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Effectiveness of screening in allocating psycho-oncological counselling

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Dedication

I dedicate my dissertation work to my family and many friends. A special feeling of gratitude to my loving husband, Mateo Rojas-Carulla, who was my rock during the entire process and who made showed me that there is a solution even to the toughest problems.

I also dedicate this dissertation to my loving family: my siblings, Nóra and Bálint, who were always there for me after busy all-nighters; my parents Èva Filep and Zoltán Kálya, who motivated me in the difficult times; my brother-in-law, Miguel, who knows how to cheer everybody up and my parents-in-law, Cristina and Alejandro, who were the embodiments of stability and safety in turbulent times.

I dedicate this work and give special thanks to my dear friends Rebecca Böffert, Evelyn Frießinger and Kathrin Härtig for the long years in medical school, which with them seemed like a couple of weeks only.

Finally, I dedicate this work to the breast cancer survivors in Tübingen, who were brave enough to share their most painful experiences with me and who made me realize that I am not only responsible for their cancer therapy but for their psyche too.

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Explanation of abbreviations

In order of appearance

Electronical PsychoOncology Screening	ePOS
Comprehensive Cancer Center	CCC
Center for Breast Cancer	CBC
Center for Dermatooncology	CDO
Center for Gastrointestinal Oncology	CGO
Center for Gynaecological Oncology	CGynO
Center for Head and Neck Cancer	CHNC
Center for Malignant Lymphomas	CML
Center for Neurooncology	CNO
Center for Thoracic Oncology	CTO
Center for Urogenital Cancer	CUC
Center for Sarcoma and GIST	CSG
NET-Center	NET-C
Hornheider Screening Instrument	HSI
Subjective Need	SN
Distress Thermometer	DT
Patient Health Questionnaire	PHQ
Generalized Anxiety Disorder	GAD
Hospital Anxiety and Depression Scale	HADS
Distress of Cancer Patients Questionnaire	FBK
Receiver Operating Characteristic Curve	ROC
Area Under the Curve	AUC

1. Introduction

Despite revolutionary achievements of the previous decades in cancer treatments, tumorous diseases are still one of the most feared health conditions.[1,2] Just as cancer spreads and destroys body tissues, it also grows and consumes patients' mental health, social relationships and career.[3] The National Comprehensive Cancer Network (NCCN) described this phenomenon as "*psychological distress for cancer patients"* and defined it as following: *"a multi-determined unpleasant emotional experience of a psychological (cognitive, behavioural and emotional), social and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. This emotional response extends along a continuum, ranging from common normal feelings of vulnerability, sadness and fear to problems that become disabling, such as depression, anxiety, panic, social isolation and spiritual crisis*".[4]
But a cancer diagnosis does not end with the last treatments. The National Cancer Institute (NCI) offers the following definition for cancer survivors: "*An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and caregivers are also impacted by the survivorship experience and are therefore included in this definition.*"[5] Though the initial prevalence of psychological distress was repeatedly reported between 20% and 56%, even after surviving the disease distress levels stayed increased for approximately a fifth of all patients.[3,6,7] After more than 10 years, beside psychological distress also depressive symptoms, fatigue and pain are still frequently observed.[8]
The triggers of psychological distress vary widely from internal (such as psychological traits and lack of coping mechanisms) to external factors (sociodemographic status, clinical state), but previous research show partly incongruent results. Table 1. summarises the results of a structured review, collecting peer-reviewed works about internal / external factors and clinical symptoms as detrimental or protective aspects. For identifying the papers, following key words were used: "cancer / carcinoma / tumour", "distress", "outcome", "survival". The included works had to be published after 2000. For this process the search engines PubMed (www.ncbi.nlm.nih.gov./entrez/query.fcgi) and

Google Scholar (http://scholar.google.com) were used in January 2022. Andreu et al. (2012) did not find correlations between distress, demographic and medical factors, however they assert that specific psychological aspects benefit distress.[6] Accordingly, emotional suppression, helplessness, hopelessness, anxious preoccupation, cognitive avoidance and fatalism evoked distress, while fighting spirit and perceived social support seemed to reduce it. Additionally, Ellis et al. (2009) established the influence of prior to cancer existing depressive symptoms, attachment anxiety, just as the decline of self-esteem and spiritual well-being.[9] Lester et al. (2015) demonstrated for breast cancer patients a likewise important role of emotional factors (worry, nervousness, sadness and fear), but they demonstrated the influence of physical aspects as well (disturbed sleep, fatigue, problems with own appearance, side-effects).[10] Also, supporting previous findings, they showed that the extent of treatments strongly influences distress, but no relation was found between cancer stage (i.e. extent of primary tumour in the body, metastases) and distress.[6,8] Harmoniously, Hack et al. (2010) reported an impact of treatment characteristics and involvement in the therapy decision making processes on increased distress.[11] The apparent contradiction to other studies with proof for elevated distress in case of metastases can be seen as a product of intensive therapy experience and hopelessness / helplessness rather than the cancer stage itself.[12-14] Furthermore, evidence suggests that sociodemographic factors, such as being unmarried, living alone, being under 40 and receiving less social support benefits psychological distress.[9,10,12] Considering the age and gender distribution among cancer patients in Germany (Figure 1.), there might be a mediating effect of cancer likelihood for the specific age groups.[15] Giese et. al delivered interesting insights on the interaction of commonly described sociodemographic problems and distress. They found, that even though young females are especially vulnerable, for them marriage seems to be a protective factor.[16] Surprisingly, young male patients experienced significantly more distress. For elderly patients' marriage seemed to buffer the experienced problems. More explicitly, Yang et al (2009) found that

Table 1. Summary of common aspects of psychological distress, based publications after 2000 on PubMed and Google Scholar in January 2022.

	Detrimental aspects	**Protective aspects**	**Neutral aspects**
Internal factors			
Psychological traits	Anxiousness[6,8,9,17] Depressive symptoms[9,17] Mood disorders[17] Nervousness[10] Fatalism[6] Low self-esteem[9] Loss of spiritualism[9]		
Emotions	Fear of cancer progression[10,12] Worry[7,10] Sadness[7,10]		
Coping mechanisms	Hopelessness[6] Helplessness[6] Emotional supression[6]	Fighting spirit[6]	
External factors			
Social net	Reduced social safety net[9,10,12,18]	Perceived social support[6,7,10]	
Sociodemography	Female gender[9,10,12,16,19] Unmarried status[9,10,12,16] Marital distress[20] Living alone[9,10,12] Younger age[9,10,12,16,19]	Male gender[9,10,12,16,19] Married[9,10,12,16] Living with others[9,10,12] Age > 60[9,10,12,16]	
Physical status	Fatigue[7,8,10,13,14,18] Sleep problems[7,10,13,14] Pain[8] Treatment side-effects[10,18] Problems with appearance[10]		
Clinic			
Cancer related	Cancer type[3,8-10,12,19] Illness duration[10,12] Progressing cancer, recurrence[12-14]		Cancer staging[6,8]
Treatment related	Extensive therapy[6,8]	Involvement in therapy[11]	

distressed relationships not only correlate with significantly higher psychological and practical problems, they even seem to have a negative effect on cancer progress and reaction to treatment.[20] One should not forget though, as the authors point it out, that these results could be mediated by the higher occurrence of mental disorders and psychological challenges in a distressed relationship.

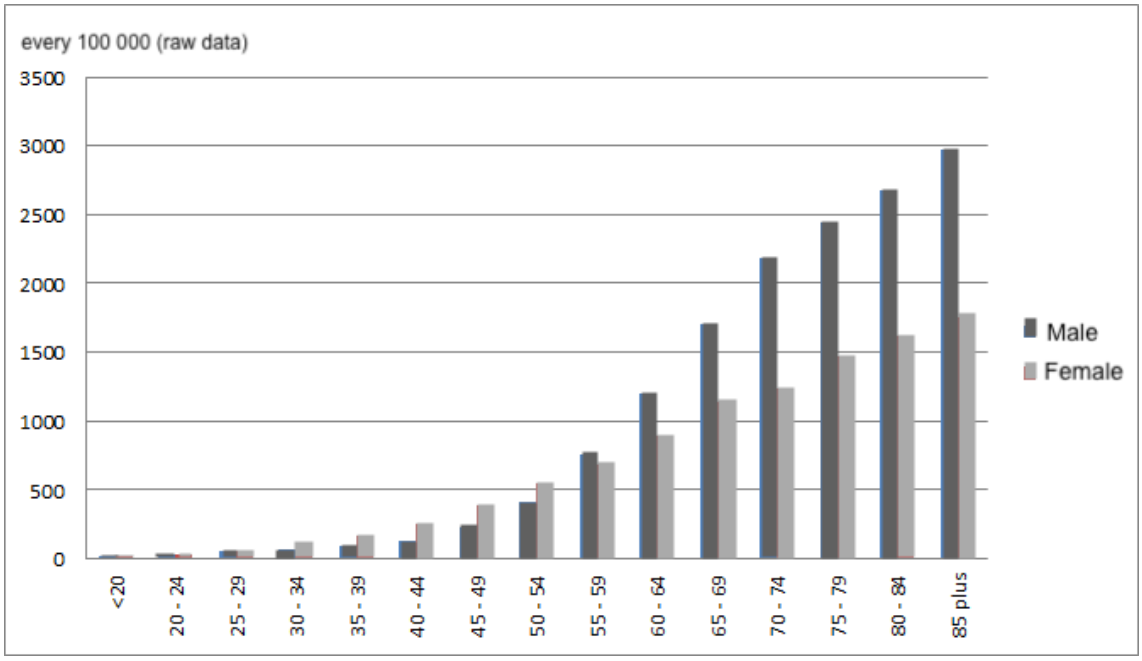

Figure 1. Age and gender distribution for cancer in Germany without melanoma in 2016. Translated and modified from https://www.krebsdaten.de/Krebs/SharedDocs/Grafiken/TdM/Lebensverlauf/grafik1.png;jsessionid=9C0DA618F1EEFCD1104505654E655DD2.internet062?__blob=poster on 18. April 2022

Even though initial cancer staging does not seem to affect the experienced distress, previous studies show that cancer type does.[3,8-10,12] Zabora et al. (2001) demonstrated that North-American patients with lung and brain cancer, just as upper gastrointestinal tumours are the most likely to cause severe distress, whereas breast cancer and gynaecological tumours tend to lead less to psychological problems.[3] Herschbach et al (2004) presented very different results for a German sample: in their study, soft tissue cancer and breast cancer were highly associated with psychological distress, whereas brain tumours were only ranked 6th out of the 12 cancer types studied and upper gastrointestinal tumours caused significantly less distress than other cancer types.[12] Both studies agreed

on urological and lower gastrointestinal cancers to be rather less correlated with distress. A meta-analysis by Linden et al (2012) provided evidence for the main findings of both studies: They found a higher prevalence of distress in haematological, lung and gynaecological/breast cancers, while the least affected cancers were urological and skin cancers. [19] Table 2. displays the similarities and differencies between both Zabora's and Herschbach' studies.

Table 2. Comparing distress level rankings between Zabora et al.[3] and Herschbach et al.[12] Note[1]: Cancer types differing greatly in ranking are highlighted. Note[2]*: Cancer types which do not occur in both of studies are labelled with *.*

Distress level ranking	**Zabora et al. (2001)**	**Herschbach et al. (2004)**
1.	Lung	Soft tissue tumours*
2.	***Brain***	***Breast***
3.	Hodgkins'	Respiratory tract
4.	Pancreas	Thyroid carcinomas*
5.	Lymphoma	ENT carcinomas
6.	Liver*	***Brain***
7.	Head and neck	Haematological neoplasias
8.	Adenocarcinoma (unknown primary)	***Gynaecological***
9.	***Breast***	***Male genitourinary tract***
10.	Leukaemia	Lower gastrointestinal tract
11.	Melanoma*	Urinary tract*
12.	Colon	Upper gastrointestinal tract
13.	***Prostate***	-
14.	***Gynaecological***	-

Why is it so important to address distress, especially for cancer patients? Affective disorders, anxiety and adjustment disorders are common for them, particularly if they undergo fatigue, pain or strong cancer-related symptoms.[21] Obviously, feeling helpless, anxious, even depressed over a longer period of time is a painful experience, which might lead to decreased self-esteem and hopelessness on the long term. Furthermore, distress correlates with increased mortality up to 12 years post treatment.[13,14] Hence, successful tumour therapy plans must consider the impact of distress as an essential part of the disease and must try to address it accordingly.

The first step in that process is recognizing those patients suffering from any cancer-related distress. For that, the Association of the Scientific Medical Societies (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, AWMF) in Germany recommends routine screenings for all tumour patients after the initial diagnosis, in case of tumour progress or changes and when patients show or express distress.[21] The use of well-established screening tools and methods are bridely suggested, mainly for three reasons: to expedite an early diagnosis, to detect affected patients who do not communicate their concerns or sufferings well and to decrease inequalities in diagnosis that result from differing clinician abilities.[22]

However, measuring cancer related psychological distress is a complex task. As mentioned above, distress is not equal to anxiety or depression, but it should be rather understood as a(n early) symptom of these.[17,22] As a wide spectrum concept, it can be associated with underlying psychiatric traits, can progress to mental disorders, but individually even the experience of non-pathological aspects like lowered self-esteem or helplessness should be considered as distress. Therefore, instead of applying single screening tests, the use of screening assortments could be reasonable. PROMIS® (Patient-Reported Outcomes Measurement Information System) was an attempt to conceive such a screening tool.[23] PROMIS® has been widely used in North-America and it underlies constant validation, with satisfying results (e.g. Schalet et al., 2016[24]). Another globally acknowledged screening instrument is Distress Thermometer (DT).[25,26] Here, next to the mental distress, somatical difficulties can be measured

as well. In german-speaking countries other instruments, specifically the Hornheider Screening Instrument (HSI) and Distress of Cancer Patients Questionnaire (FBK) have been established and used broadly.[27-31] Besides the distress specific questionnaires, screening instruments to detect depression and anxiety are universally common as well.[32,33]

Another interesting question in the current topic is the impact and success of screening in clinical routine.[22,34,35] First of all, measuring a state psychological variable means, that distress might change in the time between screening and treatment.[22] Schäffeler et al. suggested the additional standardized questioning of patients' subjective need for support to reduce "false positive" screening results.[36] In this case, a medical metaphor for distress could be the high level of C-reactive protein, which is used to detect infections (depression in the analogy). Whereas screening for infections in the blood is a well-defined process, a rise of C-reactive protein itself can point to many different causes from tissue damages after a surgery to cancer. Whether it is dangerous, depends a lot on the context and conspicuous screening does not necessarily automatically lead to treatment. Mitchell et al. (2013) found in a metaanalysis, that patients can benefit from distress screening the most if it is followed by further evaluation. Another important aspect on the practicality of screening regards the posterior treatment: if screening results were linked to treatment, training of coping strategies or support, patients profited the most from screening.[22] As it is frequently not the case in everyday clinical routine, some authors urge us to reconsider the general use of a routine screening for all cancer patients and the consequences of a conspicuous result.[34,35,37]

Summarizing, cancer distress research is traditionally rather focused on the impact of distress, how to measure it and which possible treatments are beneficial. Only a small number of studies investigate *how* to apply screening instruments in clinics' daily routine.[36,38,39] Further, computer based screening methods became more relevant as they seem to be superior to paper-pencil screening methods regarding their efficiency.[40] Based on a metaanalysis of patient-reported outcomes and face-to-face consensus meeting experts, Koehler et al. (2017) published the following recommendations for computerized distress

screening in routine oncological care.[38] First, actions of preparation have to be agreed on by all participating disciplines, e.g. defining the terms, screening goals (distress, but maybe also somatic symptoms, etc.). Second, a proper IT equipment should be available. Third, implementation should take place, i.e. standard operating procedures should be available, personnel should be schooled and all steps of the process should be known for participating personnel. Fourth, the practicality should be continuously tested and optimized in everyday routine, e.g., during morning rounds, regular boards. And fifth, regular quality measures for research and for further optimization should take place.

Teufel et al. implemented an electronical screening system (**e**lectronical **P**sycho**O**ncology **S**creening, *ePOS*), which is valid in all the cancer centers at the University of Tübingen.[39] Furthermore, they developed a clinical pathway with an automatically triggered emergency counselling system in case of conspicuous screening results and/ or expressed subjective need. For that, they combined well established screening instruments, such as HSI or DT and patients' subjective evaluation of their own needs.[36] If the screening instruments measured increased distress or if patients communicated the same, psycho-oncologists offered them counselling, tailored to their accute needs. The system is well accepted and accessible among a wide range of patients.[41]

In this current study we intended to evaluate the efficiency of ePOS and to provide basis for future improvement of the system. The system is considered efficient, when all patients who experience high distress and would like to be supported are recognized by the screening system and receive a consecutive counselling appointment. Because of the nature of the 12-month data collection at the Comprehensive Cancer Center Tübingen, we are not only able to measure and compare patient distress and identify socio-demographic or clinical factors, but we can also focus on the relevance of screening results for clinical routine. With that, we aim to provide data for the practicability of distress screening and investigate, whether high scores and the wish for counselling are statistically dependent.

2. Material and methods

Sample

In the calendar year 2018 all neoplasia inpatients of the participating Comprehensive Cancer Center (CCC) were considered for the ePOS (Electronical PsychoOncology Screening) study. They could participate in the routine screening if they were fluent in German both written and spoken, they had sufficient technical skills to operate a tablet and if they not showed signs of delusional disorders or severe accompanying symptoms impacting cognitive skills. An ethics comittee approval was provided for retrospective analysis of these screenings (s. section "*Ethics committee approval"*).

The following cancer centers joined the study: Center for Breast Cancer (CBC, Universitäts-Brustzentrum), Center for Dermatooncology (CDO, Zentrum für Dermatoonkologie), Center for Gastrointestinal Oncology (CGO, Zentrum für Gastrointestinale Onkologie), Center for Gynaecological Oncology (CGynO, Zentrum für Gynäkologische Onkologie), Center for Head and Neck Cancer (CHNC, Zentrum für Kopf-Hals-Tumoren), Center for Malignant Lymphomas (CML, Zentrum für Maligne Lymphome), Center for Neurooncology (CNO, Zentrum für Neuroonkologie), Center for Thoracic Oncology (CTO, Zentrum für Thoraxonkologie), Center for Urogenital Cancer (CUC, Zentrum für Urogenitale Tumoren), Center for Sarcoma and GIST (CSG, Zentrum für Weichteilsarkome, GIST und Knochentumoren), NET-Center (NET-C, Zentrum für Neuroendokrine Tumoren).

Screening instruments

Table 3. provides a review of the applied screening instruments and the locations they were used at.

Table 3. Screening instruments' main characteristics and locations of their use. Note: HADS has been used only in CHNC for one study. FBK-10 was experimentally used for a limited amount of time and has not been selected as a permanent screening tool.

Screening instrument	Items	Scales	Cutoff score	Cancer center
Hornheider Screening Instrument (HSI)	7	Distress	Discrimination function ≥ .3 Total score ≥ 4	All
Subjective need	1	Subjective distress	Answered with yes	All
Distress-Thermometer (DT)	1 + 36	Distress	Total score ≥ 4	Dermatooncology Gynaecological Oncology Breast Cancer
Patient Health Questionnaire (PHQ8)	8	Depression	Total score ≥ 10	Dermatooncology Gynaecological Oncology Breast Cancer Head and Neck Cancer
Patient Health Questionnaire (PHQ2)	2	Depression	Total score ≥ 3	All
Generalized Anxiety Disorder Scale (GAD7):	7	GAD	Total score ≥ 8	Dermatooncology Gynaecological Oncology Breast Cancer Head and Neck Cancer
Generalized Anxiety Disorder Scale (GAD2):	2	GAD	Total score ≥ 3	All
Hospital Anxiety and Depression Scale (HADS):	14	Anxiety (7 items) Depression (7 items)	Total score ≥ 15	Dermatooncology Head and Neck Cancer
Fragebogen zur Belastung von Krebskranken (FBK-10)	10	Psychosocial distress	Total score ≥ 14	Dermatooncology Head and Neck Cancer

The simplified **Hornheider Screening Instrument** (HSI, Appendix 1.) was constructed for the self-assessment of oncological patients to identify ominous mental and physical strains. [30] The test receives seven inputs, each with a score between 0 and 2 or 3. These inputs correspondent to 1: perception of the body, 2: perception of the mental state, 3: disease independent stressors, 4: social support, 5: stressed family members due to the disease, 6: capability to find peace, and 7: perception of being informed about the disease. For items 1, 2, and 7 the answer categories range from “rather good”, “medium” and “rather bad”. For the rest of the items the answer categories are “yes” or “no”. Summarizing the scores of the singular items provides the mean score with a maximum value of 14. To distinguish between patients in need for help and patients who do not need help a discriminant function can be computed from the item scores. The total value and discrimination coefficients as follows: $Y = b_1 X_1 + b_2 X_2 + b_3 X_3 + b_4 X_4 + b_5 X_5 + b_6 X_6 + b_7 X_7 + b_8 X_8 - b_0$ (Y: discriminant variable, $X_{1\text{-}7}$: item scores, X_8 : total value, b_0: constant, $b_{1\text{-}8}$: discriminant coefficients, $Y = 0{,}569\ X_1 + 0{,}476\ X_2 + 0{,}444\ X_3 + 0{,}057\ X_4 - 0{,}081\ X_5 + 0{,}063\ X_6 + 0{,}973\ X_7 + 0{,}109\ X_8 - 1{,}722$)[27]. Further counselling is recommended above Y > 0.3 or a total score of 3. Cronbach ´s alpha is the measure of internal consistency, which indicates how well a group of items asses a unidimensional construct. For HSI it is .60. Furthermore, HSI correlates significantly with other widely used screening instruments (e.g. HADS[27]).

The single item **Subjective Need** (SN) was developed in the University of Tübingen and is in daily use since 2012 to identify oncological patients’ need for psychological assistance.[41] Its main purpose is to provide additional information about the current balance of required and experienced support. If the question “Do you currently need support in coping with the disease or psycho-oncological counselling?” is answered with “yes”, it is strongly recommended to further establish the patient’s distress level.[36] (Appendix 2.).

The **Distress Thermometer** (**DT,** Appendix 4-5.) was designed to detect both level and source of distress for oncological patients[26,27,42]. The visual scale (a thermometer ranging from 0 to 10) is especially suited for ultra-rapid screenings, the connecting problem list collects detailed information about specific distress factors (practical, family, emotional, physical problems, or spiritual/religious

concerns) in 36 items. The results are interpreted without further statistical analysis: a higher level of distress is to be assumed if the visual scale is above 4 or 5, or if at least one item of the distress factors is marked as conspicuous[26]. In the present study we chose a cutoff of 5 on the visual scale. A metaanalysis from Donovan et al. revealed a sensitivity of .83 and a specificity of 0.68 for translated versions of the DT[25]. Because of the virtual nature of DT it is especially challenging to test the validity, however numerous empirical findings show, that DT is comparable with other self-assessment tools[25,27].

The Patient Health Questionnaire-8 (**PHQ-8,** Appendix 6) is a widely used, unidimensional, 8-item depression assessment tool. This from PHQ-9 simplified version contains the main time and symptomatic criteria of major depression. Kroenke et al. showed significant correlations between DSM-IV scales to diagnose depression and PHQ-8[33]. A total score ≤ 4 out of 24 indicates no significant depressive symptoms, scores between 5-9 mild depressive symptoms, 10-14 moderate, 15-19 moderately severe and 20-24 severe symptoms. A cutoff of >10 is recommended based on empirical data for various patient groups[33,43].

