) are 0.76 (0.70-0.83) for the HADS, 0.68 (0.60-0.75) for the GHQ-12; p = 0.26 (test for equality of areas).

(35%) is related to the lower number of patients with comorbid mental disorders in the sample, as this value in particular is dependent on prevalence rates of cases in the study population.

The optimal cut-off points for the GHQ-12 vary between 2 and 6. Sensitivity is lower than for the HADS in all diagnostic categories, except for depressive disorders (93%). However, this high sensitivity value can only be reached through a low cut-off and therefore low specificity (49%). The specificity for the GHQ-12 is lower than for the HADS in all analyses except for anxiety disorders (76%), in which group the GHQ-12 also reached the best positive predictive value (60%).

#### Discussion

Clinical diagnostic interviews with a standardized assessment system (CIDI) were carried out with 188 inpatients and outpatients and enabled reliable and valid diagnosis of mental disorders (lifetime and four-

**Figure 4:** Receiver Operating Characteristics (ROC) Curves for the Detection of Comorbid Mental Disorders. The areas under the curve (AUC) (95% CI) are 0.78 (0.72-0.84) for the HADS, 0.77 (0.70-0.82) for the GHQ-12; p = 0.82 (test for equality of areas).

week prevalence) according to DSM-IV criteria. Therefore, specific analyses regarding the screening ability of HADS and GHQ-12 for different diagnostic categories could be performed. The Hospital Anxiety and Depression Scale showed a better screening performance than the General Health Questionnaire in its 12-item version for all four diagnostic specifications. Its superiority was especially marked for the detection of depressive and anxiety disorders.

Because recent findings have questioned the discriminant validity of the two HADS subscales, the suggestion of several authors to use the total scale as a single measure of emotional disturbance according to the concept of mixed emotions was followed. The best screening performance was found for depressive disorders (AUC = 0.80, 79% sensitivity; 76% specificity). For the other diagnostic categories, sensitivity and specificity values were either lower or less balanced, meaning that higher percentages of false positive and false negative cases respectively, have to be considered.

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	HADS score				GHQ-12 score					
	Cut- off	Sensitivity (in %)	Specificity (in %)	PPV (%)	NPV (%)	Cut- off	Sensitivity (in %)	Specificity (in %)	PPV (%)	NPV (%)
Any Mental Disorder	16	60	79	47	86	5	55	73	39	84
Base rate: 23.8%										
Depressive Disorder	17	79	76	69	84	2	93	49	55	91
Base rate: 7.4%										
Anxiety Disorder	13	88	57	53	90	6	67	76	60	81
Base rate: 6%										
Comorbid Mental Disorder	16	87	67	35	96	3	75	55	25	91
Base rate: 4.2%										

**Table 3:** Sensitivity, Specificity, Positive and Negative Predictive Value (PPV 1 NPV) for the Optimal Cut-off Points (N = 188 Cancer Patients)

The reported values for the HADS score vary between 70% and 91% for sensitivity (Razavi et al., 1990; Kugaya et al., 1998) and 66% and 96% for specificity (Razavi et al., 1992; Kugaya et al., 1998) depending on the homogeneity of the sample, the prevalence of disorders in the sample, the measure used as criterion (for example structured or clinical interview) and the diagnosis included (for example major depression and/without adjustment disorder). Within this spectrum the sensitivity and specificity values of the present study are situated among the lower results.

Some authors have recently suggested questioning the suitability of the HADS as a screening instrument because of poor validation results (Hall et al., 1999; Ramirez et al., 1995). On the one hand, it is possible that the HADS's capacity for detection of mental disorders in cancer patients has been overestimated for a long time and therefore more realistic values appear through the use of structured or/and standardized assessment methods for mental disorders (such as SKID, CIDI). On the other hand, the results of this study might be due to the fact that subthreshold disorders had not been included and therefore the prevalence of cases in the four analyses was rather low. It had been demonstrated before that the inclusion of adjustment disorders, being less severe and specific in their symptomatology had a positive effect on screening performance (Razavi et al., 1990; Kugaya et al., 1998).