PHQ - 2 (Appendix 6.) was designed for rapid depression screening in the clinical setting[44]. With only the first 2 items of the PHQ-8 questionnaire (see the section above) it focuses on the depression criteria anhedonia and depressed mood. At a cutoff score ≥3 out of 6 a specificity of .92 and a sensitivity of .83. for major depression were shown.

The **Generalized Anxiety Disorder Scale** (**GAD - 7,** Appendix 7.) is a 7-item screening tool for generalized anxiety disorder for the general population. A total score ≤ 4 represents no significant anxiety symptoms, scores between 5-9 mild anxiety symptoms, 10-14 moderate, 15-19 moderately severe and 20-24 severe symptoms. For a cutoff score of 10 out of 24 both specificity and sensitivity exceeded .80[32,43,45]. A cronbach's alpha of 0.92 was reported.

GAD - 2 (Appendix, 7.) uses the first 2 items of GAD-7 to focus on the two important criteria of anxiety: experiencing severe anxiety/tension and having uncontrollable anxious thoughts. A systematic review found acceptable sensitivity (.76) and specificity (.81) for a cutoff of ≥ 3 out of 6[45].

Hospital Anxiety and Depression Scale (HADS, copyright at Hans Huber Verlag, 2011) is a self-assessment tool to screen physical disorder patients for typical vegetative symptoms of anxiety and depression. It contains two subscales (HADS-Anxiety and HADS-Depression) with 7 items respectively. The results on each subscales are categorized as non-cases (≤7 points out of 46), borderline cases (8-10 points) or as definitive cases (≥11 points). Correlations between both scales are on average .56, the sensitivity and specificity are for both scales approximately .80, Cronbach´s alpha for HADS-A is .83 and for HADS-D .82 [29]. Concerns were repeatedly reported in case of testing patients with somatic symptoms, as their results can be false positive.

Distress of Cancer Patients Questionnaire (**FBK - 10,** Appendix 8.) is a 10-item long, simplified version of FBK-23, which was developed to qualify and quantify psychosocial strains for cancer patients.[27] For a cutoff ≥ 14 out of 50, the sensitivity was .81, the specificity .72 compared with HADS.

Procedure

The ePOS study was based on an already established routine clinical pathway, which was performed daily to monitor and plan psycho-oncological care in the cancer center. In the standard process, the health care provider introduced the ePOS screening to patients during their treatment in one of the cancer centers. If they agreed to participate in the study, their date was recorded for later analysis. In this current work only the participants will be referred as patients.

All patients received a tablet with the screening tool (sociodemographic and clinical questionnaire, HSI, SN, displayed in Appendices 1-10.) or in the CDO a paper-pencil screening sheet. They had unlimited time to fill the questionnaires. The screening was deemed conspicuous, if the HSI discrimination function was above 0.3, the patient claimed a subjective need for psychological counselling or if both cases were true (s. Figure 2, based on Schaffeler, Pfeiffer, Grischke, Wallwiener, Garbe, Zipfel, Teufel [41].).

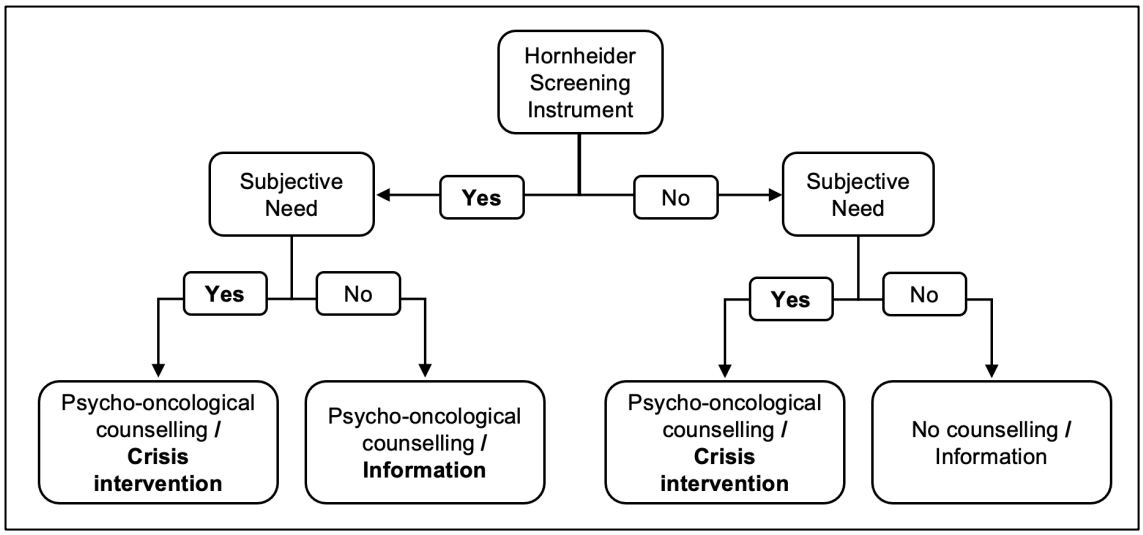

Figure 2. Decision making algorithm for psycho-oncological counselling based on the standard screening.

In case of conspicuous screening the psycho-oncological service was involved and a specialized psychologist offered the affected patients an emergency counselling session. If HSI was conspicuous but SN was not, patients were automatically informed and offered a short counselling session with information about counselling options. The exact pathway has been documented in the gynaecological clinics, in other clinics only the results of HSI and SN. Either way, the contact has been documented in the patient management platform of the University Tübingen (SAP® ECC 6.0 EHP-7 with SAP® HANA 1.0 SPS 12 for Healthcare IS-H and Cerner Clinical Modul® i.s.h.med). In specific cancer centers additional screening instruments were given to routine screening, either in electronical or in paper-pencil format (as shown in Table 3.). If the results in those instruments were above the cutoff score, a psycho-oncologist contacted the patients for crises intervention.

The data was stored in ePOS and extracted in a Microsoft Excel file for later analysis. After the data collection ended, in this present work further information has been gained from SAP. All patients with conspicuous screening results were identified and examined, whether they had a counselling appointment documented during their inpatient treatment, whether they agreed to the counselling or declined it and whether there were follow-up appointments documented.

Also, a sample of patients with unremarkable screenings was randomly chosen and underwent the same data collection. For the random selection of approximately 200 of all patients with unremarkable screening, a number of 1 to 20 was generated by Microsoft Excel and assigned to each patient. Accordingly, the following formula was used: ROUND(RAND()*(20-1)+1,0).) Then, using RStudio v1.1.463 [46] a random number was chosen with the following command: "floor(runif(1, min=1, max=20))". As result, group number 4 with 195 patients was chosen for further analysis. The new data was added to Microsoft Excel file and after that the file has been completely made anonymous.

Statistical analyses

All statistical analyses were completed with Statistical Package for the Social Sciences (SPSS®, IBM Corp. Released 2019)[47], IBM® SPSS® Statistics for Macintosh (macOS Catalina 10.15.5.), Version 26.0. Routledge, NY: IBM Corp. All statistical analyses base on the recommendations of SPSS Survival Manual (Pallant, 2016)[48]. First, to understand the connections between distress and intrapersonal variables, descriptive statistics were computed for each of the cancer centers, sociodemographic, clinical data, counselling related data. Second, we performed univariate analyses and analyses of variance to understand the dependence between different testing instruments and intrapersonal variables. Univariate analyses were calculated between dichotomic screening test results (HSI, SN, DT, PHQ, GAD), counselling, counselling readiness and the variables cancer centers, sociodemographic and clinical groups, using a Chi-squared test for independence with Spearman and Pearson correlation coefficients. Between metric tests results of HSI and DT and the other variables, Analysis of Variance (ANOVA) with post hoc Bonferroni comparisons were performed. Third, receiver operating characteristic curves (ROCs) were computed stepwise for each screening instruments' fixed and redetermined cutoff scores (s. Table 3.) on predicting counselling readiness. The correct discrimination probabilities were estimated with areas under the curve (AUCs), based on Wilcoxon-Mann-Whitney statistics. Fourth, ROCs were performed on each screening instrument to estimate the impact of discrimination probabilities

when combined with the standard tests HSI + SN. Fifth, Chi-squared tests for independency were conducted on HSI, SN and PHQ – 2 such as GAD – 7. ROCs and AUCs of aforementioned tests were compared to estimate the differences between their prediction accuracy.

Ethics committee approval

A study approval application of the ethics committee of the University of Tübingen were submitted on the 7th of February 2017 with the title "*Rollout des elektronischen psychoonkologischen Screenings (ePOS) am Südwestdeutschen Tumorzentrum (Comprehensive Cancer Center Tübingen): Einflüsse auf die psychoonkologische Versorgung von Patienten mit Krebs*". The votum of approval was delivered on the 28th of February 2017 (086/2017BO2). We filed an amendment on the 17th of December 2018 for specific changes regarding patients' data for this present work and received the approval for retrospective data collection on the 31st of January 2019.

Hypotheses

In this current study following hypotheses will be investigated:

1. Patients' level of distress differs significantly among the Comprehensive Care Centers.
2. Patients' sociodemographic data influences their experienced distress level and readiness for psycho-oncological counselling.
3. Patients' clinical data influences the experienced distress level and readiness for psycho-oncological counselling.
4. Patients with conspicuous screening results consecutively received psycho-oncological counselling.
5. The applied screening instruments effectively predicted patients' readiness for psycho-oncological counselling.
6. The specificity and sensitivity of the core screening test (HSI and SN) can be improved by adding other screening instruments.
7. The short versions of the screening instruments GAD - 2 and PHQ - 2 are comparable sensitive and specific as their long versions GAD - 7 and PHQ - 8.

3. Results

Sample

In total N=7568 measures are available. With some repeated measures M=5732 patients were screened, 57% of them were female. The average age was 61.17 years (the youngest patient was only 12 years old, the oldest 94). The age distribution was according to the expected incident rates in Germany (s. Figure 1. and 3.)

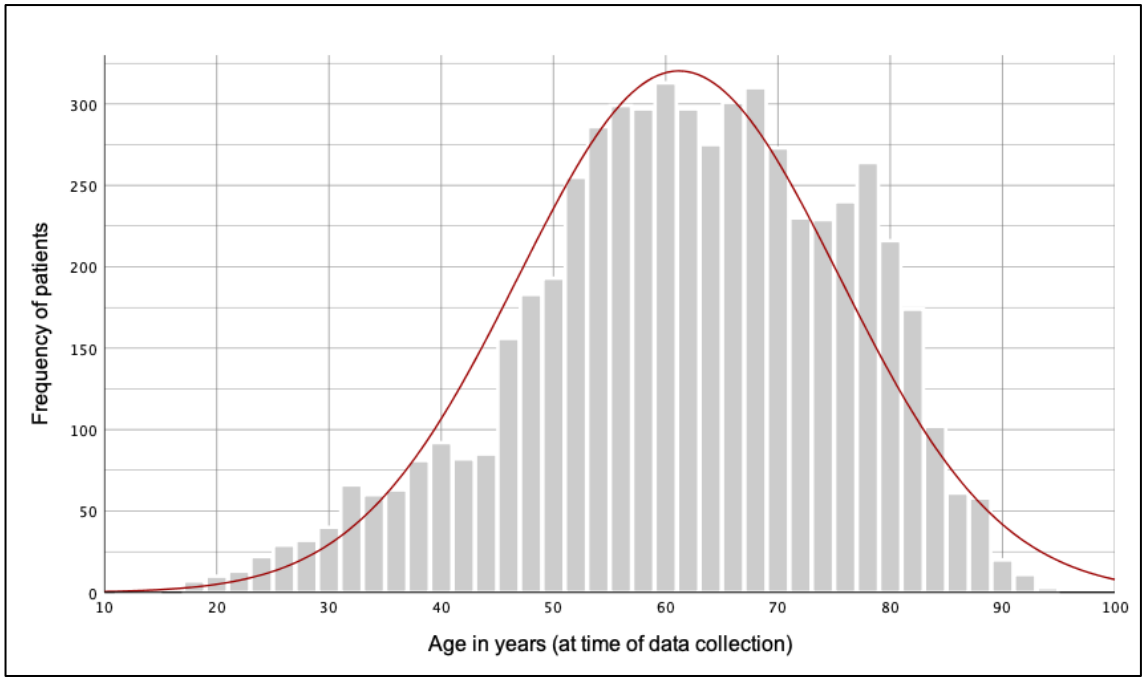

Figure 3. Age distribution of all patients at the time of data collection.

The number of patients in each cancer center is displayed in Figure 4. A significant difference in age between the centers was observed, F (2, 1040.887) = 68.974, p = .001 at p<.05. Post hoc comparisons using Bonferroni correction indicated that the mean age between the Center for Neurooncology (CNO, M = 52.78, SD = 15.597), the Center for Sarcoma and GIST (CSG, M = 56.02, SD = 17.941), the Center for Gynaecological Oncology (CGynO, M = 57.94, SD = 13.537), the Center for Breast Cancer (CBC, M = 58.07, SD = 12.910) and Center for Malignant Lymphomas (CML, M = 61.29, SD = 14.994) did not differ

significantly. Also, the mean age did not differ significantly between the CML, the Center for Head and Neck Cancer (CHNC, M = 62.43, SD = 12.554), the Center for Dermatooncology (CDO, M = 62.57, SD = 15.042), the Center for Gastrointestinal Oncology (CGO, M = 63.95, SD=12.764),

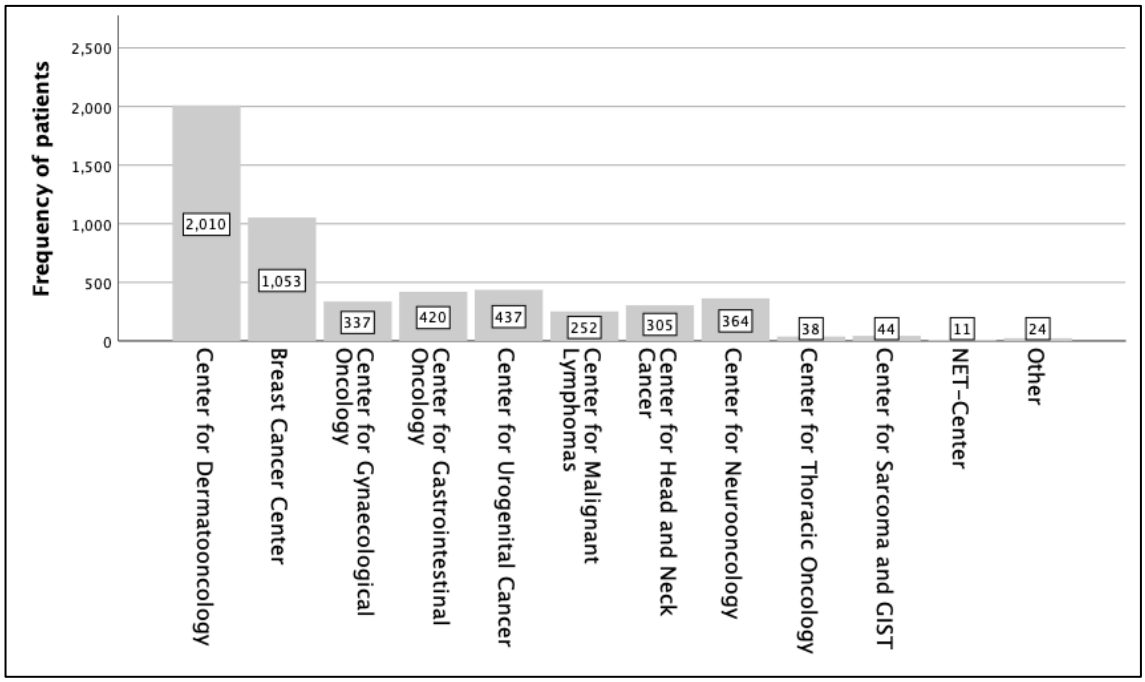

Figure 4. Patients' frequencies by Cancer Centers. Note: Centers under 10 participants were summerized under "Other".

the Center for Thoracic Oncology (CTO, M = 66.47, SD = 9.217) and Center for Urogenital Cancer (CUC, M = 67, SD = 11.249). Other age differences between these two groups appeared significant.

Screening

66% of all patients participated in the computer based routine screening, 25% in the paper form of the routine screening 9% of the patients screening was either not possible or has been rejected. 85% of all the patients completed the Hornheider Screening Instrument (HSI), and 87% completed the Subjective Need (SN, s. Table 4.). Distress Thermometer (DT) was used for 41% of the patients.

34% filled the Generalized Anxiety Disorder Scale (GAD) 2/7 and the Patient Health Questionnaire (PHQ) 2. The PHQ8, the Hospital Anxiety and Depression Scale (HADS) and the Distress of Cancer Patients Questionnaire (FBK-10) was used for less than 1% of the patients.

Table 4. Frequency of patients performing the screening instruments.

Screening instrument	*n*	*%*
Hornheider Screening Instrument (HSI)	4889	85.29
Subjective Need (SN)	4979	86.86
Distress-Thermometer (DT)	2336	40.75
Generalized Anxiety Disorder Scale (GAD2)	1921	33.51
Generalized Anxiety Disorder Scale (GAD7)	1928	33.64
Patient Health Questionnaire (PHQ2)	1920	33.47
Patient Health Questionnaire (PHQ8)	415	.07
Hospital Anxiety and Depression Scale (HADS)	49	.01
Distress of Cancer Patients Questionnaire (FBK-10)	22	.004

Sociodemographic data

Sociodemographic data has been collected in the CBC, CDO and on the radiooncological outpatient ward. Occasionally in the CML, CNO and CGO patients completed the questionnaire. In the other centers no sociodemographic data has been collected.

N = 1611 patients declared their civil status: 77.1% of them lived in a partnership (in total 66.6% were married), 22.4% did not live in a partnership (6.6% were divorced or separated, 7% were widowers). Out of n = 1602 patients 17.4% lived alone, 78% lived either with their partner, children or both, 2.8% with their parents,

1.9% in institutions or other facilities. Out of n = 1609 patients 80.7% had at least one child. Out of n = 1604 patients 30.7% had finished high school or studied, 29.2% finished secondary school, 35.5% finished elementary school or still attended school. Out of n = 1616 patients 39% were employed, 12.2% were self-employed, 3% were unemployed and 44.8% were pensioners or were unable to work.

Clinical data

9% of the n = 3412 patients had an either unknown tumour status, or it was not recorded by the medical personnel at the time of data collection. 61% had primary tumours, 6% had metastases, 4% had recurrent cancer and under 1% had an additional secondary tumour.

N = 1611 patients were asked whether they consumed regularly psychotropic medication. 84% answered with no, 10% consumed medication on a daily and 6% on a regular basis. Out of n = 1611 patients 80% never need psychological counselling, 15% used to have and 6% were in psychological treatment at the time of study.

Hypothesis 1.

In order to investigate whether patients´ average distress level differs significantly between the cancer centers, screening instruments above 40% utilization were analysed (HSI, SN, DT, s. Table 4.). Table 5. summarizes the dichotomic screening results of each instruments (conspicuous vs. unremarkable) in each of the centers. Further, Chi-squared tests for independence were performed to examine the relationship between the cancer centers and the screening instruments. After a Bonferroni correction for multiple testing a p-value of .02 was set.

The positive-negative ratio differs significantly in the centers. Conspicuous HSI results are disproportionally associated with the CGynO, unremarkable screening results with CUC, $X^2(11, N = 4567) = 72.159$, p = .001. Also, there is a significant relationship between some of the cancer centers and SN. There are disproportional associations between positive answers and CGynO and between negative answers and CUC, $X^2(11, N = 4643) = 311.96$, p = .001. Further, a significant association between some cancer centers and DT was observed. Unremarkable screening results related disproportionally with CDO and CUC, conspicuous screenings with CGynO, $X^2(10, N = 2306) = 124.76$, p = .001.

In a second step one-way ANOVAs of the average scores of the discriminant function in HSI and DT were performed. Figure 5. displays the mean discriminant function scores in each of the centers. The HSI scores were standardized by taking their natural logarithm, to meet the assumptions of ANOVA. Mean HSI scores differ significantly between the centers, F(11, 4555) = 17.51, p = .001 at p<.02.

Table 5. Comparison between dichotomic screening results of Hornheider Screening Instrument (HSI), Subjective Need (SN) and Distress Thermometer (DT) for each cancer center.

Cancer Center	HSI *n (%)*			SN *n (%)*			DT *n (%)*		
	Neg.	Pos.	Chi- squared X^2	Neg.	Pos.	Chi-squared X^2	Neg.	Pos.	Chi-squared X^2
Dermatooncology *(CDO)*	1375 *(71.8)*	540 (*21.8)*	X^2 = 72.16 *df* = 11 **p = .001** *n* = 4567	1855 *(94.8)*	101 *(5.2)*	X^2 = 311.96 *df* = 11 **p = .001** *n* = 4643	983 *(59.5)*	668 *(40.5)*	X^2 = 124.76 *df* = 10 **p = .001** *n* = 2306
Breast Cancer Center *(CBC)*	544 *(59.9)*	364 (*40.1)*		700 *(75.3)*	229 *(24.7)*		107 *(33.5)*	212 *(66.5)*	
Gynaecological Oncology *(CGynO)*	167 *(58.6)*	118 *(41.4)*		222 *(74.5)*	76 *(25.5)*		28 *(38.4)*	45 *(61.6)*	
Gastrointestinal Oncology *(CGO)*	219 *(64.0)*	123 *(36.0)*		280 *(81.4)*	64 *(18.6)*		22 *(34.9)*	41 *(65.1)*	
Urogenital Cancer (CUC)	279 *(76.6)*	85 *(23.4)*		336 *(92.1)*	29 *(7.9)*		7 *(50.0)*	7 *(50.0)*	
Malignant Lymphomas *(CML)*	106 *(65.0)*	57 *(35.0)*		117 *(71.8)*	46 *(28.2)*		1 *(12.5)*	7 *(87.5)*	
Head and Neck Cancer *(CHNC)*	122 *(61.9)*	75 *(38.1)*		161 *(80.9)*	38 (*19.1)*		20 *(28.2)*	51 *(71.8)*	

Table 5. (continuation)

Neurooncology *(CNO)*	199 *(65.5)*	105 *(34.5)*		243 *(81.3)*	56 *(18.7)*		30 *(36.1)*	53 *(63.9)*	
Sarcoma and GIST *(CSG)*	21 *(58.3)*	15 *(41.7)*		27 *(73.0)*	10 *(27.0)*		8 (*50.0)*	8 *(50.0)*	
Thoracic Oncology *(CTO)*	19 *(63.3)*	11 *(36.7)*		29 *(100)*	0 *(0)*		.	.	
NET-Center *(NET-C)*	7 *(77.8)*	2 *(22.2)*		7 *(70.0)*	3 *(30.0)*		0 *(0)*	1 *(100)*	
Other	11 *(78.6)*	3 *(21.4)*		12 *(85.7)*	2 *(14.3)*		3 *(42.9)*	4 *(57.1)*	

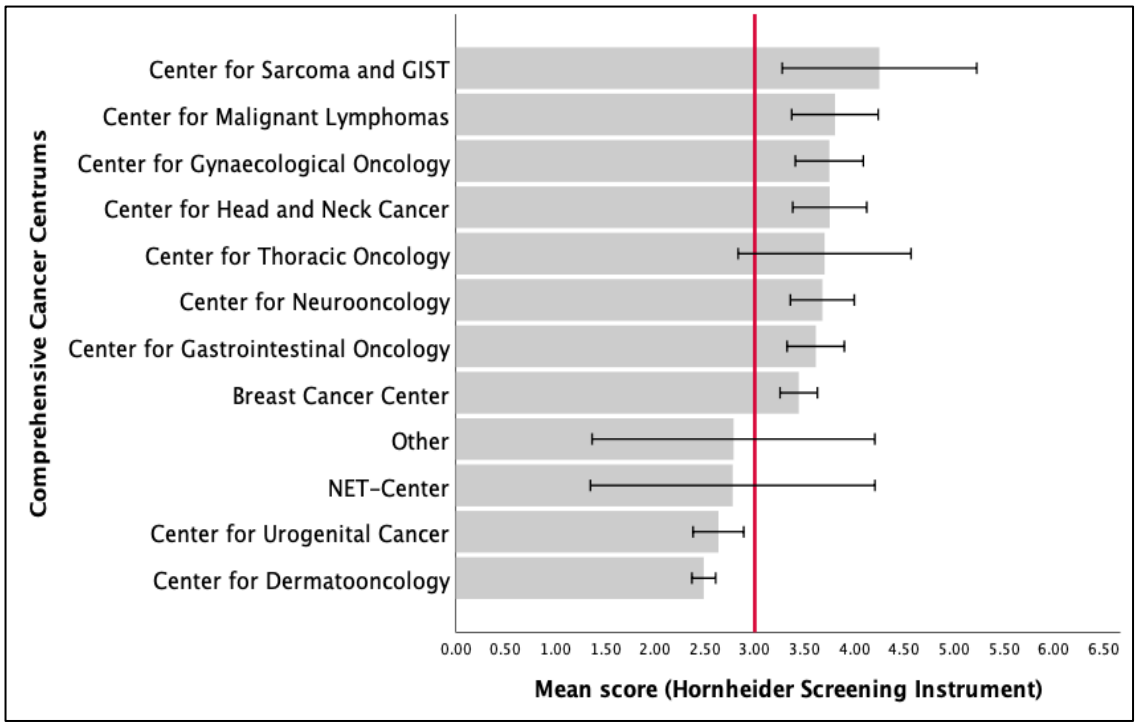

Figure 5. Mean scores of Hornheider Screening Instrument (HSI) with error bars and cutoff score at 3 for each of the cancer centers.

Post hoc comparisons using Bonferroni correction revealed non-significant differences between CDO (M = 2.49, SD = 2.66) and CUC (M = 2.63, SD = 2.47). Also, mean scores in CBC (M = 3.44, SD = 2.87), CGynO (M = 3.75, SD = 2.93), CGO (M = 3.61, SD = 2.70), CML (M = 3.80, SD = 2.80), CHNC (M = 3.75, SD = 2.64), CNO (M = 3.7, SD = 2.32) and CSG (M = 4.2, SD = 2.88) did not differ significantly. Mean scores between CDO, CUC and the other centers differ significantly in each of the cases.

Hypothesis 2.

In order to establish whether there is an effect of sociodemographic data on the experienced distress, screening instruments above 40% utiliziation (i.e. HSI, SN, DT) were included in the analysis. First, Chi-squared tests were performed on the binary screening results. The p-level was set at $p \leq .01$ after Bonferroni correction for multiple testing. Table 6. displays the results. Age is significantly associated with all three screening instruments. Unbalanced correlations are observed between conspicuous screenings and younger age in all screening tools. There is a significant relationship between gender and all three screening instruments. A disproportional association between females and conspicuous screening, was observed for all three instruments. The same was found for males and unremarkable screening. Further, single patients seemed to have an unbalanced relationship for conspicuous screening in HSI and SN, but not in DT. There is a significant association between housing situation and HSI, whereas a disproportional relationship between single living and conspicuous screening results was revealed. There is no relationship between SN, DT and housing situation. There is no significant relationship between having children and any of the screening instruments. Similarly, no significant relationship was revealed for education level and the screening instruments. A significant association was established between SN and employment status. An unbalanced relationship between employed status and conspicuous screening was indicated. In a second step, one-way ANOVAs for mean scores in HSI and DT were performed, as shown in Table 7. The HSI scores were standardized by taking their natural logarithm, to meet the assumptions of ANOVA. Age groups from 0-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90 and 91-100 were computed. The analysis revealed significant higher HSI scores for the age under than above 60. Though, there are no significant HSI differences between the refined age groups under 60 (< 40: M = 1.21, SD = .76; 40 – 49: M = 1.25, SD = .76; 50 – 59: M = 1.19, SD = .78). Same applies for age groups above 60 (60 – 69: M = 1.10, SD = .75; 70 – 79: M = 1.05, SD = .77; 80 – 89: M = 1.17, SD = .72, 90 ≤ : M = 1.14, SD = .69). For DT the same trends are valid. Women (M = 1.21, SD = .75) had significantly higher mean HSI scores than men (M = 1.06, SD = .77). The same

observation was implied for DT scores for women (M = 4.46, SD = 2.81) and men (M = 3.73, SD = 2.80). Further, single patients reached significantly higher scores in HSI (M = 1.29, SD = .70) than espoused patients (M = 1.42, SD = .64). Patients who lived alone had as well significantly higher HSI scores (M = 1.42, SD = .66) than those who lived with their partner, family or friends (M = 1.28, SD = .70).

Table 6. Mean score differences of Hornheider Screening Instrument (HSI), Subjective Need (SN) and Distress Thermometer (DT) for sociodemographic data.

	HSI n *(%)*			SN n *(%)*			DT n *(%)*		
Sociodemographic data	Neg.	Pos.	Chi- squared X^2	Neg.	Pos.	Chi-squared X^2	Neg.	Pos.	Chi-squared X^2
Age									
< 60	1468 *(65.2)*	784 *(34.8)*	X^2 = 6.85 *df* = 1	1841 *(80.5)*	445 *(19.5)*	X^2 = 92.85 *df* = 1	531 *(47.2)*	593 *(52.8)*	X^2 = 22.70 *df* = 1
60 ≤	1812 *(68.7)*	825 *(31.3)*	**p = .01** *n* = 4889	2427 *(90.1)*	266 *(9.9)*	**p = .001** *n* = 4979	692 *(57.1)*	520 *(42.9)*	**p = .001** *n* = 2336
Gender									
Female	1786 *(62.5)*	1072 *(37.5)*	X^2 = 67.85 *df* = 1 **p = .001** *n* = 4883	2398 *(82.0)*	526 *(18.0)*	X^2 = 81.83 *df* = 1 **p = .001** *n* =4973	641 *(47.8)*	700 *(52.2)*	X^2 = 26.18 *df* = 1 **p = .001** *n* =2336
Male	1493 *(73.7)*	532 *(26.3)*		1867 *(91.1)*	182 *(8.9)*		582 *(58.5)*	413 *(41.5)*	
Civil status									
In partnership	911 *(66.8)*	452 *(33.2)*	X^2 = 14.69 *df* = 1	1093 *(80.3)*	268 *(19.7)*	X^2 = 6.62 *df* = 1	218 *(36.2)*	384 *(63.8)*	X^2 = 2.35 *df* = 1
Single	119 *(53.6)*	103 *(46.4)*	**p = .001** *n* =1585	160 *(72.7)*	60 *(27.3)*	**p = .01** *n* = 1581	28 *(28.3)*	71 *(71.7)*	p = .13 *n* = 701

Table 6. (continuation)

Housing									
Alone	143 *(52.4)*	130 *(47.6)*	X^2 = 23.02	204 *(75.3)*	67 *(24.7)*	X^2 = 3.06	38 *(30.9)*	85 *(69.1)*	X^2 = .1.27
With partner/ children / parents	881 *(67.6)*	422 *(32.4)*	*df* = 1 **p = .001** *n* = 1576	1041 *(80.0)*	260 *(20.0)*	*df* = 1 p = .08 *n* =1572	208 *(36.2)*	366 *(63.8)*	*df* = 1 p = .26 *n* =697
Children									
Yes	852 *(66.5)*	430 *(33.5)*	X^2 = 5.30	1026 *(80.4)*	250 *(19.6)*	X^2 = 5.01	193 *(34.8)*	361 *(65.2)*	X^2 = .03
No	182 *(59.5)*	124 *(40.5)*	*df* = 1 p = .02 *n* = 1588	229 *(74.6)*	78 *(25.4)*	*df* = 1 p = .02 *n* = 1583	53 *(35.6)*	96 *(64.4)*	*df* = 1 p = .87 *n* = 703
Education									
Elementary/ secondary school	614 *(64.7)*	335 *(35.3)*	X^2 = .157 *df* = 1 p = .69	762 *(80.4)*	186 *(19.6)*	X^2 = 1.71 *df* = 1 p = .07	160 *(34.5)*	304 *(5.5)*	X^2 = .19 *df* = 1 p = .66
High school/ university degree	417 *(65.7)*	218 *(34.3)*	*n* = 1584	490 *(77.7)*	141 *(22.3)*	*n* =1432	86 *(36.1)*	152 *(63.9)*	*n* =702
Occupational status									
Self-employed	119 *(68.0)*	56 *(32.0)*	X^2 = 7.14	145 *(83.3)*	29 *(16.7)*	X^2 = 23.02	30 *(41.1)*	43 *(58.9)*	X^2 = 3.70
Employed	355 *(67.2)*	173 *(32.8)*	*df* = 3 p = .07	384 *(73.0)*	142 *(27.0)*	*df* = 3 **p = .001**	91 *(32.2)*	191 *(67.7)*	*df* = 3 p = .30
Unemployed/ pension	451 *(63.0)*	265 *(37.0)*	*n* = 1432	597 *(83.5)*	118 *(16.5)*	*n* = 1428	96 *(36.5)*	167 *(63.5)*	*n* = 625
In school	5 *(38.5)*	8 *(61.5)*		9 *(69.2)*	4 *(30.8)*		1 *(14.3)*	6 *(85.7)*	

Table 7. Mean score differences of Hornheider Screening Instrument (HSI), Subjective Need (SN) and Distress Thermometer (DT) for sociodemographic data. Note: HSI scores were normalised with the natural logarithms.

Sociodemographic data	HSI, *M (SD)*	One-way ANOVA, *F*	DT, *M (SD)*	One-way ANOVA, *F*
Age				
< 40	1.21 (.76)	*F* = 6.49	4.34 (2.80)	*F* = 11.05
40 – 49	1.25 (.75)	***p* = .001**	4.69 (2.82)	***p* = .001**
50 – 59	1.19 (.78)	*SS* = 22.51	4.59 (2.86)	*SS* = 517.91
60 – 69	1.10 (.75)	*n* = 4888	4.07 (2.71)	*n* = 2335
70 – 79	1.05 (.77)		3.38 (2.76)	
80 – 89	1.17 (.72)		3.77 (2.82)	
90 ≤	1.14 (.69)		3.88 (2.95)	
Gender				
Female	1.21 (.75)	*F* = 45.48	4.46 (2.81)	*F* = 38.77
Male	1.06 (.77)	***p* = .001**	3.73 (2.80)	***p* = .001**
		SS = 26.12		*SS* = 305.63
		n = 4883		*n* = 2336
Civil status				
In partnership	1.29 (.70)	*F* = 6.73	5.24 (2.55)	*F* = 2.25
Single	1.42 (.64)	***p* = .01**	5.66 (2.66)	*p* = .13
		SS = 3.23		*SS* = 14.81
		n = 1585		*n* = 701
Housing situation				
Alone	1.42 (.66)	*F* = 7.19	5.37 (2.62)	*F* = .12
With partner/ children parents	1.28 (.70)	***p* = .01**	5.28 (2.56)	*p* = .73
		SS = 3.46		*SS* = 3.46
		n = 1576		*n* = 697
Children				
Yes	1.29 (.70)	*F* = 4.129	5.31 (2.53)	*F* = .02
No	1.38 (.66)	*p* = .042	5.28 (2.68)	*p* = .89
		SS = 1.99		*SS* = .118
		n = 1588		*n* = 703
Education				
Elementary / secondary school	1.30 (.70)	*F* = .291	5.34 (2.54)	*F* = .37
Highs school / university degree	1.32 (.69)	*p* = .59	5.21 (2.56)	*p* = .54
		SS = .14		*SS* = 2.42
		n = 1584		*n* =702
Occupational status				
Self-employed	1.27 (.69)	*F* = .98	4.75 (2.50)	*F* = 3.17
Employed	1.30 (.71)	*p* = .40	5.60 (2.53)	*p* = .02
	1.33 (.68)	*SS* = 1.41	5.18 (2.58)	*SS* = 61.51
Unemployed / pension		*n* =1432		*n* = 625
In school	1.58 (.61)		6.57 (2.15)	

Hypothesis 3.

To examine whether clinical data affects the experienced distress, screening instruments above 40% utiliziation (i.e. HSI, SN, DT) were included in the analysis. First, Chi-squared tests were performed on the binary screening results. The p-level was set at $p \leq .02$ after Bonferroni correction for multiple testing. Table 8. summarizes the results. Patients with metastases have a significant higher mean score in HSI than patients with not classified tumours. Patients with metastases, primary and recurrent tumours scored significantly higher on DT than patients with not classified tumours. Patients with daily and occasionally psychotropic medication achieved significantly higher scores both in HSI and in DT compared to patients with no psychotropic medication. Also, patients who attended psychotherapy either in the past or currently, scored significantly higher in both HSI and DT in comparison to those, who never had psychotherapy. To further investigate the relationship between distress and clinical data, one-way ANOVAs were performed on standardized HSI and on DT scores (s. Table 9.). Patients with metastases have a significant higher mean score in HSI than patients with not classified tumours. Patients with metastases, primary and recurrent tumours scored significantly higher on DT than patients with not classified tumours. Patients with daily and occasionally psychotropic medication achieved significantly higher scores both in HSI and in DT compared to patients with no psychotropic medication. Also, patients who attended psychotherapy either in the past or currently, scored significantly higher in both HSI and DT in comparison to those, who never had psychotherapy.

*Table 8. Mean score differences of Hornheider Screening Instrument (HSI), Subjective Need (SN) and Distress Thermometer (DT) for clinical data. Note: data with * have been rounded.*

Clinical data	HSI *n (%)*			SN *n (%)*			DT *n (%)*		
	Neg.	Pos.	Chi- squared X^2	Neg.	Pos.	Chi- squared X	Neg.	Pos.	Chi- squared X^2
Tumour classification									
No classification	573 *(64.7)*	313 *(35.3)*	X^2 = 13.75	790 *(86.6)*	122 *(13.4)*	X^2 = 16.62	245 *(55.2)*	199 *(44.8)*	X^2 = 23.02
Primary	1157 *(68.3*)	538 *(31.7)*	*df* = 4	1405 *(82.9)*	289 *(17.1)*	*df* = 4	394 *(44.5)*	491 *(55.5)*	*df* = 4
Metastasis	84 *(64.1)*	47 *(35.9)*	**p = .01***	100 *(76.9)*	30 *(23.1)*	**p = .001***	17 *(33.3)*	34 *(66.7)*	**p = .001**
Recurrent	48 *(54.5)*	40 *(45.5)*	*n* = 2820	66 *(75.0)*	22 *(25.0)*	*n* =2844	13 *(18.3)*	30 *(69.8)*	*n* =1440
Secondary	9 *(45.0)*	11 *(55.0)*		15 *(75.0)*	5 *(25.0)*		7 *(17.9)*	10 *(58.8)*	
Psychotropic medication									
Never	916 *(68.3)*	425 *(31.7)*	X^2 = 41.34	1096 *(81.8)*	244 *(18.2)*	X^2 = 40.24	224 *(37.7)*	370 *(62.3)*	X^2 = 11.39
Daily	77 *(47.8)*	84 *(52.2)*	*df* = 2	97 *(60.6)*	63 *(39.4)*	*df* = 2	13 *(18.3)*	58 *(81.7)*	*df* = 2
Occasionally	41 *(46.1)*	48 *(53.9)*	**p = .001**	64 *(74.4)*	22 *(25.6)*	**p = .001**	10 *(27.8)*	26 *(72.2)*	**p = .001***
			n = 1591			*n* =1586			*n* =701
Psychotherapy									
Never	874 *(68.6)*	400 *(31.4)*	X^2 = 36.79	1070 *(84.3)*	199 *(15.7)*	X^2 = 99.49	213 *(38.2)*	345 *(61.8)*	X^2 = 11.39
In the past	120 *(51.9)*	111 *(48.1)*	*df* = 2	138 *(60.0)*	92 *(40.0)*	*df* = 2	27 *(25.7)*	78 *(74.3)*	*df* = 2
Currently in treatment	41 *(47.1)*	46 *(52.9)*	**p = .001**	49 *(56.3)*	38 *(43.7)*	**p = .001**	7 *(17.9)*	32 *(82.1)*	**p = .001***
			n = 1592			*n* = 1586			*n* = 702

Table 9. Mean score differences of Hornheider Screening Instrument (HSI), Subjective Need (SN) and Distress Thermometer (DT) by clinical data. Note*: HSI scores were normalised with the natural logarithms.*

Clinical data	HSI, *M (SD)*	One-way ANOVA *F*	DT, *M (SD)*	One-way ANOVA *F*
Tumour classification				
No classification	1.15 (.77)	*F* = 6.48	4.06 (2.84)	*F* = 7.30
Primary	1.21 (.73)	***p* = .001**	4.60 (2.80)	***p* = .001**
		SS = 14.15		*SS* = 230.81
Metastasis	1.41 (.61)	*n* = 2820	5.51 (2.68)	*n* = 1440
Recurrent	1.38 (.79)		5.77 (2.66)	
Secondary	1.63 (.58)		5.41 (3.41))	
Psychotropic medication				
Never	1.26 (.69)	*F* = 20.83	5.09 (2.56)	*F* = 12.83
Daily	1.56 (.67)	***p* = .001**	6.62 (2.13)	***p* = .001**
		SS = 19.56		*SS* = 163.71
Occasionally	1.56 (.68)	*n* = 1591	5.94 (2.57)	*n* = 701
Psychotherapy				
Never	1.25 (.69)	*F* = 23.68	5.10 (2.56)	*F* = 9.11
In the past	1.55 (.64)	***p* = .001**	5.88 (2.38)	***p* = .001**
		SS = 22.19		*SS* = 22.19
Currently in treatment	1.51 (.74)	*n* = 1592	6.54 (2.30)	*n* = 702

Hypothesis 4.

Whether conspicuous screening results were consecutively followed by psycho-oncological counselling, counselling records in the electronic patients' files were evaluated. For that, patients with missing data about gender, age, treating cancer center and multiple screenings were excluded from further analysis. In total 1837 patients showed conspicuous screening either in HSI or claimed subjective need for counselling. After comparing these results with the internal psycho-oncological list for gynaecological patients, additional 10 patients received counselling before participating in the screening process. They were included in the further analysis as well. All the 1847 patients' files were analysed (s. Table 10.). 67% of this subpopulation were female, the age ranged between 18 and 94 years with a mean of 59.26 years (SD 14.24). In 58% of the cases there were no

Table 10. Counselling for patients with conspicuous screening (n = 1847).

Counselling records	n	%
No record	1080	58.5
No records, patient probably already under psycho-oncological supervision	101	5.5
Record: conspicuous screening is justified	197	10.6
Record: conspicuous screening is not justified	56	3.0
Record: a followup appointment was recommended	96	5.2
Record: a followup appointment was recorded as well	167	9.0
Record: counselling not possible	44	2.4
Record: short contact, information about counselling options	106	5.8

documented counselling in SAP©. 5% eventually did not need counselling, as record showed that they underwent psychological treatment during the study. In 2% of the cases counselling was not possible (e.g. the patient has already left the clinic, language difficulties, cognitive or physical barriers). In total we have psycho-oncological recordings for 28% of the patients with conspicuous screening. In 11% of these cases the conspicuous screening could be justified, that is, patients did wish further counselling or support. For 5% a new appointment has been offered but not documented. 9% of the patients met the psycho-oncologists more than one time. 6% of the patients received information in a short counselling appointment. For 3% the conspicuous screening could not be justified.

Further, 195 patients with unremarkable screening results in both HSI and SN were randomly selected as described in the materials section and the counselling records were evaluated. 54 % of this subpopulation were female, the average age was 63.05 years with a range between 18 and 94 years and SD of 15.15. In 35 of the cases (17.95 %) there was a record of counselling despite the unremarkable screening results. Table 11. shows the evaluation in detail.

Table 11. Counselling frequencies for patients with unremarkable screening (n = 195).

Counselling records	n	%
No record	141	72.29
No records, patient probably already under psycho-oncological supervision	17	8.72
Record: counselling is justified	16	8.21
Record: a followup appointment was recommended	7	3.58
Record: a followup appointment was recorded as well	6	3.08
Record: counselling not possible	2	1.03
Record: short contact, information about counselling options	6	3.08

The relationship between cancer centers and counselling was investigated with Chi-squared tests (Table 12.). There is an unbalanced association between counselling and CDO, CGynO, CGO, CML and CHNC. The lack of counselling was associated with CGO and CML.

Table 12. Comparison of counselling frequencies after conspicuous screening results in each of the cancer centers.

Cancer center	Counselling n *(%)*		Chi- squared X^2
	No	Yes	
Dermatooncology *(CDO)*	571 *(93.1)*	42 *(6.9)*	
Breast Cancer Center *(CBC)*	274 *(56.6)*	210 *(43.3)*	X^2 = 286.01
Gynaecological Oncology *(CGynO)*	94 *(60.6)*	61 *(39.4)*	*df* = 11
Gastrointestinal Oncology *(CGO)*	82 *(47.4)*	91 *(52.6)*	**p = .001**
Urogenital Cancer *(CUC)*	69 *(67.6)*	33 *(32.4)*	*n* = 1882
Malignant Lymphomas *(CML)*	40 *(43.5)*	52 *(56.5)*	
Head and Neck Cancer *(CHNC)*	50 *(54.9)*	41 *(45.1)*	
Neurooncology *(CNO)*	85 *(64.9)*	46 *(35.1)*	
Sarcoma and GIST *(CSG)*	9 *(69.2)*	4 *(30.8)*	
Thoracic Oncology *(CTO)*	8 *(44.4)*	10 *(55.6)*	
NET-Center *(NET-C)*	3 *(60.0)*	2 *(40.0)*	
Other	2 *(40.0)*	3 *(60.0)*	

For the comparison between sociodemographic data and counselling a p-value of $p \leq .01$ was set after the Bonferroni correction for multiple testing. The Chi-squared tests between counselling and civil status, $X^2(1, N = 751) = 3.96$, $p = .05$, housing situation $X^2(1, N = 748) = 1.59$, $p = .21$, children, $X^2(1, N = 749) = 3.10$, $p = .08$, education, $X^2(1, N = 315) = .02$, $p = .88$ and employment, $X^2(3, N = 671) = 8.13$, $p = .04$ indicated no significant association between sociodemographic data and counselling. With $X^2(1, N = 2037) = 15.66$, $p = .001$ there is a significant

relationship between gender and counselling. There is an unbalanced association between men and counselling.

For the Chi-squared tests between clinical data and counselling a Bonferroni-adjusted p-value of $p \leq .02$ was set. Neither psychotropic medication, $X^2(2, N = 753) = 6.63$, $p = .04$ nor psychotherapy, $X^2(2, N = 753) = 6.64$, $p = .04$ differ significantly between their subgroups. Cancer classification is significantly associated with counselling, $X^2(4, N = 2037) = 67.21$, $p = .001$. There are unbalanced relationships between counselling and no classification, metastases and secondary tumours, just as between the lack of counselling and metastases and secondary tumours.

As Table 12. points out, in some cancer centers conspicuous screening results maye not have been followed by counselling. An underlying cause could have been the disproportional ratio of outpatients in those centers. In general, for outpatients it can be more challenging to organize the needed counselling (e.g. difficulties in finding an appointment that fits both the patients and the psycho-oncologists, as they are only temporarly in the cancer centers). To investigate whether outpatients played a role in counselling efficacy, they were excluded from further analysis (s. Table 13. in Hypothesis 5.).