The cut-off points varied between 16 and 17. Only for anxiety disorders did a lower cut-off point of 13 maximize sensitivity and specificity. Compared to the range of cut-off points between 10/11 (Razavi et al., 1992, Kugaya et al., 1998; Costantini et al., 1999) and 18/19 (Hopwood et al., 1991; Ibbotson et al., 1994; Malasi et al., 1991; Razavi et al., 1990) that have been reported for the overall scale, the optimal cut-off points for the four diagnostic groups showed relative consistency. Even though this means that similar severity of case definition on the scale is needed for the best trade-off between sensitivity and specificity in all four diagnostic groups, the scores are not necessarily the best. The cut-off points have to be chosen in relation to the screening strategies required by specific clinical and economic situations (for example, choosing a high cut-off for high specificity in order to minimize false positive results).

Compared to the well-implemented HADS, little experience is available at this point about the use of the GHQ-12 in clinical settings. For assessing unspecific psychological distress, it has been well validated for the detection of mental disorders in community-based and cross-cultural studies. The results demonstrated good overall ability of detection (AUC = 0.88 to 0.96) as well as satisfying values for sensitivity (83% to 97%) and specificity (76% to 90%) (Goldberg et al., 1997, 1998; Jacobs et al., 1997; Schmitz et al., 1999). This study with a clinical sample shows less satisfying results for the GHQ-12. The highest overall ability of detection was reached for comorbid mental disorders (AUC = 0.77). Sensitivity and specificity were, except for depressive disorders, in all diagnostic groups far below 80%. The wide range of cut-off points reflects the variety of thresholds between 1 to 6 that have been reported before (Goldberg et al., 1998). In contrast, the findings from the cross-cultural WHO-study, relating higher cutoffs with those samples having higher percentages of multiple diagnoses (comorbid mental disorders) were not confirmed here (Goldberg et al., 1998).

Corresponding to Le Fevre et al. (1999) who compared the screening ability of the HADS with the GHQ-12 in a palliative care setting, the HADS is superior to the GHQ-12 for cancer care. Even though the screening performance of the HADS could not confirm the outstanding results of earlier studies, the scale proved to be a valid screening instrument for the detection of depressive and anxiety disorders as specific diagnostic categories. When other, less prevalent mental disorders are included, the superiority of the HADS is less evident. This means that the GHQ-12, based on a non-specific concept of psychological distress, might be considered as an alternative instrument to the HADS for the screening of mental disorders in general.

The validity of screening for comorbid mental disorders has until now only been investigated in population surveys (Sandanger et al., 1998; Goldberg et al., 1998). As in comorbid mental disorders psychopathology vary more and might be more severe than in single disorders the consideration of comorbidity for screening in clinical samples is important. Similar to the results for single mental disorders, the overall accuracy of HADS and GHQ-12 doesn't differ as much as for the specific diagnosis of anxiety and depressive disorders. However, as in most patients with comorbid mental disorders, anxiety and/or depressive disorders are present, sensitivity and specificity of the HADS are still considerably better than of the GHQ-12.

The results of this study have to be looked at under the restriction of relatively small sample sizes of the four diagnostic groups, heterogeneous patients regarding duration and severity of illness, and the fact that rather severe criteria for mental disorders were applied, excluding adjustment and subthreshold disorders. Further studies are needed, which investigate the performance of screening instruments for specific questions regarding diagnostic subgroups, because the continuous comparison of existing instruments today is seen as one important condition for the improvement of screening procedures (Payne et al., 1999; Hall et al., 1999; Hopwood et al., 1991; Chochinov et al., 1997).

Furthermore, one must realize that like most screening inventories, the HADS and the GHQ-12 measure emotional and psychological distress with a dimensional approach, whereas the diagnosis of mental disorders is based on a categorical approach through the assessment of psychopathological syndromes. Therefore, the validity, especially the specificity, of dimensional instruments for the screening of psychiatric disorders will always be limited, because tests and criteria are based on different methodologies. Symptom-oriented instruments that screen for mental disorders following the criteria of DSM-IV could close this gap in the future. New and promising instruments in that sense are the Anxiety and Depression Screening Questionnaires (ASQ-15 and DSQ-15) developed within the German CIDI-version (Wittchen and Boyer, 1998; Wittchen and Pfister, 1997), as well as the Patient Health Questionnaire (PHQ) developed and validated within the Prime-MD, an interview for mental disorders in primary care (Spitzer et al., 1994, 1999; Loerch et al., 2000). Equal to conventional screening inventories, their use should be investigated for cancer care and the field of somatic medicine in general, comparing its screening validity

with implemented instruments on the basis of relevant diagnostic questions. This allows detection of incremental screening abilities of new instruments that might be useful in different medical care settings.

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