Hypothesis 5.

To understand whether the applied screening instruments correctly measured patient's need for counselling, the electronic patients' files were analysed. All n = 1847 patients with conspicuous HSI or SN were included. Additional 195 with unremarkable screenings were randomly chosen as described in Hypothesis 4. The construct validity (i.e. counselling readiness or indication) was labelled as correct, if at least one of the screenings was conspicuous and patients accepted at least once a counselling appointment. The indication was incorrect, if patients rejected the counselling appointment despite of conspicuous screening results or there was at least one record of counselling despite of the screening results. Unclear counselling needs resulted from imprecise records, documented language barriers or patients' absence. Table 13. displays the relationship between counselling and screening (n = 1167 without outpatients).

Table 13. Counselling records summary. Note[1]: screening based on Hornheider Screening Instrument and / or Subjective Need. Note[2]: Outpatient care was excluded from further analysis.

Counselling records	n	%
Conspicuous screening, counselling record	403	69.1
Conspicuous screening, patient rejects counselling	39	6.7
Unremarkable screening, no counselling recorded	74	12.7
Unremarkable screening, counselling record	45	7.7
Conspicuous screening, but patient already under psycho-oncological counselling	22	3.8
No post hoc analysis possible	584	56.0

For the gynaecological clinics (CGynO and CBC) detailed information were ad hoc automatically collected by ePOS (ePOS-react). The relationships between the automatically offered intervention (based on the sreening results) and whether counselling occured, were documented in an Excel file. Table 14. summarizes the results of the 286 patients. If both HSI and SN indicated need for counselling (91 cases), 56% of the patients met with a psycho-oncologist. 21%

chose information above counselling and 2 % did not wish any interventions. 21 % of them did not see a psycho-oncologists despite their counselling wish in ePOS and a reason for that was not systematically recorded. When HSI indicated counselling, but patients answered SN with ‘no’ (112 cases), 76% did not receive counselling.11 of those, who wanted to receive informations, ended up having counselling and only 1% wanted to meet with a psycho-oncologist. In 48 of the cases, when HSI did not indicate the need for counselling, but patients answered SN with ‘yes’, 44% received counselling and 35% chose information instead. Surprisingly, 32% of the 34 patients with no indication at all chose to receive further information, 6% of them wished to meet a psycho-oncologist.

Table 14. Ad hoc collected correlations between automatically offered interventions, chosen interventions, and whether counselling occurred (n = 286).

HSI	**SN**	**Suggested intervention**	**Patients’ choice**	**POD n** (%)	
				Yes	**No**
Yes	Yes	Counselling	Counselling	51 *(56.0%)*	19 *(20.9%)*
			Information	14 *(15.4%)*	5 *(5.5%)*
			No intervention	1 *(1.1%)*	1 *(1.1%)*
	No	Information	Information	12 *(10.62%)*	10 *(8.9%)*
			Counselling	1 *(0.9%)*	2 *(1.8%)*
			No intervention	3 *(2.7%)*	85 *(75.9%)*
No	Yes	Counselling	Counselling	21 (*43.8%)*	7 *(14.6%)*
			Information	3 *(6.3%)*	14 (*29.2%)*
			No intervention	0 (*0.0%)*	3 *(6.3%)*
	No	No intervention	No intervention	4 *(11.8%)*	17 (50*.0%)*
			Information	8 *(23.6%)*	3 *(8.8%)*
			Counselling	1 *(2.9%)*	1 *(2.9%)*

In a second step, all the screening instruments were compared whether the screening results predicted counselling correctly. To achieve that, only unambigous data from the post hoc collection were included in further analysis. That is, at least one meeting with a psycho-oncologist was recorded, or records distinctively show that patients did not wish counselling when offered. All other possibilities (s. Table 10. and 11.) were excluded from this analysis. Further, as discussed earlier, outpatients were excluded as well. After that, the mean age in the subpopulation changed to 57.88 years with a range between 18-94 (SD 13.96). Moreover, the ratio of female patients increased to 74%.

As for the screening tools, HADS and FBK -10 were not included in the analysis due to too small sample sizes (n = 3 for HADS). The p-values were Bonferroni adjusted to $p \leq .01$. The results in detail are offered in Table 15. There is a significant relationship between GAD - 7 and the predicted counselling readiness, $X^2(4, N = 261) = 12.72$, $p = .01$. Unbalanced associations were found for rejecting the counselling and minimal, just as mild anxiety. Further, there is a connection between PHQ - 2 and counselling readiness, $X^2(1, N = 260) = 10.97$ $p = .001$. A disproportional relationship was found for rejecting the counselling and no signs of depression. All the other performed Chi-squared tests brought no significant relationships between the screening results and counselling readiness (s. Table 15.)

In a third step ROC curves were calculated for the screening instruments to investigate their ability to predict counselling, under the same conditions as mentioned before. Furthermore, outpatients have been excluded from this part of the analysis to avoid falsely underestimation of the counselling ratio. HADS and FBK - 10 could not be included to the analysis due to small sample sizes (HADS = 3, FBK – 10 = 22). As in the standard screening procedure SN was the crucial instrument to decide whether counselling was offered (s. Figure 2.), DT, PHQ and GAD were always compared to SN. Despite SN not providing fine grained scores, the ROC analysis is still a meaningful method to compare its efficacy with the other instruments which have continuous scores. Figure 6. displays the results for HSI and SN. For a subpopulation of 1107 patients HSI had an Area under the curve (AUC) of 0.469 and SN 0.717. These findings are not surprising as

*Table 15. Comparison counselling readiness by screening instruments. Note[1]: Outpatient care was excluded from further analysis. Note[2]: Hospital Anxiety and Depression Scale (HADS), Distress of Cancer Patients Questionnaire (FBK-10) could not be included in the analysis due to small sample sizes. Note[3]: with * marked data are rounded.*

Screening Instruments	Counselling n *(%)*		Chi- squared X^2
	No	Yes	
Hornheider Screening Instrument			
Unremarkable	131 *(51.4)*	124 *(48.6%)*	X^2 = 6.44
Conspicuous	528 *(60.3)*	348 *(39.7)*	*df* = 1 **p = .01*** *n* = 1131
Subjective Need			
No	470 *(77.2)*	139 *(22.8)*	X^2 = 199.55
Yes	183 *(35.5)*	333 *(64.5)*	*df* = 1 **p = .001** *n* = 1125
Distress Thermometer			
Practical problems			
No problems	682 *(58.0)*	493 *(42.0)*	X^2 = . p = . *n* = 1175
≥1 problems named	0 *(0)*	0 *(0)*	
Family problems			
No problems	664 *(58.2)*	476 *(41.8)*	X^2 = .648
≥1 problems named	18 *(51.4)*	17 *(48.6)*	*df* = 1 p = .42* *n* = 1175
Emotional problems			
No problems	640 *(58.4)*	456 *(41.6)*	X^2 = .83*
≥1 problems named	42 *(53.2)*	37 *(46.8)*	*df* = 1 p = .36* *n* = 1175
Spiritual or religious concerns			
No problems	670 *(58.0)*	486 *(42.0)*	X^2 = .208
≥1 problems named	12 *(63.2)*	7 *(36.8)*	p = .65* *df* = 1 *n* = 1175
Physical problems			
No problems	682 *(58.0)*	493 *(42.0)*	X^2 = . p = . *n* = 1175
≥1 problems named	0	0	
Generalized Anxiety Disorder - 2			
Unremarkable	246 *(58.4)*	175 *(41.6)*	X^2 = 14.74*
Conspicuous	51 *(40.8)*	79 *(60.8)*	*df* = 1 **p = .001** *n* = 551
Generalized Anxiety Disorder -7			
No anxiety	222 *(61.7)*	138 *(38.3)*	X^2 = 26.13*
Minimal anxiety	51 *(40.8)*	74 *(59.2)*	*df* = 4 **p = .001** *n* = 554
Mild anxiety	15 *(36.6)*	26 *(63.4)*	
Moderate anxiety	9 *(40.9)*	13 *(59.1)*	
Severe anxiety	1 *(20.0)*	4 *(80.0)*	

Table 15. (continuation)

Patient Health Questionnaire- 2			
Unremarkable	72 *(68.6)*	33 *(31.4)*	X^2 = 11.366*
Conspicuous	224 *(50.3)*	221 *(49.7)*	*df* = 1 **p = .001*** *n* = 550
Patient Health Questionnaire- 8			
No depression	24 *(51.1)*	23 *(48.9)*	X^2 = 4.49*
Minimal depression	43 *(48.3)*	46 *(51.7)*	*df* = 4 p = .34*
Mild depression	19 *(38.8)*	30 *(61.2)*	*n* = 206
Moderate depression	4 *(24.0)*	12 *(75.0)*	
Severe depression	2 *(40.0)*	3 *(60.0)*	

indication for counselling in HSI always has been followed by the answering of SN and the results of SN decided whether counselling is necessary or not. The right side of Figure 4 displays the ROC curves for SN and DT for a subpopulation of 249. SN shows here an AUC of 0.681 and DT 0.541, SN whereas shows higher accuracy at a false positive ratio under 0.2 and at 0.7. Given the binary nature of SN, it will never achieve an accuracy above 0.8. Additionally, a combined model for SN and DT was computed (s. Hypothesis 6.).

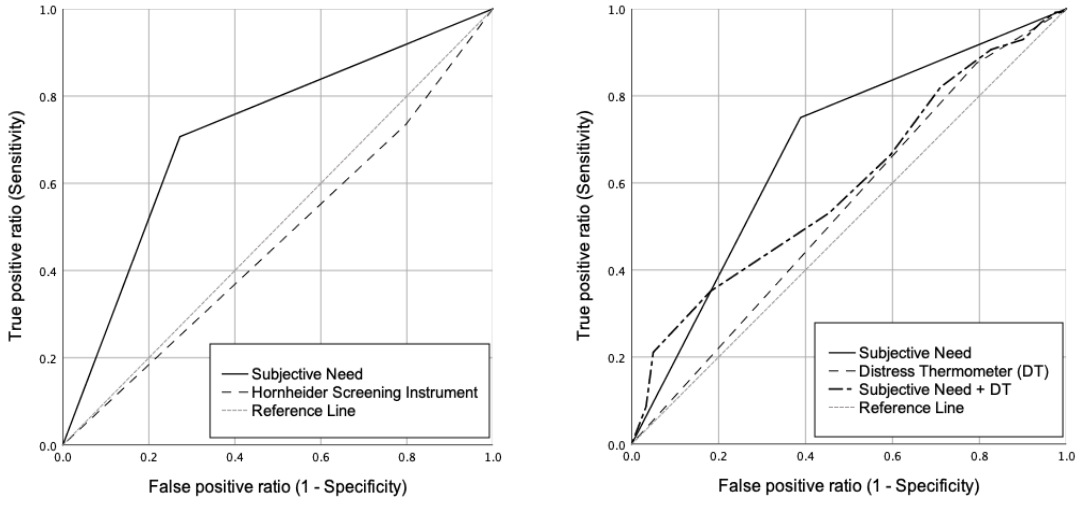

Figure 6. ***Left:*** *ROC curves of the Hornheider Screening Instrument (AUC = 0.469) and Subjective Need (AUC = 0.717) as predictors of counselling (n = 1107).* ***Right****: ROC curves of Subjective Need (AUC = 0.681), Distress Thermometer (AUC = 0.541) and their combined model (AUC = 0.596) as predictors of counselling (n = 249).*

Figure 7. summarises the findings for PHQ – 2 and -8. PHQ -2 had an AUC of 0.599 for a subpopulation of 549, whereas SN showed 0.735. PHQ – 8 could be tested on 206 patients with an AUC of 0.582 and increased false positive predictions for central scores. SN had in the same subpopulation an AUC of 0.691. The combined models of SN and respectively PHQ – 2 and – 8 will be presented in the next section (s. Hypothesis 6.).

For GAD – 2 and GAD – 7 the sample sizes were almost equal (respectively n = 551 and n = 553). GAD – 2 had an AUC of 0.605 (whereas SN 0.735) and GAD – 7 of 0.638 (SN had 0.736). The combined models of GAD – 2 and SN, just as GAD – 7 and SN will be described in Hypothesis 6.

Taken all together, because of the binary nature of SN it will never reach more than 0.8 sensitivity. Nonetheless, compared to all other screening instruments it shows a clearly higher sensitivity at a false positive ratio of 0.4.

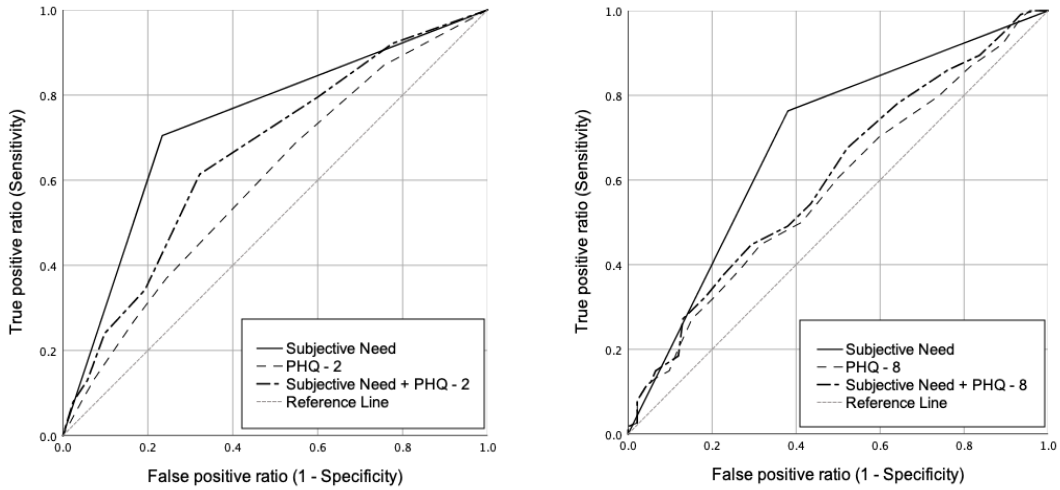

Figure 7. ***Left:*** *ROC curves of Subjective Need (AUC = 0.735), Patient Health Questionnaire 2, PHQ - 2 (AUC = 0.599) and their combined model (AUC = 0.663) as predictors of counselling (n = 549)****. Right****: ROC curves of Subjective Need (AUC = 0.691), Patient Health Questionnaire 8, PHQ - 8 (AUC = 0.582) and their combined model (AUC = 0.606) as predictors of counselling (n = 206)****.***

Hypothesis 6.

To examine whether the specificity and sensitivity of the standard screening instruments (HSI and SN) can be improved by adding additional instruments, SN was combined with DT, PHQ – 2 / -8 and GAD – 2 / - 7 (s. Figures 6-8.). The methods of the analysis were the same as described in Hypothesis 5.

When combining DT with SN, the AUC of the new model was 0.596, which does not improve the ROC curve of SN. The combined model of PHQ – 2 and SN was 0.663 and here neither seemed to be beneficial for SN. The combination of PHQ – 8 and SN showed an AUC of 0.606, which was slightly higher than the AUC of of PHQ – 8. At last, both the combined model with SN and GAD – 2 (AUC of 0.666) and with GAD – 7 (AUC of 0.671) did not bring an increase of AUC compared to SN alone.

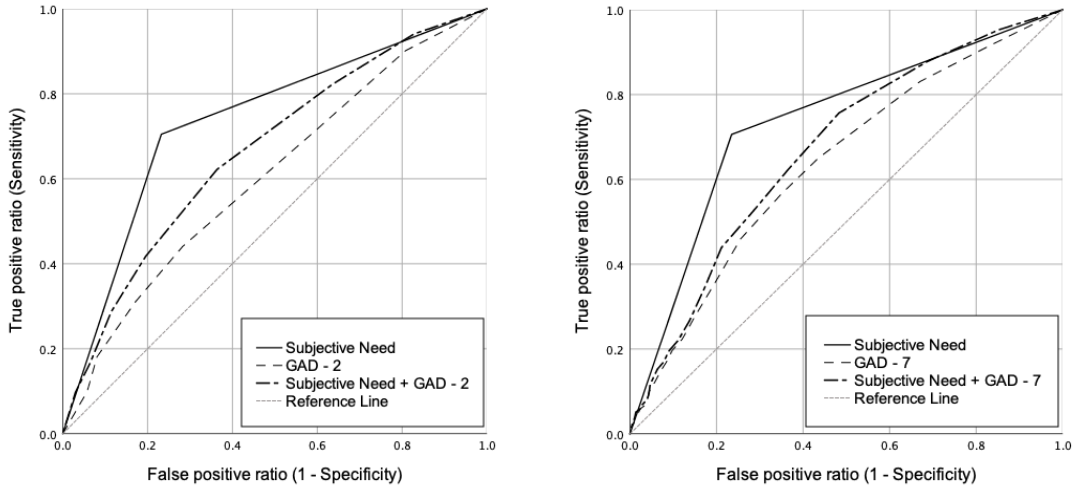

Figure 8. ***Left:*** *ROC curves of Subjective Need (AUC = 0.736), General Anxiety Disorder Scale 2, GAD – 2 (AUC = 0.605) and their combined model (AUC = 0.666) as predictors of counselling (n = 551)****. Right:*** *ROC curves of Subjective Need (AUC = 0.735), General Anxiety Disorder Scale 7, GAD – 7 (AUC = 0.638) and their combined model (AUC = 0.671) as predictors of counselling (n = 553)****.***

Hypothesis 7.

To investigate whether the short versions of PHQ and GAD are comparable sensitive and specific as their long versions and as the standard screening instruments (HSI and SN) Chi-squared tests were performed. Therefore, the same procedure was implemented as described in Hypothesis 5 and 6. Results regarding the construct validity (i.e. counselling readiness) are offered in Table 13. Both the short and the long versions of PHQ and GAD had similar or lower p-values than HSI and SN. For PHQ - 2 and GAD - 7 significant associations with counselling readiness were found (s. Hypothesis 5.).

In a second step, ROC analysis was implemented for both GAD and PHQ (s. Hypothesis 5. and 6.). As already described before, neither the short, nor the long versions of these tests were beneficial for the sensitivity of SN. However, the visual comparison of their ROC curves does not show a significant difference between short and long versions either.

4. Discussion

The aim of this current study was not only to evaluate the effectivity and optimize the screening tools in the **e**lectronical **P**sycho**O**ncology **S**creening (ePOS) system, but also to identify vulnerable patient clusters with distinct need for psycho-oncological care. For that, a retrospective analysis was performed on the screening, sociodemographic and clinical data gained from ePOS in the year 2018. When after conspicuous screening results in Subjective Need (SN) and Hornheider Screening Instrument (HSI) the psycho-oncological service was involved, their electronical notes were included in this current study. To grant that, over 2000 patients files have been read and analysed. Additionally, further possibilities to enhance ePOS with other screening instruments were investigated. Due to a rather heterogenous, large sample size and regular data collection current discoveries are well suited for adaptation in the clinical routine.

Our analysis revealed significantly different distress levels among the cancer centers. Patients with gynaecological cancer types showed the highest levels of subjective and objective distress, whereas patients with urogenital and dermatological tumours suffered the least from it. These and some further findings align to previous research results, e.g. the especially high distress for soft tissue cancer and brain tumours, the elevated distress for head and neck cancer and lymphomas or the comparable lower distress for breast cancer and dermatological tumour types.[3,7,12,18] However, our results show two rather surprising phenomena.

First, in the Center for Thoracic Oncology (CTO) screening tools as SN, HSI or Distress Thermometer (DT) revealed lower distress ranking than in any of the reference studies[3,12,40,49]. On the one hand, CTO was one of poorest represented cancer center with n = 38 patients included in the analysis, which could explain these results. On the other hand, since the early 2000's terminal lung cancer treatment underwent significant changes, which induced longer survival times and better quality of life for some lung cancer types.[50-52] These positive changes might be mirrored in decreased distress levels as previously suggested by Polanski et al. (2016)[49]. In the current study we did not differentiate lung cancer

types, which could have affected our results. On the other hand, belief in self-induced cancer (e.g. due to smoking) has been shown to be related to higher guilt and shame, such as to lower help-seeking behaviour[53,54] Additionally, the high variance of distress and small number of patients in CTO allows biases in the interpretation of our results.

Second, the relationship of distress levels between breast cancer and gynaecological cancers, which was shown to be identical by both Herschbach[12] and Zabora[3], changed. Our results show higher distress for gynaecological cancer types than for breast cancer. Interestingly, the same phenomenon has been showed by Mehnert et al. (2018)[7] and Herschbach et al. (2020)[55]. As both centers were well represented in our dataset, statistical biases are very unlikely. The lower distress for CBC might be due to the improved psycho-oncological care for breast cancer patients in the last decade, as this trend reflects in previous findings too. Furthermore, there is strong evidence that the most important single distress is fear of cancer progression.[12,55-57] A reduction of disease related fear can be evoked by the counselling options, as frequently observed in clinical psychotherapy[56,58]. Strong evidence suggests, that actively asking about the subjective need for psycho-oncological treatment, but also just providing information about the support options, lead to decreased distress in the longterm.[40,59] Regarding the treatment policies in CBC, as soon as breast cancer patients receive their diagnosis, medical personnel automatically and repeatedly presents them a handful of counselling options: self-help groups, psycho-oncological counselling, mindfulness programs, etc.[36,39] In the CBC the decision regarding treatment was recorded as well, and it shows, that approximately 75% of the patients with conspicuous screening chose further psycho-oncological care. More interestingly, half of the patients whose screening turned out to be unremarkable, chose treatment or information anyways. These results might open a new point of view: they suggest that screenings per se are an important part of psycho-oncological counselling, as they motivate patients for structured self-reflection. Günther et al. (2021) point out that especially historically undervalued groups as e.g. elderly men can profit from routine screenings.[37] Our results could offer a novel explanation for their findings if we consider, that

targeted questions about cancer patients well-being, distress and resources could lead patients to realize their deficits and need for support – even if they did not consciously noticed them before.

In addition, progressed treatments and mortality decline for breast cancer can be considered as an underlying cause for low distress in CBC.[60,61] In the first half of the 20th century the classical treatments, such as radical mastectomy and radiochemotherapy took toll on both the physical and the mental state without convincing results. In the last two decades not only the surgical methods became less radical and more aesthetics-orientated, but fine-tuned screening methods, targeted hormonal therapies and personalized medicine with gene expression analysis improved patients' well-being and life expectancies.[62,63]

At the same time, a clear development of prevention and screening methods in gynaecological oncology led to decreasing incident of cervix carcinomas and earlier diagnostic of hereditary ovarian cancer[64-66]. However, therapy options did not change drastically: especially in the presence of metastases still radical surgery and intensive chemotherapy are recommended to improve the 5-years survival chances.[67-69] Overall, though these actions generated less hospitalization, current inpatient collectives possibly involve more late stages carcinomas with poor recovery prospects. Hence, the changed distress level order for breast cancer and gynaecological carcinomas seems plausible. It also implies that cancer specific distress levels might be characteristic, but they can respond to advanced recovery standards.

Our results on sociodemographic correlates of distress showed higher vulnerability and more help-seeking for patients who were younger than 60 years, female and spouseless or single living. These findings were congruent to previous research results.[6,9-13,19,53,55,56,70-72] First, as opposed to the results of Ellis et al. (2009) and Lester et al. (2015) we did not find significantly increased distress specifically under 40, but rather for under 60. The analyses did not reveal significant differences between other age groups either. It is important to note, that our sample had an almost identical mean age and standard deviation to aforementioned study and the age distribution matched the expectancies for cancer incident in Germany (s. Figure 1). Moreover, we found unbalanced age

distributions between the cancer centers, most likely given by the nature of tumour types[15]. As specific cancer types tend to occur in a certain age and given the nature of their progression they lead to (more or less) distress, which could mean that age possibly interacts as a mediator between cancer types and distress.

Second, we found higher distress in case of a reduced close support net, such as being spouseless or living alone. Notably, the existence of children did not affect the distress level, hence the comparable high average age of the participating patients suggests reduced anxiety regarding grownup children. The heterogenous average age in the cancer centers could impact these findings as well.

As an additional finding, higher distress levels for women are commonly explained with gender-specific social norms, different coping mechanisms and communication tools which may benefit higher scores on verbal screening tests.[72,73 7,9,11,12,72]

Fourth, the applied screening tests seem suitable for a wide range of patients, as educational and employment status surprisingly did not impact the distress level. However, employed patients claimed more frequently subjective need for counselling. Several factors could contribute to these findings (e.g. other sociodemographic factors, personality traits, health system infrastructure etc.). As in the current study we could not investigate those correlations, the interpretations of these results are limited and require further research.

As for the correlations between clinical data and distress, our findings showed higher distress for recurrent cancer types or metastases, for patients who were consuming psychotropic medication and for those, who underwent psychological treatment currently or in the past. Supporting previous evidence, expectancies regarding the tumour status seem to have a large effect on distress.[12,14] We found that recurrent cancer was correlated to elevated distress, more than secondary tumours or even metastases. However, our findings are strongly limited due to the naturalistic data collection as clinical data was not recorded systematically by trained personnel. Nonetheless, learning experiences with a cancerous disease and the related difficulties or else the lack of these might correlate with these

findings.[6,9,55,74,75] Second, tumours with high tendency of recurrence are commonly considered more life-threatening, associated more with a seriously impacted health and therapy can be more aggressive than benign tumour types[6,9,11,74]. Thus, it could plausibly result in high distress levels. In addition, it stays unclear, whether especially vulnerable patients tend to turn to regular psychotropic medication and engage counselling services or rather patients with improved self-observing skills detect their elevated distress and try to cure it with the best available method from early on.[6,11,14,71,75]

An additional goal of the present work was to evaluate the psychometric distress screening in clinical routine (ePOS) and its psycho-oncological clinical pathways. Approximately for 40% of the patients with conspicuous screening existed a recorded contact with psycho-oncologists. At the time of data collection, clinic-wide screening and the ePOS system was primarily a clinical routine pathway and only secondary a research project. Hence, recordings were not systematic, and they rather provided supporting information for the psycho-oncologists than offered basis for post-hoc studies. We do not have further information about why only 40% of the remarkable screenings were followed by psycho-oncological contact. Furthermore, we cannot imply for sure, whether the remaining 60% of patients did not have contact or the contact was simply not recorded. To properly examine this issue, further studies with systematic, clinic-wide recordings are needed. (Following the first analysis in this current study, significant changes in the psycho-oncological care took place in the CCC. Thenceforth outpatients receive systematically information about supportive programs and their routine screening is being optimized as well.)

Another explanation could be, that in the CDO, the most represented cancer center patients from same-day-surgery and chemotherapy were recruited. These patients were screened just before their treatment and in most of the cases their future oncological care took place as an outpatient. This setting complicates the follow-up for psycho-oncologists and reduces patients' interest in counselling. To avoid structural biases, outgoing patient have been excluded from further analysis. This led to an increased counselling rate of 70%, whereas 7% actively rejected counselling. We additionally analysed a randomly selected subgroup

with unremarkable screenings. Here we found that later 18% of them underwent counselling.

As already discussed, the received counselling and rejection rates are overall comparable with the rates in the CBC, where we know that a quarter of conspicuous screenings and positive subjective need was not followed by a wish for counselling. Shimizu et al. (2010) showed similar results to ours.[76] In their study those 25% who did not get further counselling reported, that they received sufficient support from their social support net.[40] Furthermore, previous findings suggest, that the timing of screening might be crucial as well.[8,77] Distress, as a normal reaction to the cancer diagnoses can be transient and eventually fades away with time, but it can become stronger as well.[78] Some patients showed strong distress before treatment, but they might not have experienced overwhelming distress later on and therefore they did not accept counselling. On the other hand, a fifth of the patients with unremarkable screening sought help later. This is not surprising, as distress is a highly variable concept which not only depends on stable factors (e.g. personality traits), but also on momentary internal and external influences.[6,8,9] Correspondingly, we found a higher rejection rate among patients who showed milder signs of anxiety or depression at the time of data collection. Salmon et al. (2015) recommends therefore targeted screenings in critical moments during the oncological progress instead of pinpointed single measurements.[59] In the recent study patients have been only screened when admitted to the hospital, when distress expected to be at the peak and we have no data about the development of their distress. Furthermore, our results indicate differences between the amount of counselling appointments in the cancer centers. On one hand, tumour-specific malignity and related distress could lead to recurrent counselling sessions.[79,80] Supporting this explanation, we found evidence for a correlation between tumour status and counselling readiness. However, as already mentioned, our study's conclusion is limited regarding tumour status. On the other hand, a less reactive counselling emergency system might lead to less counselling.[40] Especially in CGynO and CBC, where the ePOS system was already established, patients are likely to receive counselling.

However, in the Center for Gastrooncology (CGO) where routine screening looks back at a shorter history, counselling rates are rather low.

Patients' true need for psychological support is difficult to measure. In this study, we used patients' counselling readiness as a proxy to it. The current screening tests seem not to predict this concept adequately. However, the answers to one's subjective need rather correlated with counselling readiness. Then again, this fits Salmon's[59] and van Scheppingen's[40] proposition about a paradigm shift in the psycho-oncological screening. They suggest repeated measurements and instead of traditional screening instruments to actively query subjective and unmet needs. Commonly, psycho(onco)logical screening instruments are developed to allocate anxiety, depression and distress. Even if these dimensions might be increased, it possibly does not mean that further counselling is necessary.[59,78,80] Instead, the lack of support in times of high distress (such as being spouseless or living alone) seems to have a higher impact on counselling readiness.[76,80] As Mehnert suggested, alternative treatments to counselling should be individually considered: psychoeducation, mindfulness trainings, family counselling, prescribing psychotropic medications and antidepresiva.[18] Allocating the source of distress seems just as important as screening distress itself, as different underlying causes behalf different treatment methods. E.g. anxiety can be reduced long-lastingly with short interventions, such as short psychoeducation sessions, mindfulness interventions, time-limited prescription of psychotropic medication and antidepressiva – but all these rapid methods did not have a permanent effect on depression, even though regular, long term psychotherapy had.[79] For that, different screening instruments could be used, as it will be discussed in the next section. Alternatively, as previously discussed, repeated screenings might be appropriate to precise measurement of counselling need. Counselling readiness should be rather understood as a product of high distress over a longer amount time and difficulties to find or use a proper coping strategy. From the economical point of view, our results indicate that shorter screening instruments can complement SN without compromising the predicting value. Of course, these results should be treated with caution. Our algorithm for counselling was triggered by SN, and this could have led to a strong mediating effect on the

other performed tests. In order to exclude such effects, future studies with independent triggers are needed.

Nevertheless, both the short and the long versions of PHQ and GAD were not able to produce better predictions of the counselling readiness than HSI. It is still plausible to note, that they can be used for ultra-rapid screenings of anxiety and depression, whenever resources are not sufficient for longer testing periods. Their significance lies in differentiating the underlying cause of distress, which can be more efficiently addressed during the counselling. However, the single use of one of the tests might not be efficient. As the instruments all measure different facets of distress (general distress with DT, specific distress with HSI, depression with PHQ, anxiety with GAD), they should be combined for indicating counselling offer.

In summary, our analysis could replicate important findings about cancer-related distress in the last decades. We confirmed the importance of social support, age, gender and previously measured vulnerability for reduced distress. Changed trends in cancer-specific distress suggests regular revisions, as both somatical and psycho-oncological treatment developments might permanently decrease distress. Yet, distress screening instruments should be carefully used to predict patients' need for counselling. We recommend multiple screenings, as distress can change rapidly during treatment. For that, a slightly modified ePOS might be beneficial; where the first question regards subjective need and in case of a positive answer further instruments are used. (I.e., HSI would be the second and not the first question). Because this is a challenging task in clinics' everyday routine, we suggest the use of efficient instruments, which validity is comparable with longer well-established tests, like SN; DT, PHQ-2 and GAD-2. Further, we recommend the use of multiple tests instead of the use of one single instrument. Fortunately, psycho-oncological aspects became more researched, accepted, and applied over the last 50 years. Address patients' fears, anxiety and depression is crucial to their long-lasting recovery. With this past study, we could offer numerous new aspects, strategies, and considerations to support future patients even more efficiently.

5. Summary

Approximately a third of all cancer patients experience strong distress during their oncological path. Even more patients' distress might not even be detected. Though distress is not a strictly defined construct, numerous screening instruments were developed to allocate patients' need for support. At the University Hospital of Tübingen, an electronical screening tool, ePOS (**e**lectronical **P**sycho**O**ncology **S**creening) triggers the pathway of psycho-oncological counselling for each cancer patient if needed. In this study we intended to evaluate ePOS and at the same time, review sociodemographic and clinical correlates of distress. Overall 5732 patients' data from 2018 of 12 cancer centers were included in the descriptive and univariate analyses. Our findings support previously established evidence on the correlation between high distress and lack of social support, younger age, and female gender, whereas education and employment did not affect distress significantly. Besides, we found indications that involvement in psychotherapy and psychotropic medication intake prior to cancer diagnosis could increase distress. Furthermore, while we partly replicated previously reported relationships between distress level and cancer types, we also found changed trends for lung cancer, and gynaecological cancer types. We assume that novel cancer treatment discoveries and their impact on patients' quality of life is responsible for this shift of distress levels. At last, we found that a quarter of all conspicuous screenings were not followed by a consecutive counselling appointment. This could partly depend on an overrepresented outpatient ratio and the lack of automated pathways. However, previous research showed that high distress scores alone not always led to wish for counselling. Accordingly, positive answers to subjective need for counselling correlated with more psycho-oncological appointments. Therefore, we recommend multiple screening, beginning with asking for subjective need. In case of positive answer, multiple distress screening instruments should follow, to understand the underlying cause. For higher practicability, we suggest the use of rapid-screening instruments, which validity is comparable with longer well-established tests (Hornheider Screening Instrument; Distress Thermometer, Patient Health Questionnaire - 2 and Generalized Anxiety Disorder – 2).

6. Zusammenfassung

Etwa ein Drittel aller Krebspatienten leidet während ihrer onkologischen Behandlung unter starken Belastungen (*Distress*). Bei noch mehr Patienten wird Distress möglicherweise gar nicht erkannt. Obwohl Distress kein streng definiertes Konstrukt ist, wurden zahlreiche Screeninginstrumente entwickelt, um den Unterstützungsbedarf von Patienten zu erfassen. Am Universitätsklinikum Tübingen wird ein elektronisches Screening-Instrument, **ePOS** (**e**lektronisches **P**sycho**o**nkologisches **S**creening), eingesetzt, welches bei Bedarf eine psychoonkologische Beratung einleitet. In dieser Studie wollten wir ePOS evaluieren und gleichzeitig soziodemographische und klinische Korrelate von Distress untersuchen. Insgesamt wurden 5732 Patientendaten aus dem Jahr 2018 von 12 Krebszentren in die deskriptiven und univariaten Analysen mit einbezogen. Unsere Ergebnisse unterstützen die bisherigen Befunde zum Zusammenhang zwischen hohem Distress und mangelnder sozialer Unterstützung, jüngerem Alter und weiblichem Geschlecht, während Bildungsniveau und Berufstätigkeit keinen signifikanten Einfluss auf Distress haben. Darüber hinaus fanden wir Hinweise darauf, dass die Teilnahme an einer Psychotherapie und die Einnahme von Psychopharmaka vor der Krebsdiagnose den Distress erhöhen können. Zudem konnten wir teilweise die bereits etablierten Zusammenhänge zwischen dem Ausmaß an Distress und der Krebsart replizieren, fanden aber auch veränderte Trends bei Lungenkrebs und gynäkologischen Krebsarten. Wir vermuten, dass neue Therapieansätze und ihre Auswirkungen auf die Lebensqualität der Patienten für diese Verschiebung der Distresswerte verantwortlich sein könnten. Schließlich haben wir festgestellt, dass bei einem Viertel aller auffälligen Screenings kein Termin für eine weiterführende Beratung vereinbart wurde. Dies könnte zum Teil auf eine Überrepräsentation ambulanter Patienten und das Fehlen vollautomatisierter Arbeitsabläufe zurückzuführen sein. Frühere Untersuchungen haben jedoch gezeigt, dass hohe Distresswerte allein nicht immer zu einem Beratungswunsch führen. So korrelierten positive Antworten auf den subjektiven Beratungsbedarf mit mehr psychoonkologischen Konsultationen. Wir empfehlen daher ein mehrstufiges Screening, beginnend mit der Frage nach dem subjektiven Bedarf.

Bei positiver Beantwortung der Frage sollten mehrere Screeninginstrumente folgen, um die zugrunde liegende Ursache zu verstehen. Um die Durchführbarkeit zu erhöhen, schlagen wir die Verwendung von schnellen Screeninginstrumenten vor, deren Validität mit länger etablierten Tests vergleichbar ist (Hornheider Screening Instrument; Distress Thermometer, Patient Health Questionnaire - 2 und Generalized Anxiety Disorder - 2).

7. References

1. Interactive H, Foundation M. What America Thinks: MetLife Foundation Alzheimer's Survey: Metropolitan Life Insurance Company; 2011.
2. Bystad M, Grønli O, Lilleeggen C, Aslaksen PM. Fear of diseases among people over 50 years of age: A survey. Scandinavian Psychologist. 2016;3.
3. Zabora J, Brintzenhofeszoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. Psycho-Oncology. 2001;10:19-28.
4. Burt RW, et al. . NCCN clinical practice guidelines in oncology. Colorectal cancer screening. JNCCN Journal of the National Comprehensive Cancer Network. 2010;8(1):8-61.
5. Sanft T, Denlinger CS, Armenian S, et al. NCCN Guidelines Insights: Survivorship, Version 2.2019. J Natl Compr Canc Netw. 2019;17(7):784-794.
6. Andreu Y, Galdon MJ, Dura E, Martinez P, Perez S, Murgui S. A longitudinal study of psychosocial distress in breast cancer: prevalence and risk factors. Psychol Health. 2012;27(1):72-87.
7. Mehnert A, Hartung TJ, Friedrich M, et al. One in two cancer patients is significantly distressed: Prevalence and indicators of distress. Psychooncology. 2018;27(1):75-82.
8. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors--a systematic review. Int J Psychiatry Med. 2010;40(2):163-181.
9. Ellis J, Lin J, Walsh A, et al. Predictors of referral for specialized psychosocial oncology care in patients with metastatic cancer: the contributions of age, distress, and marital status. J Clin Oncol. 2009;27(5):699-705.
10. Lester J, Crosthwaite K, Stout R, et al. Women with breast cancer: self-reported distress in early survivorship. Oncol Nurs Forum. 2015;42(1):E17-23.
11. Hack TF, Pickles T, Ruether JD, et al. Predictors of distress and quality of life in patients undergoing cancer therapy: impact of treatment type and decisional role. Psychooncology. 2010;19(6):606-616.
12. Herschbach P, Keller M, Knight L, et al. Psychological problems of cancer patients: a cancer distress screening with a cancer-specific questionnaire. Br J Cancer. 2004;91(3):504-511.
13. Hamer M, Chida Y, Molloy GJ. Psychological distress and cancer mortality. J Psychosom Res. 2009;66(3):255-258.
14. Groenvold M, Petersen MA, Idler E, Bjorner JB, Fayers PM, Mouridsen HT. Psychological distress and fatigue predicted recurrence and survival in

primary breast cancer patients. Breast Cancer Res Treat. 2007;105(2):209-219.
15. Barnes B, Kraywinkel K, Nowossadeck E, et al. Bericht zum Krebsgeschehen in Deutschland 2016: Robert Koch-Institut; 2016.
16. Giese-Davis J WA, Carlson LE, Groff S, Zhong L, Neri E, Bachor SM, Adamyk-Simpson J, Rancourt KM, Dunlop B, Bultz BD. Screening for distress, the 6th vital sign: common problems in cancer outpatients over one year in usual care: associations with marital status, sex, and age. BMC cancer. 2012;12(1):1-12.
17. Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. The Lancet Oncology. 2011;12(2):160-174.
18. Mehnert A, Lehmann C, Koch U. Prävalenz und Diagnostik psychischer Störungen in der Onkologie. Der Onkologe. 2006;12(1):18-26.
19. Linden W, Vodermaier A, Mackenzie R, Greig D. Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. J Affect Disord. 2012;141(2-3):343-351.
20. Yang HC, Schuler TA. Marital quality and survivorship: slowed recovery for breast cancer patients in distressed relationships. Cancer. 2009;115(1):217-228.
21. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft DK, AWMF). Psychoonkologische Diagnostik, Beratung und Behandlung von erwachsenen
Krebspatienten, Langversion 1.1, AWMF-Registernummer: 032/051OL. 2014.
22. Mitchell AJ. Screening for cancer-related distress: when is implementation successful and when is it unsuccessful? Acta Oncol. 2013;52(2):216-224.
23. Pilkonis PA, Choi SW, Reise SP, et al. Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS(R)): depression, anxiety, and anger. Assessment. 2011;18(3):263-283.
24. Schalet BD, Pilkonis PA, Yu L, et al. Clinical validity of PROMIS Depression, Anxiety, and Anger across diverse clinical samples. J Clin Epidemiol. 2016;73:119-127.
25. Donovan KA, Grassi L, McGinty HL, Jacobsen PB. Validation of the distress thermometer worldwide: state of the science. Psychooncology. 2014;23(3):241-250.
26. Mehnert A, Müller D, Lehmann C, Koch U. Die deutsche Version des NCCN Distress-Thermometers. Zeitschrift für Psychiatrie, Psychologie und Psychotherapie. 2006;54(3):213-223.

27. Herschbach P, Weis J. Screeningverfahren in der Psychoonkologie: Testinstrumente zur Identifikation betreuungsbedürftiger Krebspatienten. :: DKG Eigenverlag; 2010.
28. Bjelland I, Krokstad S, Mykletun A, Dahl AA, Tell GS, Tambs K. Does a higher educational level protect against anxiety and depression? The HUNT study. Soc Sci Med. 2008;66(6):1334-1345.
29. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. Journal of psychosomatic research. 2002;52(2):69-77.
30. Strittmatter G, Mawick R, Tilkorn M. Development of the Hornheide Screening Instrument (HSI) for the identification of cancer patients in need of support. J Cancer Res Clin Oncol. 2000;126(Suppl):R36.
31. Rumpold G, Augustin M, Zschocke I, Strittmatter G, Söllner W. Die Validität des Hornheider Fragebogens zur psychosozialen Unterstützung bei Tumorpatienten. PPmP-Psychotherapie· Psychosomatik· Medizinische Psychologie. 2001;51(01):25-33.
32. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Archives of internal medicine. 2006;166(10):1092-1097.
33. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord. 2009;114(1-3):163-173.
34. Gotz A, Kroner A, Jenewein J, Spirig R. Evaluation of the adherence of distress screening with the distress thermometer in cancer patients 4 years after implementation. Support Care Cancer. 2019;27(8):2799-2807.
35. Meijer A, Roseman M, Delisle VC, et al. Effects of screening for psychological distress on patient outcomes in cancer: a systematic review. J Psychosom Res. 2013;75(1):1-17.
36. Schaeffeler N, Pfeiffer K, Ringwald J, et al. Assessing the need for psychooncological support: screening instruments in combination with patients' subjective evaluation may define psychooncological pathways. Psychooncology. 2015;24(12):1784-1791.
37. Gunther MP, Schulze JB, Jellestad L, Mehnert-Theuerkauf A, von Kanel R, Euler S. Mental disorders, length of hospitalization, and psychopharmacy-New approaches to identify barriers to psychological support for patients with cancer. Psychooncology. 2021;30(10):1773-1781.
38. Koehler M, Hornemann B, Holzner B, et al. Zukunft jetzt − Implementierung eines IT-gestützten Distress-Screenings. Der Onkologe. 2017;23(6):453-461.
39. Teufel M, Schäffeler N, Zipfel S. Computerbasiertes Screening in der Psychoonkologie: Behandlungspfade besser steuern. Deutsches Ärzteblatt. 2014;111(6):208-209.

40. van Scheppingen C, Schroevers MJ, Smink A, et al. Does screening for distress efficiently uncover meetable unmet needs in cancer patients? Psychooncology. 2011;20(6):655-663.
41. Schaffeler N, Pfeiffer K, Grischke EM, et al. [Acceptance and reliability of an electronic psychooncological screening of patients with breast cancer: a randomized controlled study]. Psychother Psychosom Med Psychol. 2013;63(9-10):374-380.
42. Roth AJ, Kornblith AB, Batel-Copel L, Peabody E, Scher HI, Holland JC. Rapid screening for psychologic distress in men with prostate carcinoma: a pilot study. Cancer: Interdisciplinary International Journal of the American Cancer Society. 1998;82(10):1904-1908.
43. Kroenke K, Spitzer RL, Williams JB, Lowe B. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-359.
44. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. Medical care. 2003:1284-1292.
45. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. Gen Hosp Psychiatry. 2016;39:24-31.
46. Team R. RStudio: Integrated Development for R. 2018.
47. Darren G, Mallery P. IBM SPSS Statistics 26 step by step: A simple guide and reference. Routledge. 2019.
48. Pallant J. EBOOK: SPSS Survival Manual. McGraw-Hill Education (UK). 2016.
49. Polanski J, Jankowska-Polanska B, Rosinczuk J, Chabowski M, Szymanska-Chabowska A. Quality of life of patients with lung cancer. Onco Targets Ther. 2016;9:1023-1028.
50. Brahmer J. R., Tykodi S., Chow L. Q. M., et al. Safety and Activity of Anti–PD-L1 Antibody
in Patients with Advanced Cancer. The New England Journal of Medicine. 2012;366(26):2455-2465.
51. Hirsch FR, Scagliotti GV, Mulshine JL, et al. Lung cancer: current therapies and new targeted treatments. The Lancet. 2017;389(10066):299-311.
52. Sullivan DR, Forsberg CW, Ganzini L, et al. Longitudinal Changes in Depression Symptoms and Survival Among Patients With Lung Cancer: A National Cohort Assessment. J Clin Oncol. 2016;34(33):3984-3991.
53. LoConte NK, Else-Quest NM, Eickhoff J, Hyde J, Schiller JH. Assessment of guilt and shame in patients with non-small-cell lung cancer compared with patients with breast and prostate cancer. Clin Lung Cancer. 2008;9(3):171-178.
54. Berterö C. Living with Social Anguish: Shame and Guilt in Lung Cancer Patients. The Open Area Studies Journal. 2008;1:26-30.

55. Herschbach P, Britzelmeir I, Dinkel A, et al. Distress in cancer patients: Who are the main groups at risk? Psychooncology. 2020;29(4):703-710.
56. Herschbach P, Berg P, Waadt S, et al. Group psychotherapy of dysfunctional fear of progression in patients with chronic arthritis or cancer. Psychother Psychosom. 2010;79(1):31-38.
57. Dinkel A, Herschbach, P. . Fear of Progression in Cancer Patients and Survivors. In: Goerling, U., Mehnert, A. (eds) Psycho-Oncology. Recent Results in Cancer Research. Springer, Cham. 2018;210.
58. Blake-Mortimer J, Gore-Felton C, Kimerling R, Turner-Cobb JM, Spiegel D. Improving the quality and quantity of life among patients with cancer: a review of the effectiveness of group psychotherapy. European Journal of Cancer. 1999;35(11):1581-1586.
59. Salmon P, Clark L, McGrath E, Fisher P. Screening for psychological distress in cancer: renewing the research agenda. Psychooncology. 2015;24(3):262-268.
60. Autier P, Boniol M, La Vecchia C, et al. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. BMJ. 2010;341:c3620.
61. Jatoi I, Miller AB. Why is breast-cancer mortality declining? The Lancet Oncology. 2003;4(4):251-254.
62. Waks AG, Winer EP. Breast Cancer Treatment: A Review. JAMA. 2019;321(3):288-300.
63. Ades F, Tryfonidis K, Zardavas D. The past and future of breast cancer treatment-from the papyrus to individualised treatment approaches. Ecancermedicalscience. 2017;11:746.
64. Small W, Jr., Bacon MA, Bajaj A, et al. Cervical cancer: A global health crisis. Cancer. 2017;123(13):2404-2412.
65. Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68(4):284-296.
66. Sehouli J, Höffken K. Ovarialkarzinom. Der Onkologe. 2019;25(2):88-89.
67. Koh WJ, Abu-Rustum NR, Bean S, et al. Cervical Cancer, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019;17(1):64-84.
68. Fehm T, Mallmann P. S3-Leitlinie Zervixkarzinom. Der Gynäkologe. 2019;52(8):568-569.
69. Mallmann P. Neueste Entwicklungen beim Zervix- und Ovarialkarzinom. gynäkologie + geburtshilfe. 2020;25:32–34.
70. Hobden B, Turon H, Bryant J, Wall L, Brown S, Sanson-Fisher R. Oncology patient preferences for depression care: A discrete choice experiment. Psychooncology. 2019;28(4):807-814.

71. Hinz A, Krauss O, Hauss JP, et al. Anxiety and depression in cancer patients compared with the general population. Eur J Cancer Care (Engl). 2010;19(4):522-529.
72. Angst J, Gamma A, Gastpar M, et al. Gender differences in depression. Epidemiological findings from the European DEPRES I and II studies. Eur Arch Psychiatry Clin Neurosci. 2002;252(5):201-209.
73. Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. British Journal of Psychiatry. 2000;177:486-492.
74. Dinkel A, Berg P, Pirker C, et al. Routine psychosocial distress screening in radiotherapy: implementation and evaluation of a computerised procedure. Br J Cancer. 2010;103(10):1489-1495.
75. Costanzo ES, Lutgendorf SK, Mattes ML, et al. Adjusting to life after treatment: distress and quality of life following treatment for breast cancer. Br J Cancer. 2007;97(12):1625-1631.
76. Shimizu K, Ishibashi Y, Umezawa S, et al. Feasibility and usefulness of the 'Distress Screening Program in Ambulatory Care' in clinical oncology practice. Psychooncology. 2010;19(7):718-725.
77. Helgeson VS, Snyder P, Seltman H. Psychological and physical adjustment to breast cancer over 4 years: identifying distinct trajectories of change. Health Psychol. 2004;23(1):3-15.
78. Hollingworth W, Metcalfe C, Mancero S, et al. Are needs assessments cost effective in reducing distress among patients with cancer? A randomized controlled trial using the Distress Thermometer and Problem List. J Clin Oncol. 2013;31(29):3631-3638.
79. Weidner K, Zimmermann K, Neises M, Distler W, Joraschky P, Hessel A. [Effects of psychosomatic interventions within the consultation service of a gynecological university hospital]. Psychother Psychosom Med Psychol. 2006;56(9-10):362-369.
80. Sollner W, Maislinger S, Konig A, Devries A, Lukas P. Providing psychosocial support for breast cancer patients based on screening for distress within a consultation-liaison service. Psychooncology. 2004;13(12):893-897.

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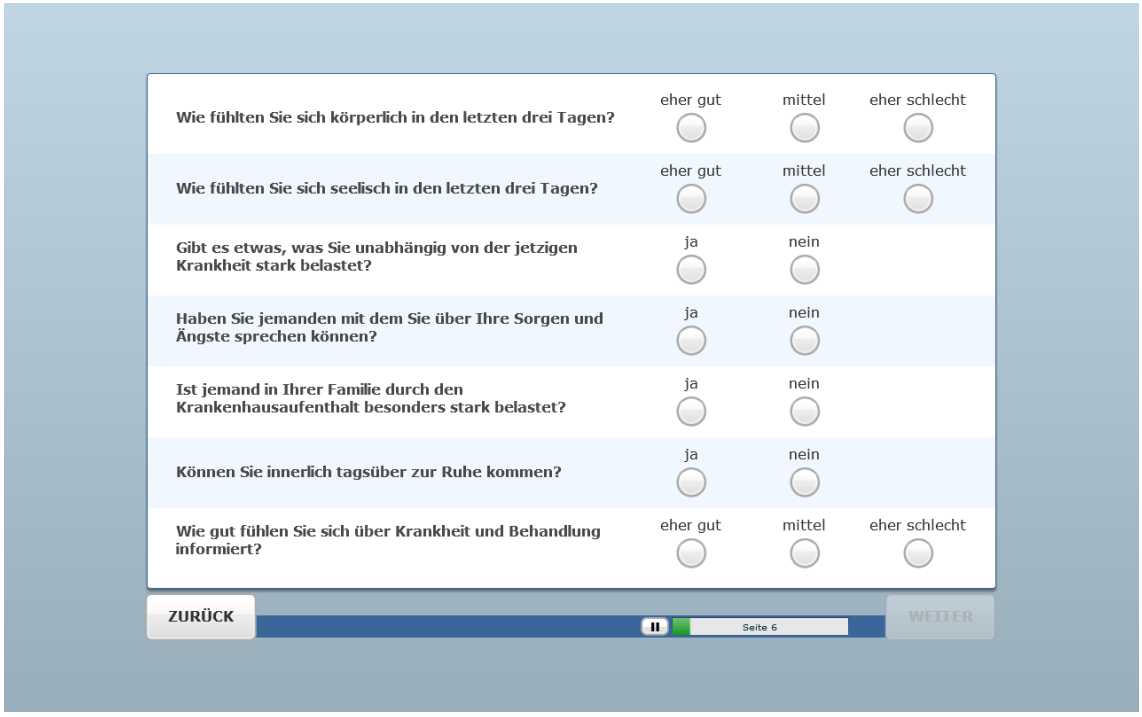
Appendices

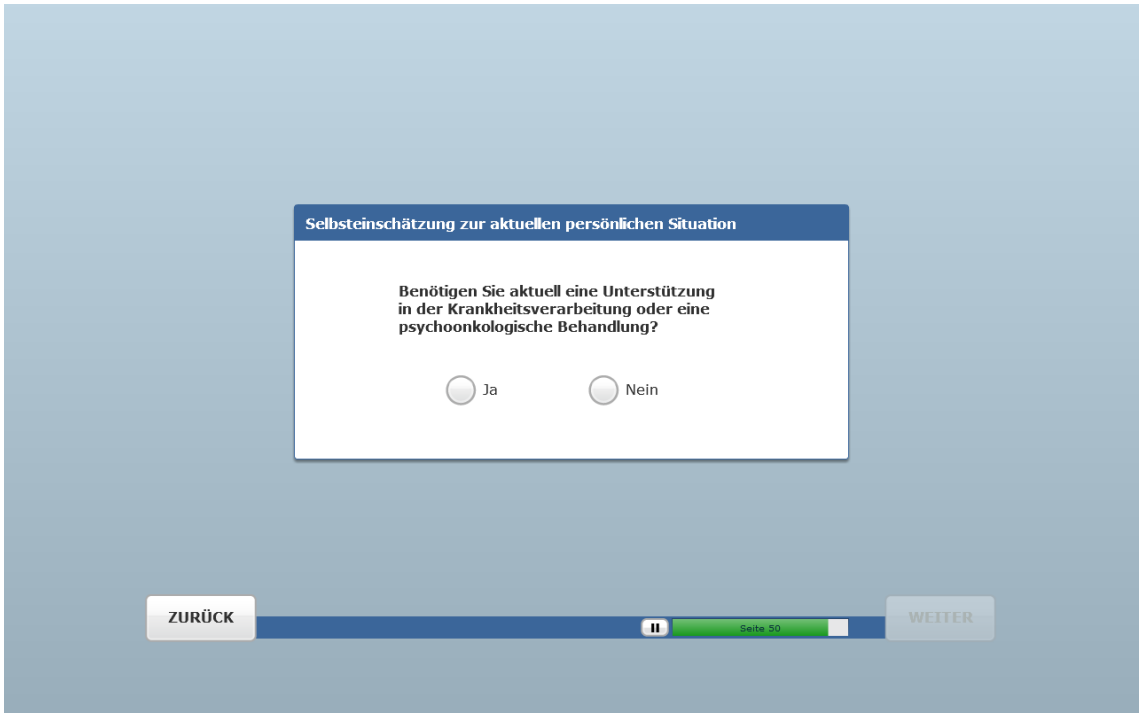
Appendix 1.

Hornheider Screening Instrument in ePOS.



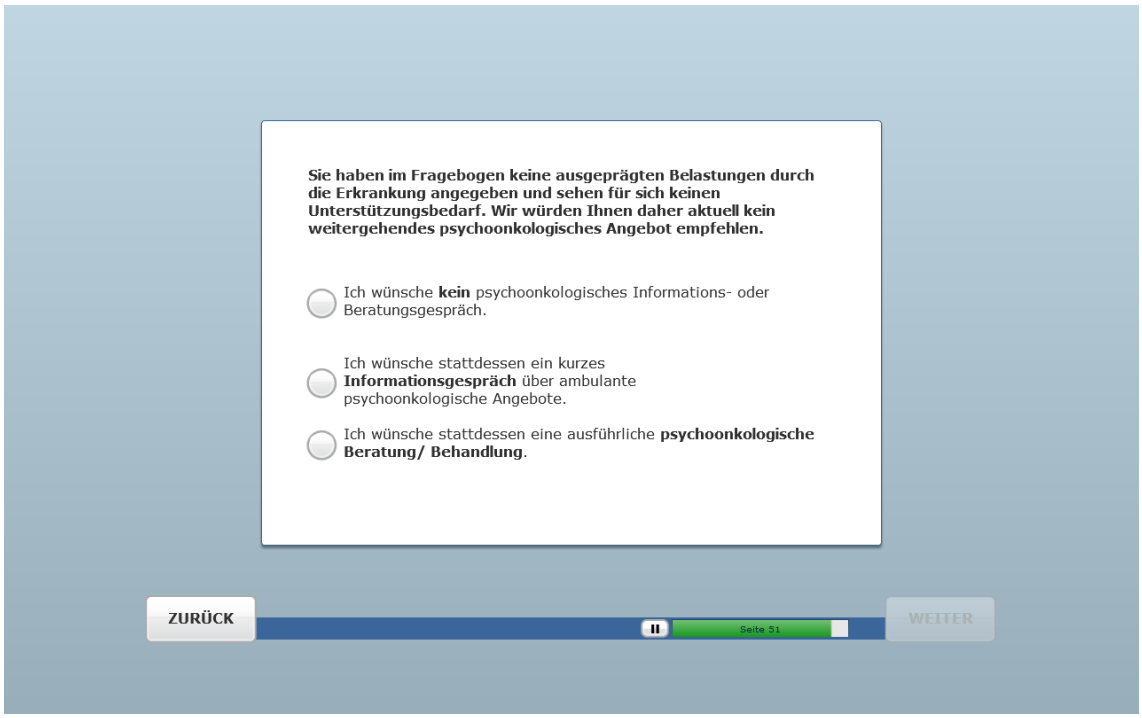
Appendix 2.

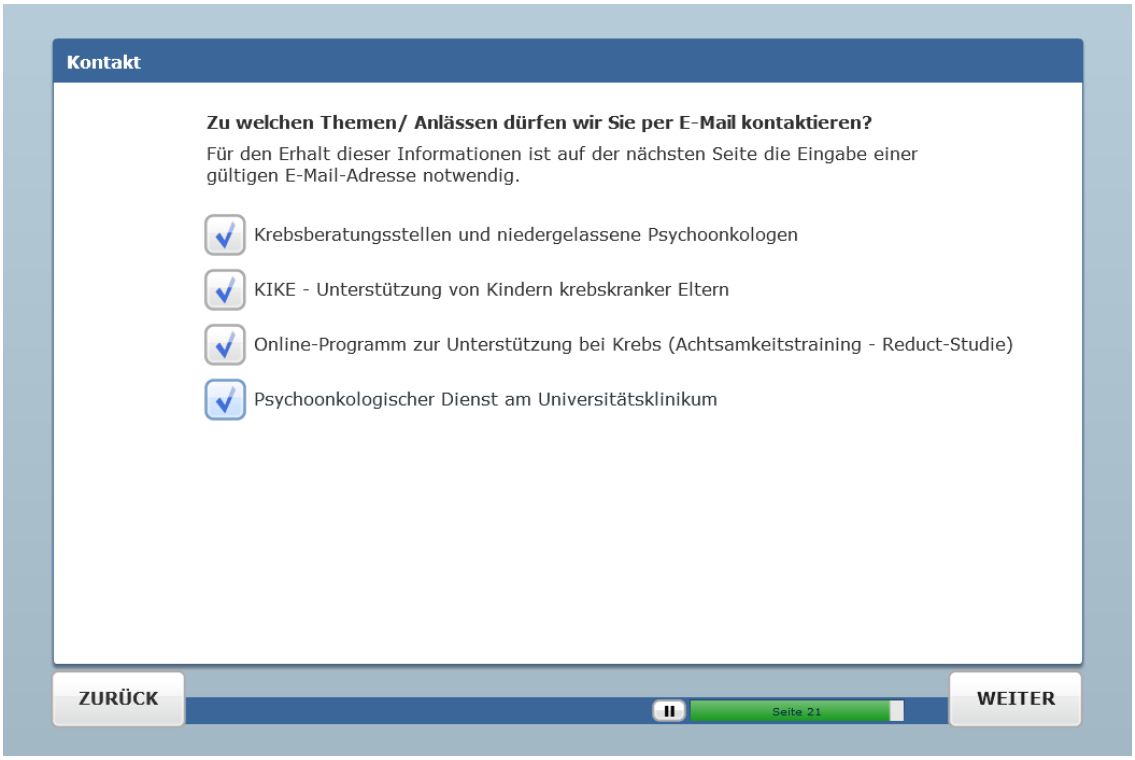
Subjective Need in ePOS.

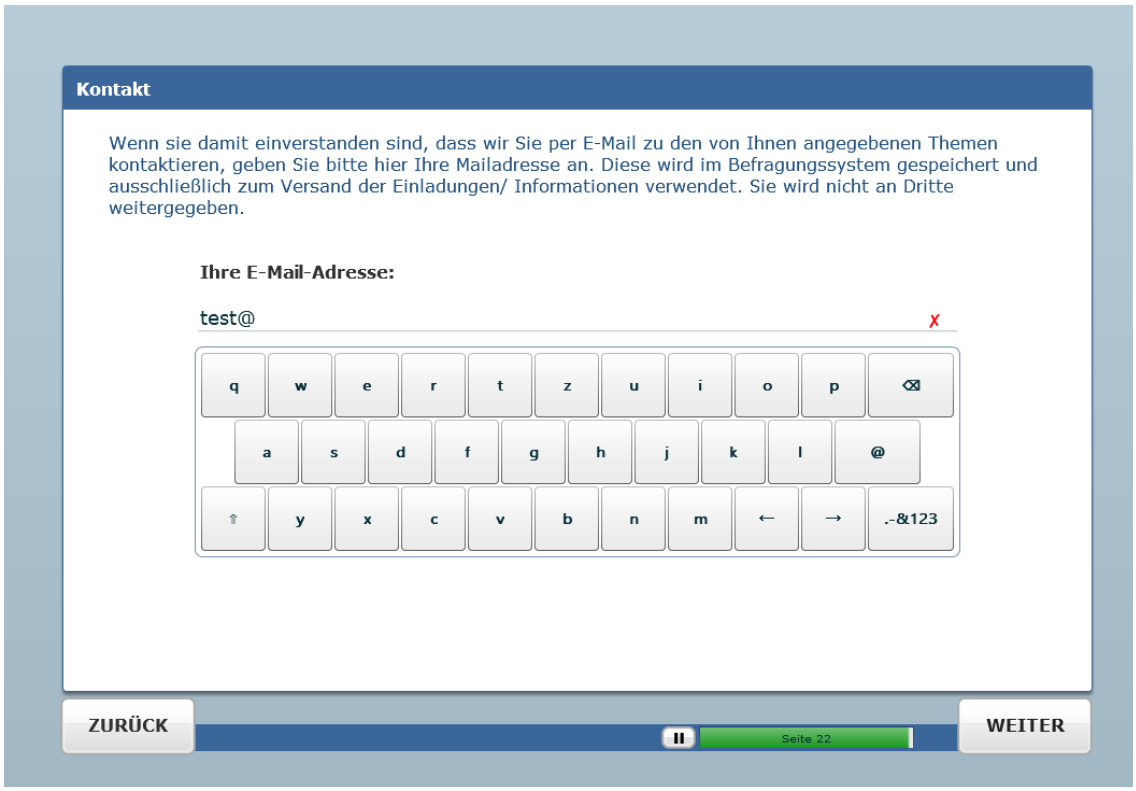


Appendix 3.

Hornheider Screening Instrument conspicuous, but unremarkable Subjective Need in ePOS.

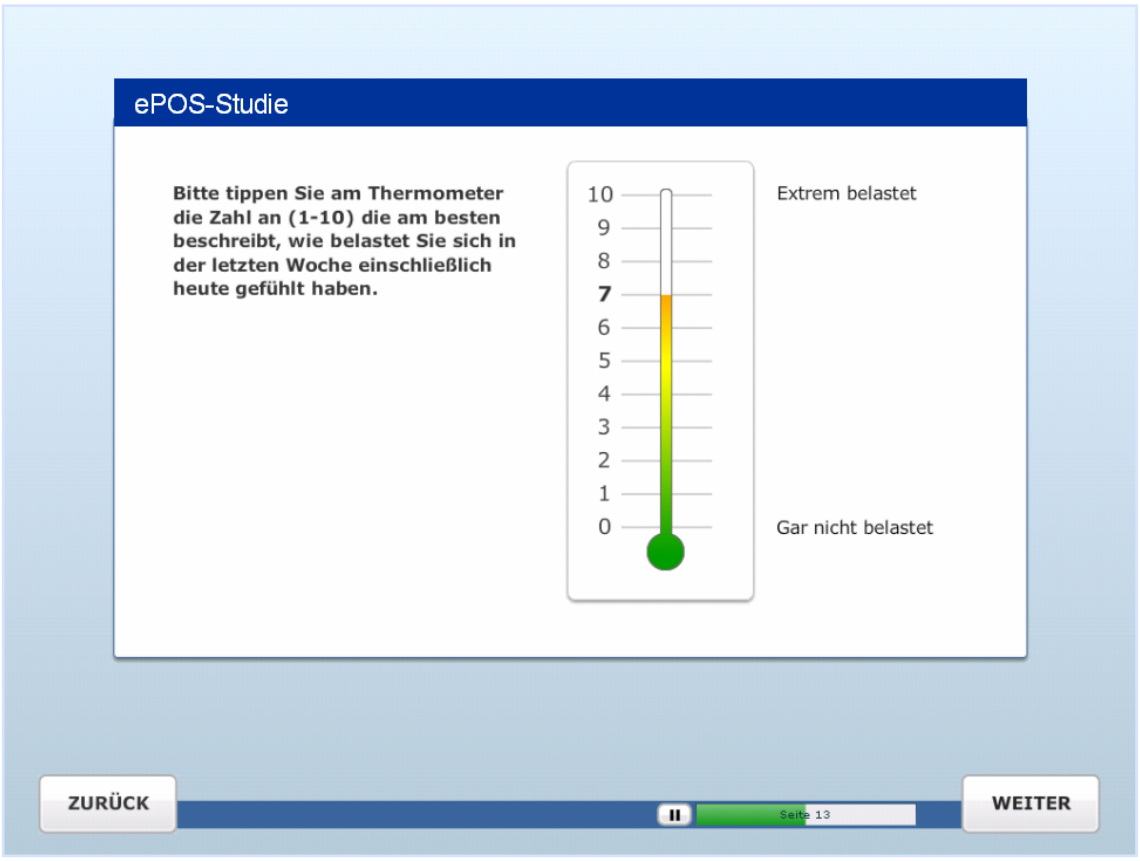





Kontakt
Wenn sie damit einverstanden sind, dass wir Sie per E-Mail zu den von Ihnen angegebenen Themen kontaktieren, geben Sie bitte hier Ihre Mailadresse an. Diese wird im Befragungssystem gespeichert und ausschließlich zum Versand der Einladungen/ Informationen verwendet. Sie wird nicht an Dritte weitergegeben.
Ihre E-Mail-Adresse:
test@
q w e r t z u i o p
a s d f g h j k l @
y x c v b n m
.-&123
ZURÜCK
Seite 22
WEITER

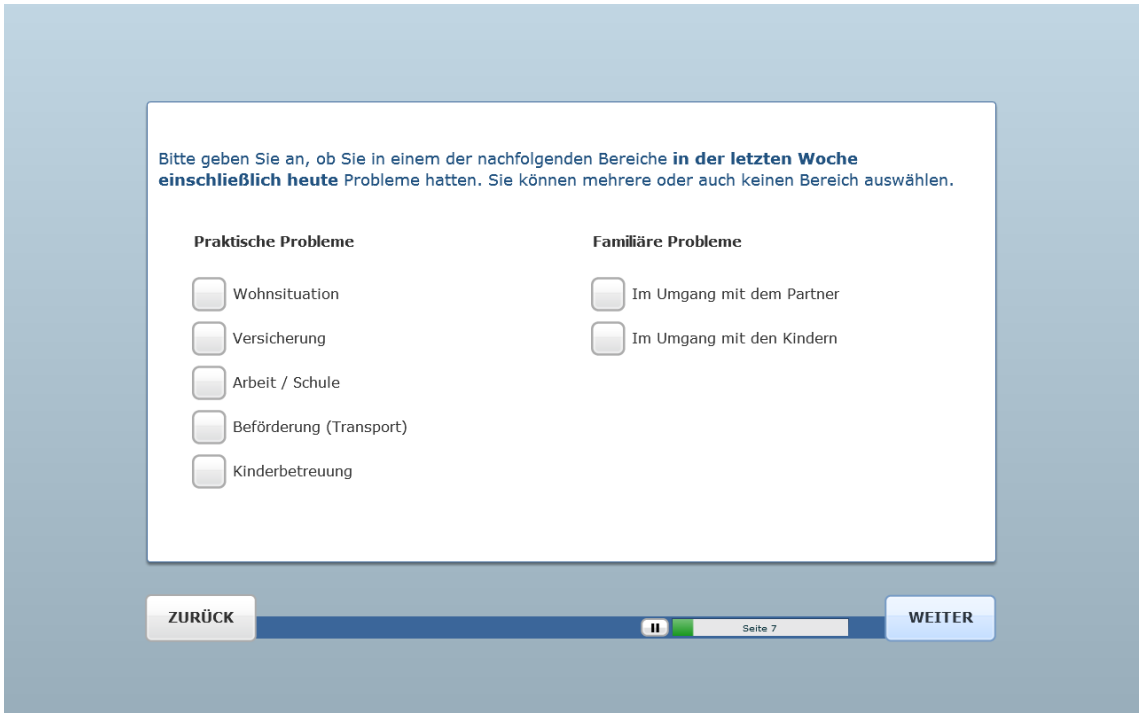
Appendix 4.

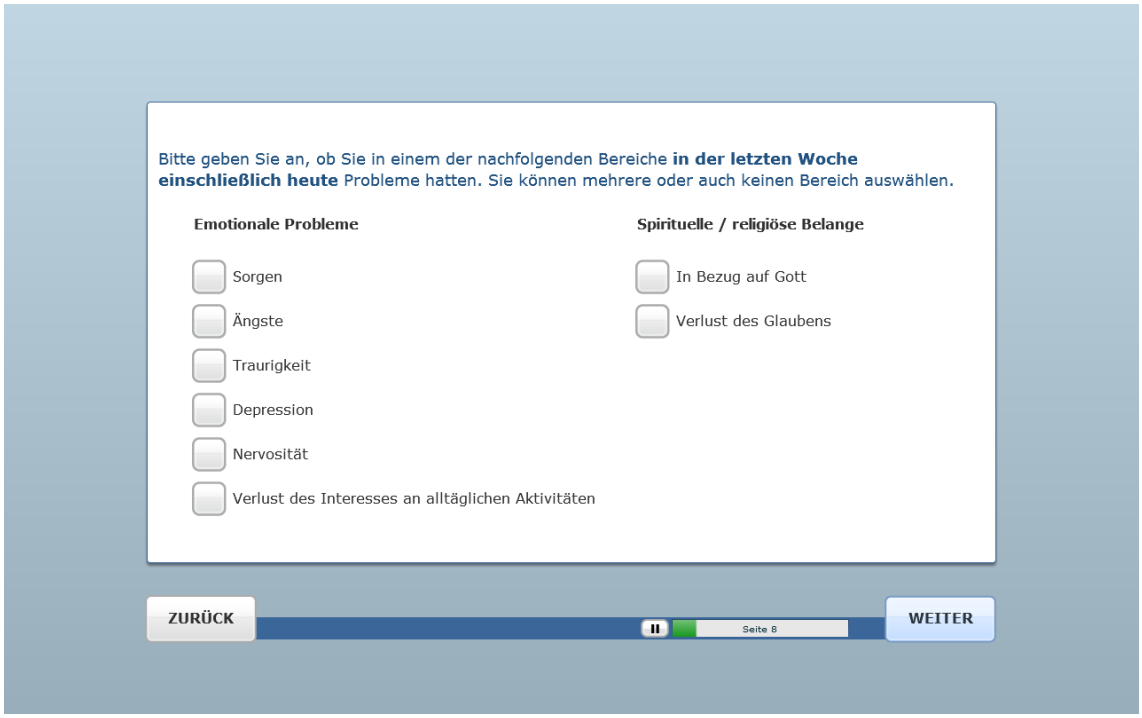
Distress Thermometer in ePOS.

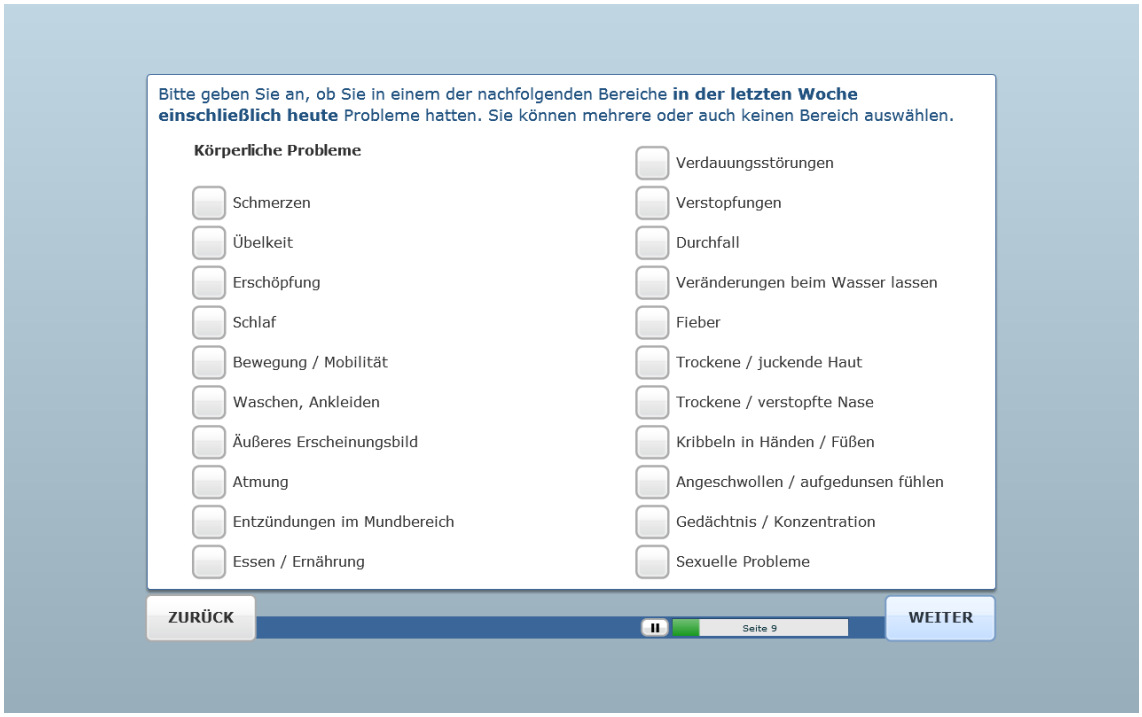


Appendix 5.

Distress Thermometer Problems in ePOS.

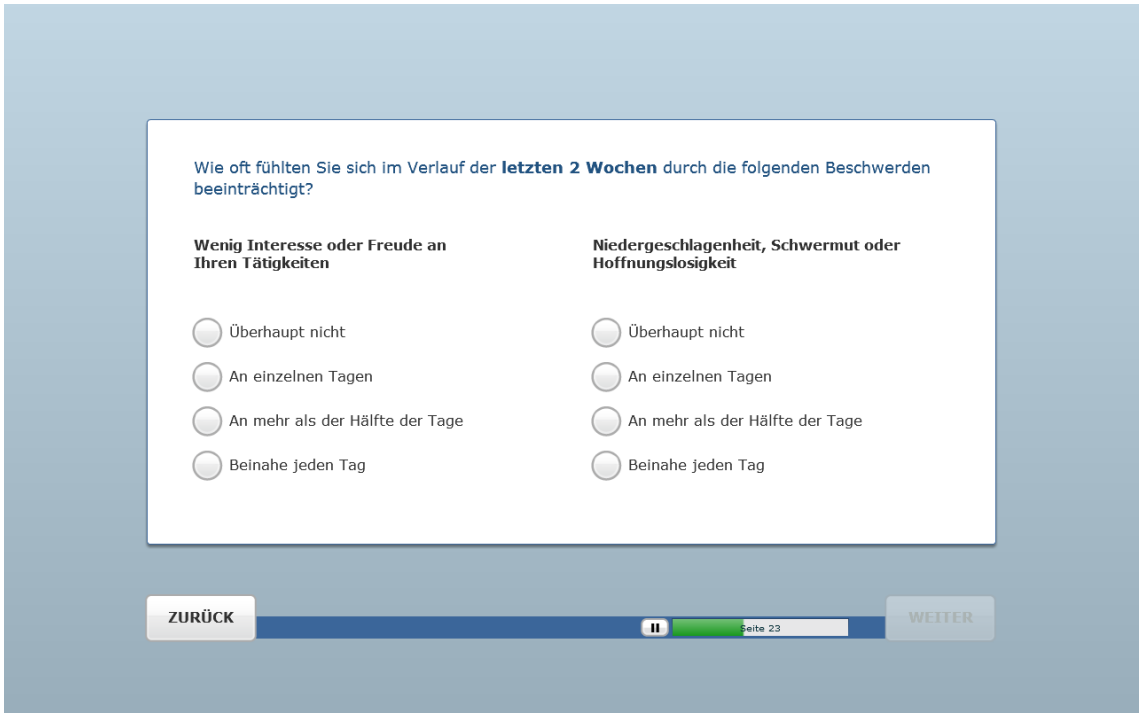


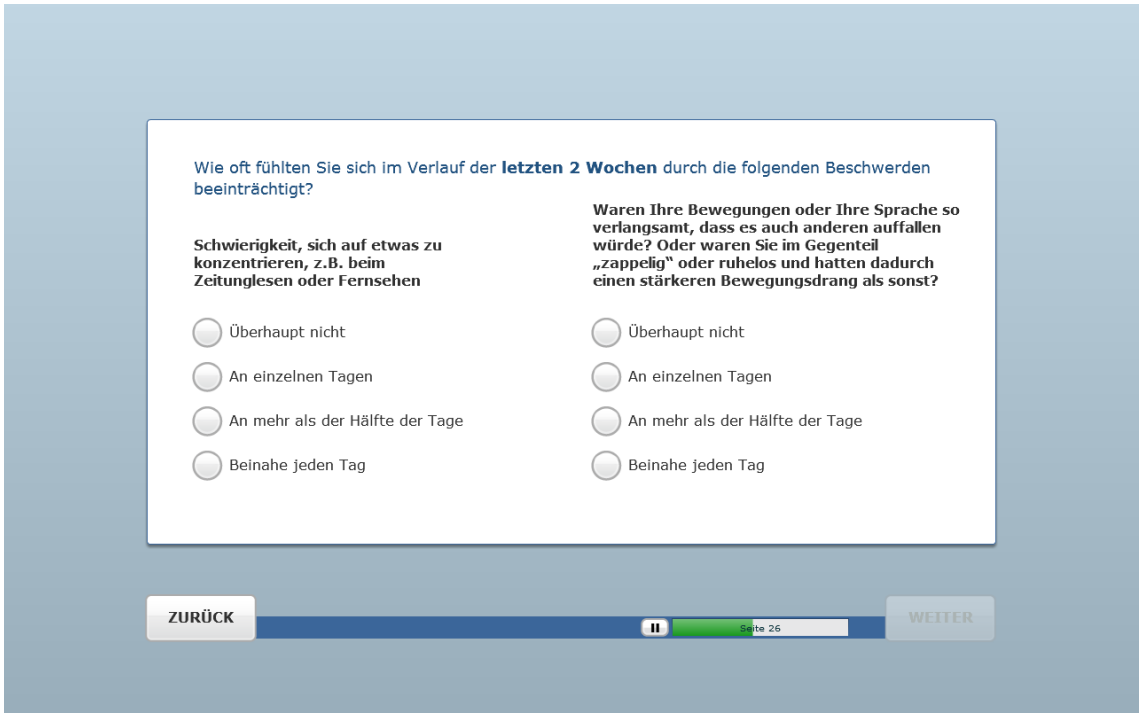


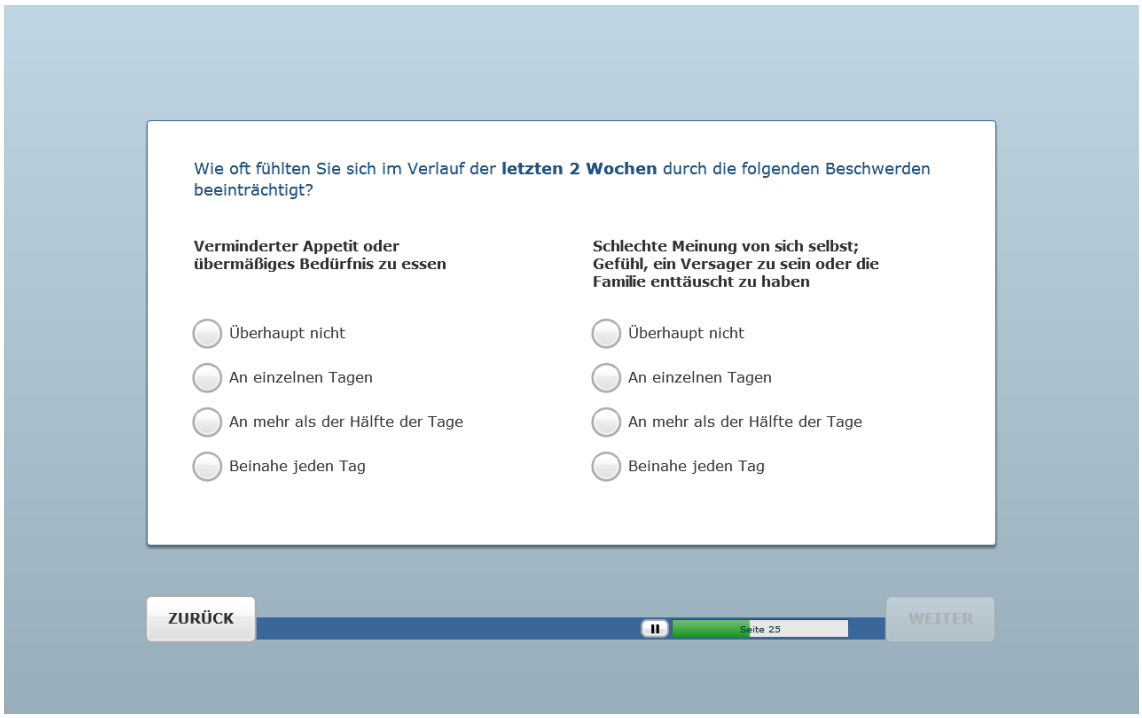

Bitte geben Sie an, ob Sie in einem der nachfolgenden Bereiche in der letzten Woche einschließlich heute Probleme hatten. Sie können mehrere oder auch keinen Bereich auswählen.
Körperliche Probleme
Schmerzen
Übelkeit
Erschöpfung
Schlaf
Bewegung / Mobilität
Waschen, Ankleiden
Äußeres Erscheinungsbild
Atmung
Entzündungen im Mundbereich
Essen / Ernährung
Verdauungsstörungen
Verstopfungen
Durchfall
Veränderungen beim Wasser lassen
Fieber
Trockene / juckende Haut
Trockene / verstopfte Nase
Kribbeln in Händen / Füßen
Angeschwollen / aufgedunsen fühlen
Gedächtnis / Konzentration
Sexuelle Probleme
ZURÜCK
Seite 9
WEITER

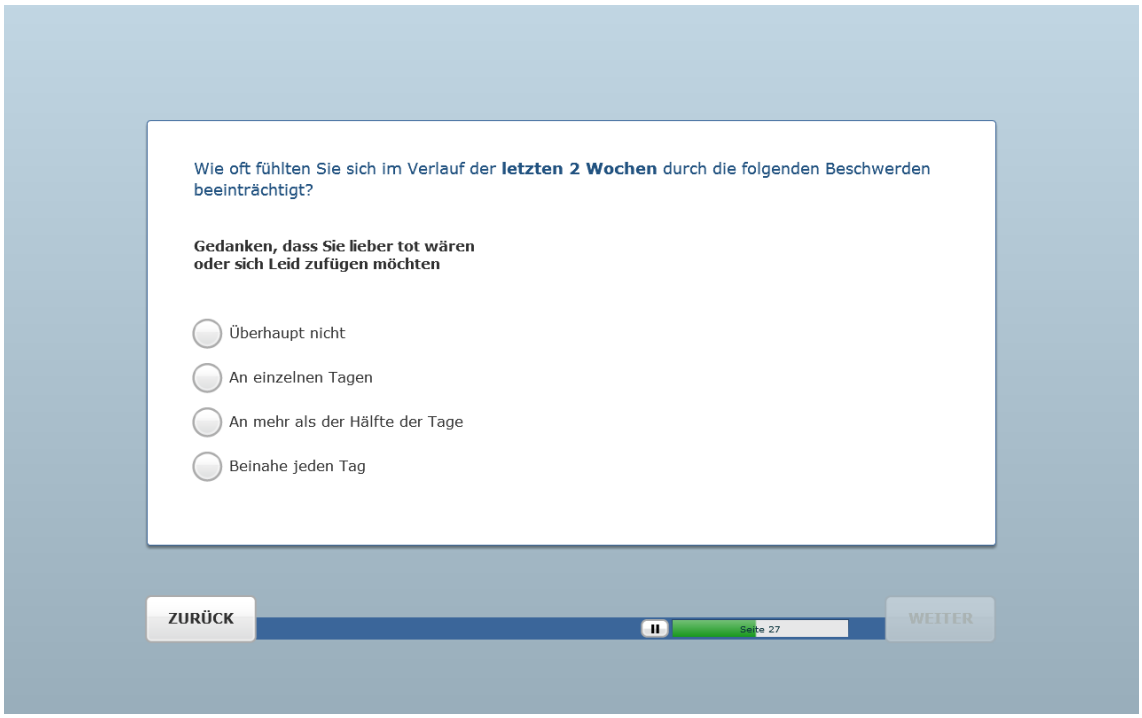
Appendix 6.

Patient Health Questionnaire (2 and 8) in ePOS.



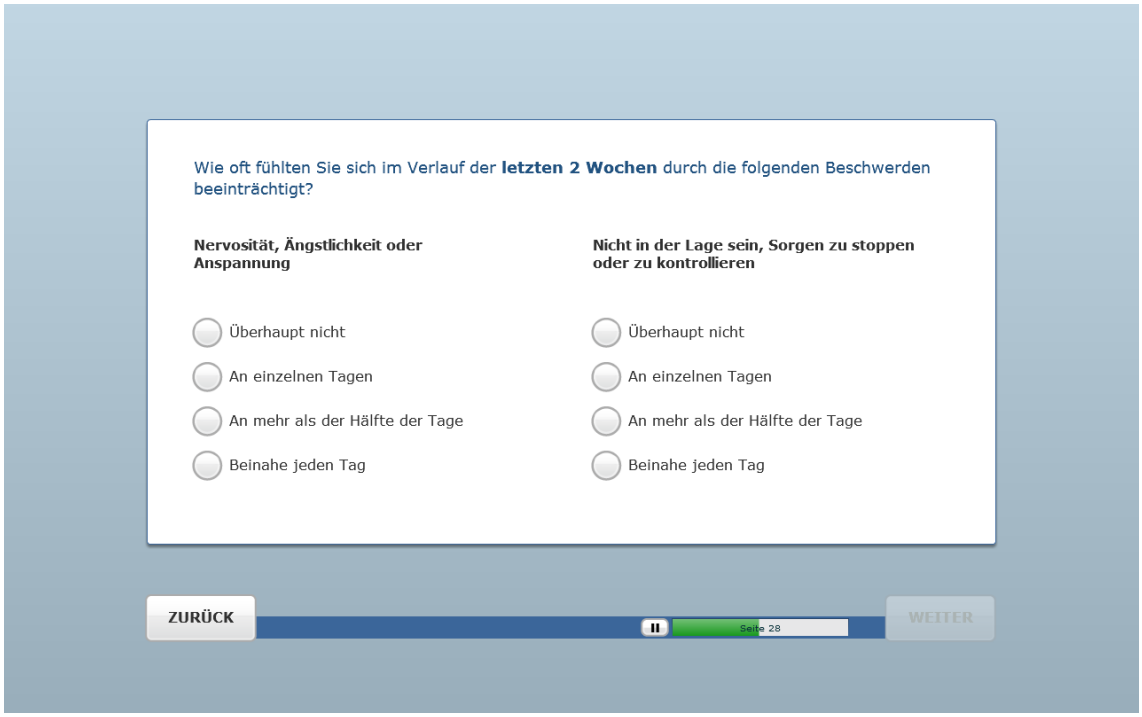


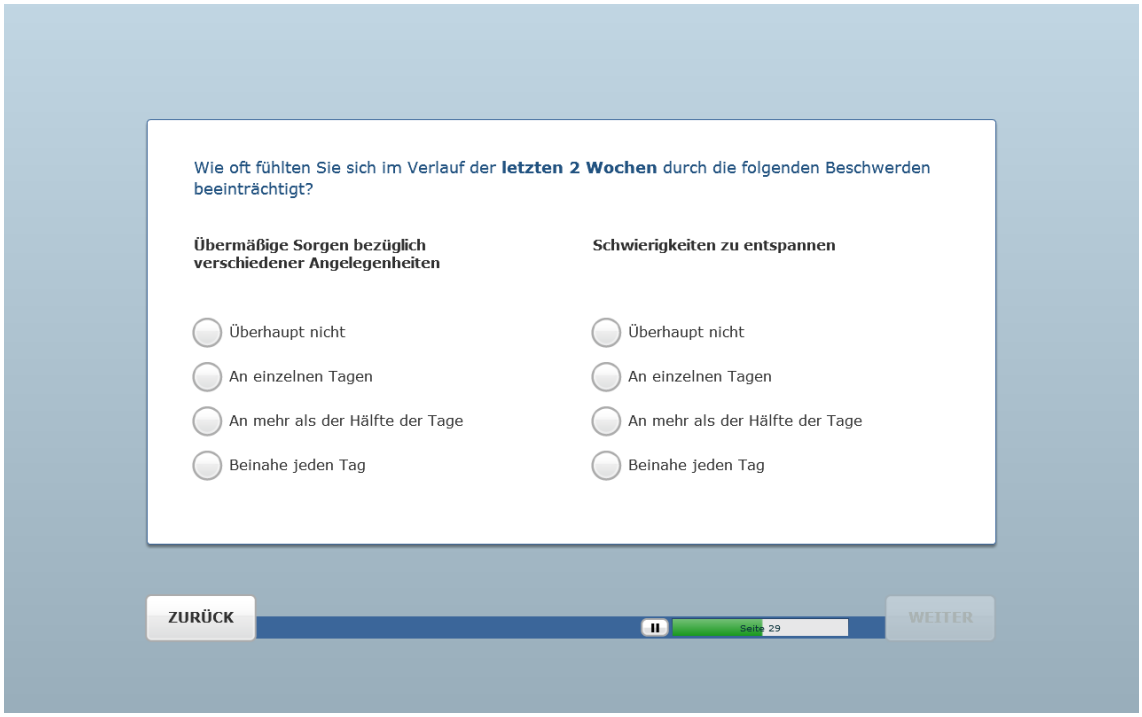

Wie oft fühlten Sie sich im Verlauf der letzten 2 Wochen durch die folgenden Beschwerden beeinträchtigt?
Verminderter Appetit oder übermäßiges Bedürfnis zu essen
Überhaupt nicht
An einzelnen Tagen
An mehr als der Hälfte der Tage
Beinahe jeden Tag
Schlechte Meinung von sich selbst; Gefühl, ein Versager zu sein oder die Familie enttäuscht zu haben
Überhaupt nicht
An einzelnen Tagen
An mehr als der Hälfte der Tage
Beinahe jeden Tag
ZURÜCK
Seite 25
WEITER

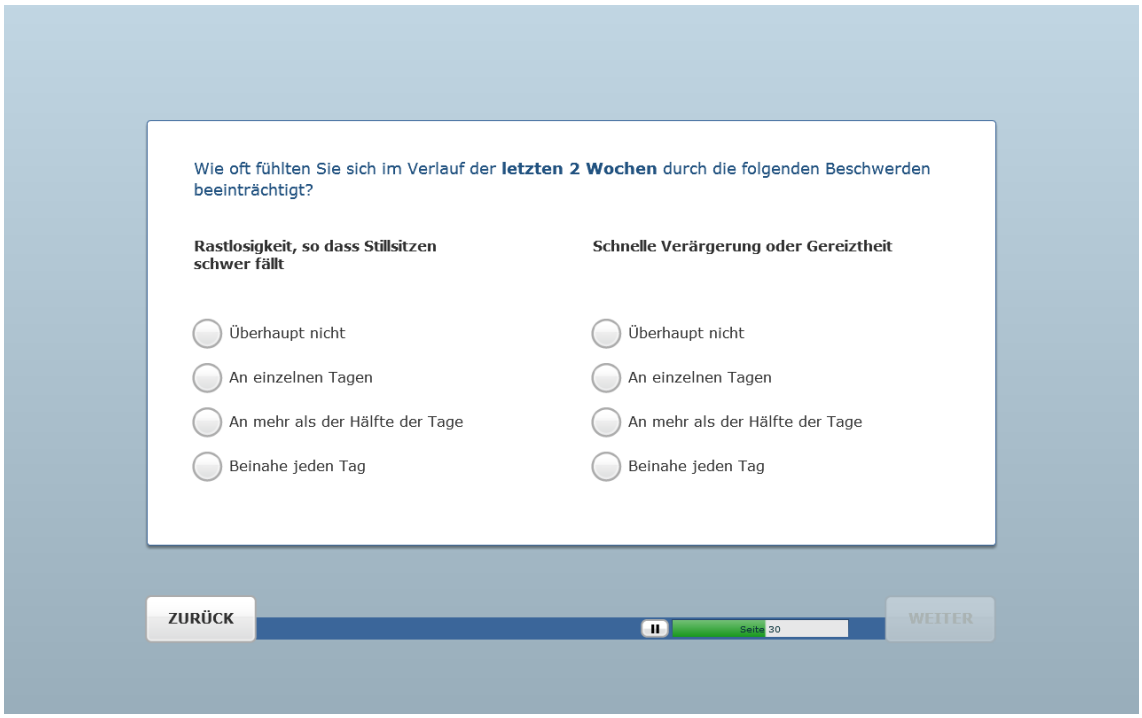

Wie oft fühlten Sie sich im Verlauf der letzten 2 Wochen durch die folgenden Beschwerden beeinträchtigt?
Gedanken, dass Sie lieber tot wären oder sich Leid zufügen möchten
Überhaupt nicht
An einzelnen Tagen
An mehr als der Hälfte der Tage
Beinahe jeden Tag
ZURÜCK
Seite 27
WEITER

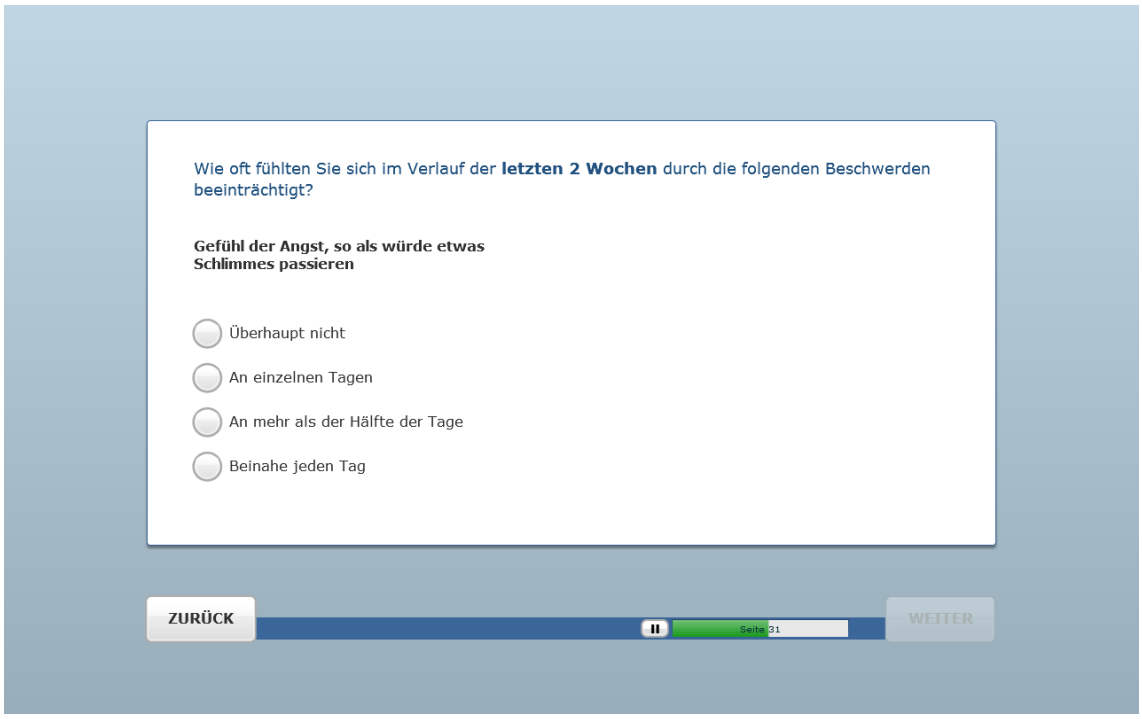
Appendix 7.

Generalized Anxiety Disorder (2 and 7) in ePOS.



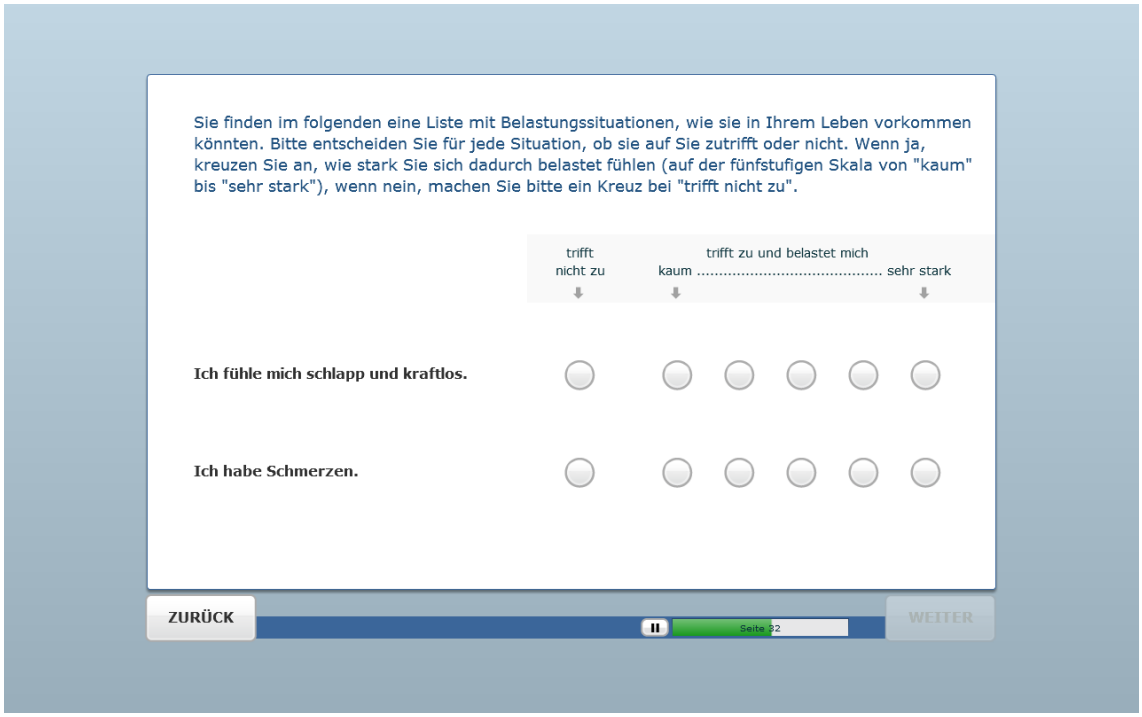


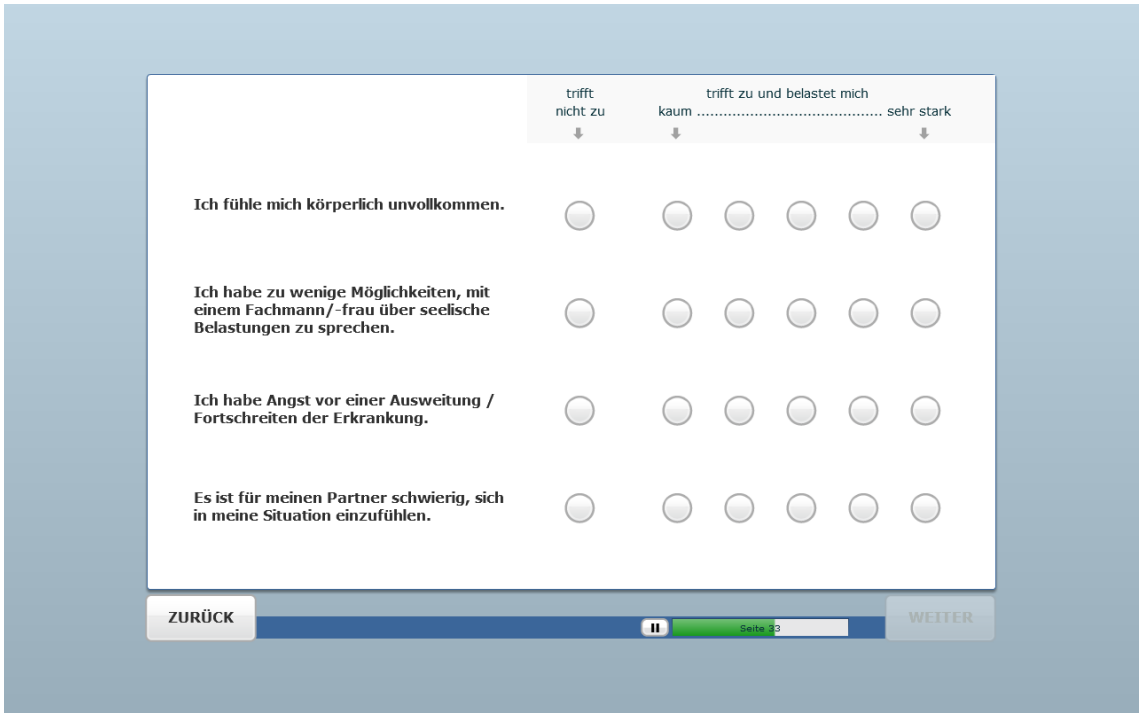

Wie oft fühlten Sie sich im Verlauf der letzten 2 Wochen durch die folgenden Beschwerden beeinträchtigt?
Rastlosigkeit, so dass Stillsitzen schwer fällt
Überhaupt nicht
An einzelnen Tagen
An mehr als der Hälfte der Tage
Beinahe jeden Tag
Schnelle Verärgerung oder Gereiztheit
Überhaupt nicht
An einzelnen Tagen
An mehr als der Hälfte der Tage
Beinahe jeden Tag
ZURÜCK
Seite 30
WEITER

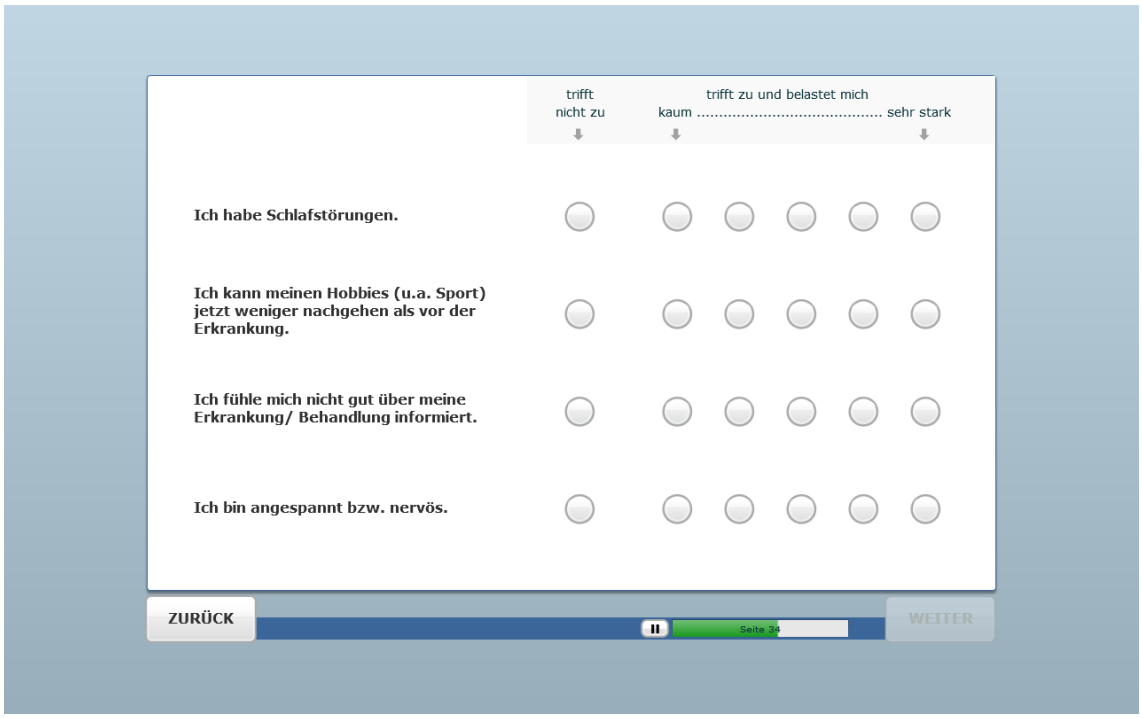

Wie oft fühlten Sie sich im Verlauf der letzten 2 Wochen durch die folgenden Beschwerden beeinträchtigt?
Gefühl der Angst, so als würde etwas Schlimmes passieren
Überhaupt nicht
An einzelnen Tagen
An mehr als der Hälfte der Tage
Beinahe jeden Tag
ZURÜCK
Seite 31
WEITER

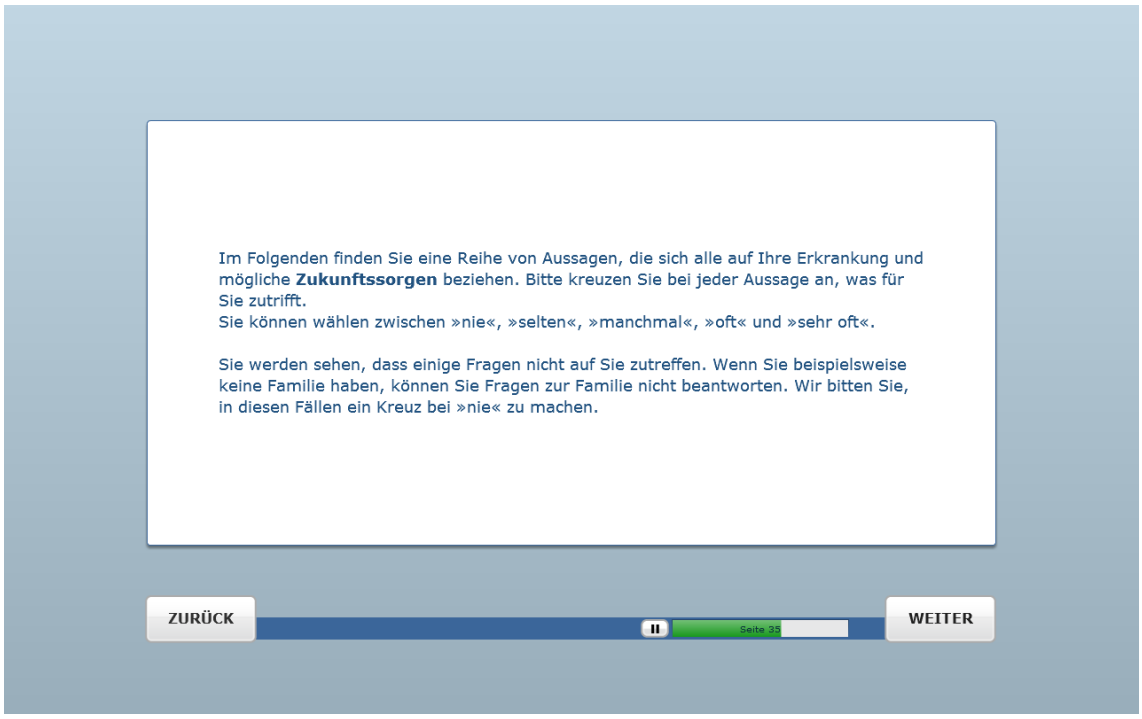
Appendix 8.

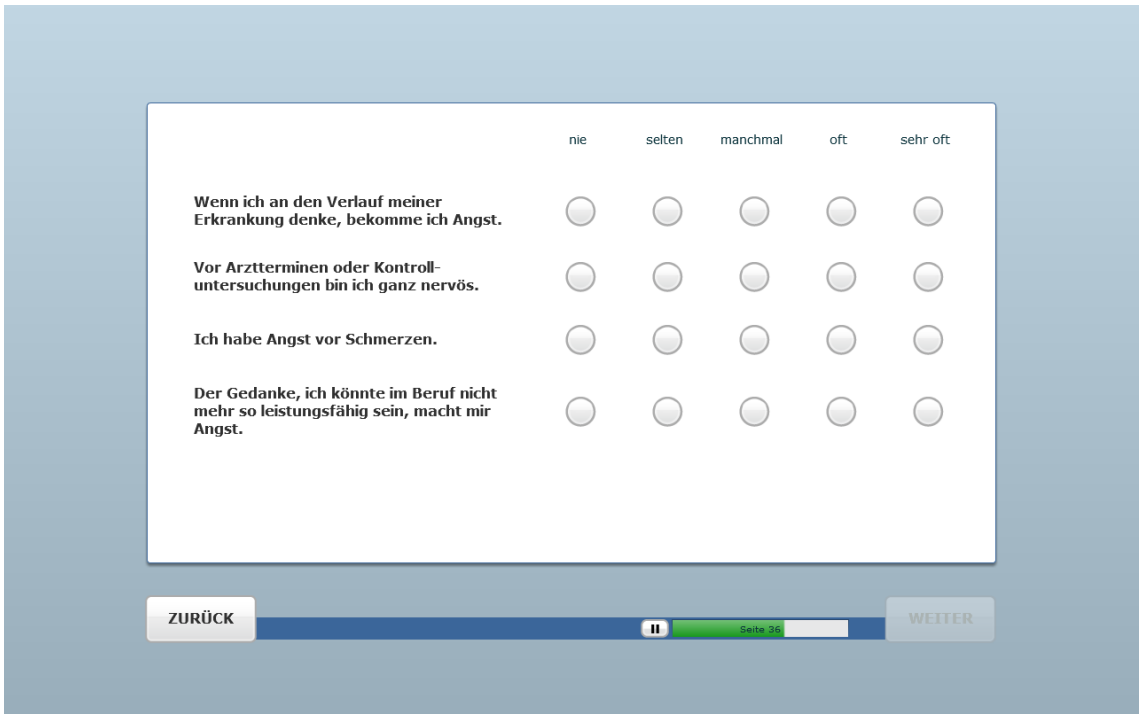
Distress of Cancer Patients Questionnaire in ePOS.

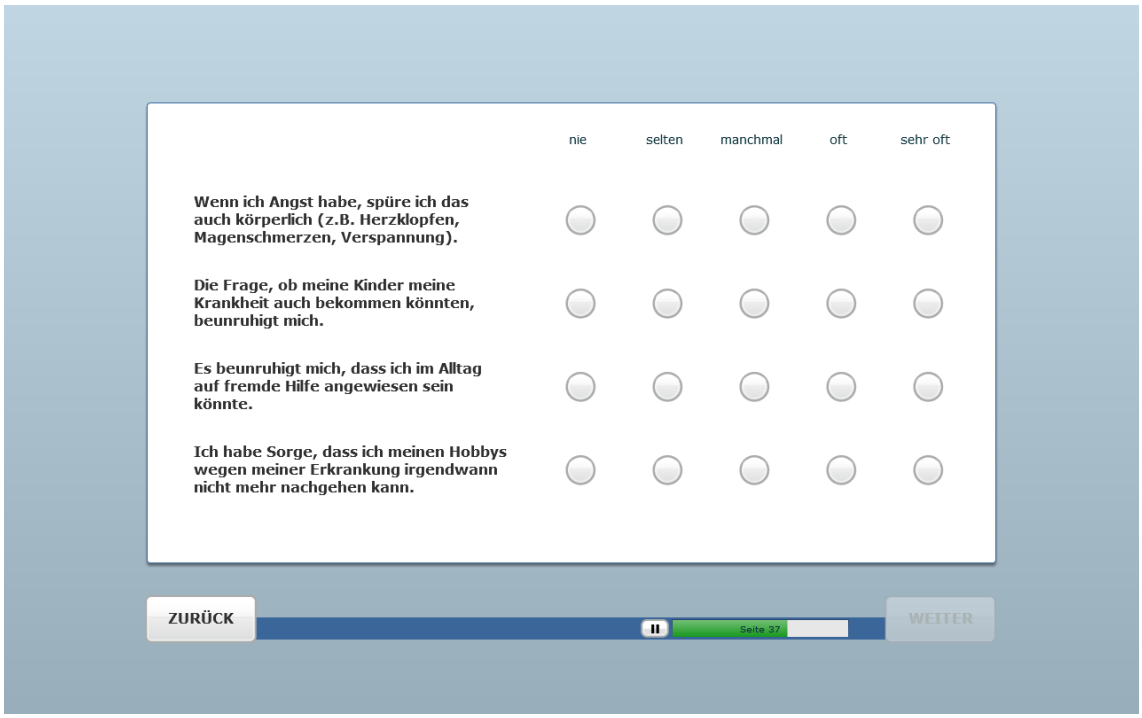


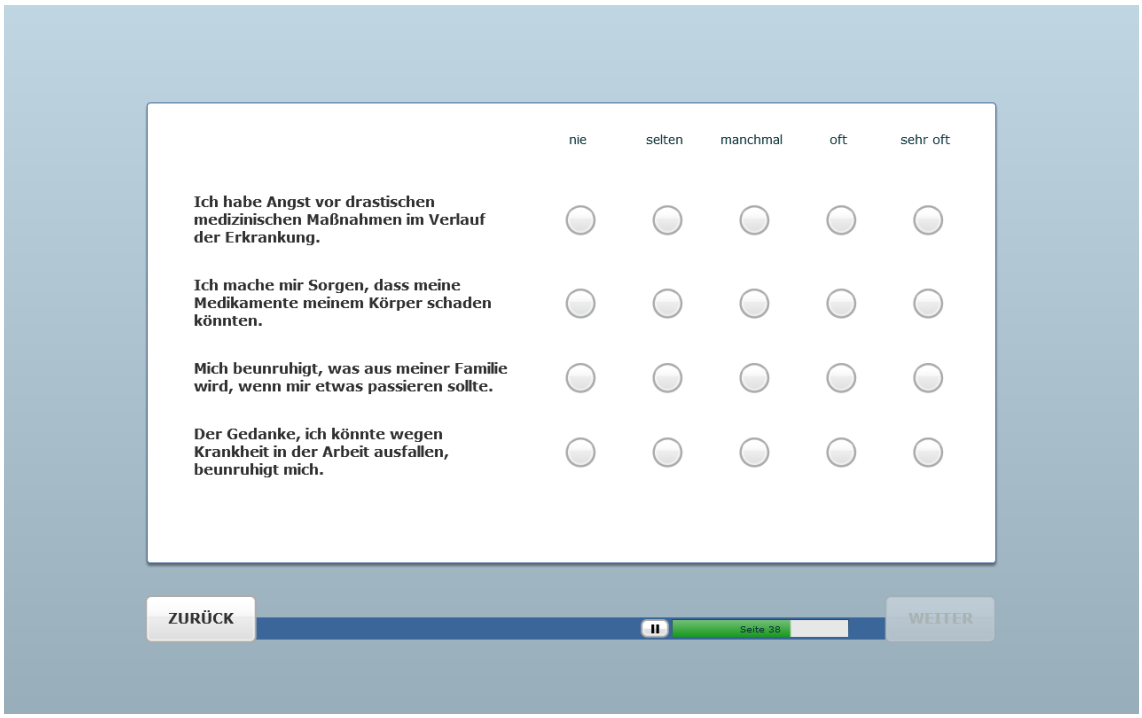


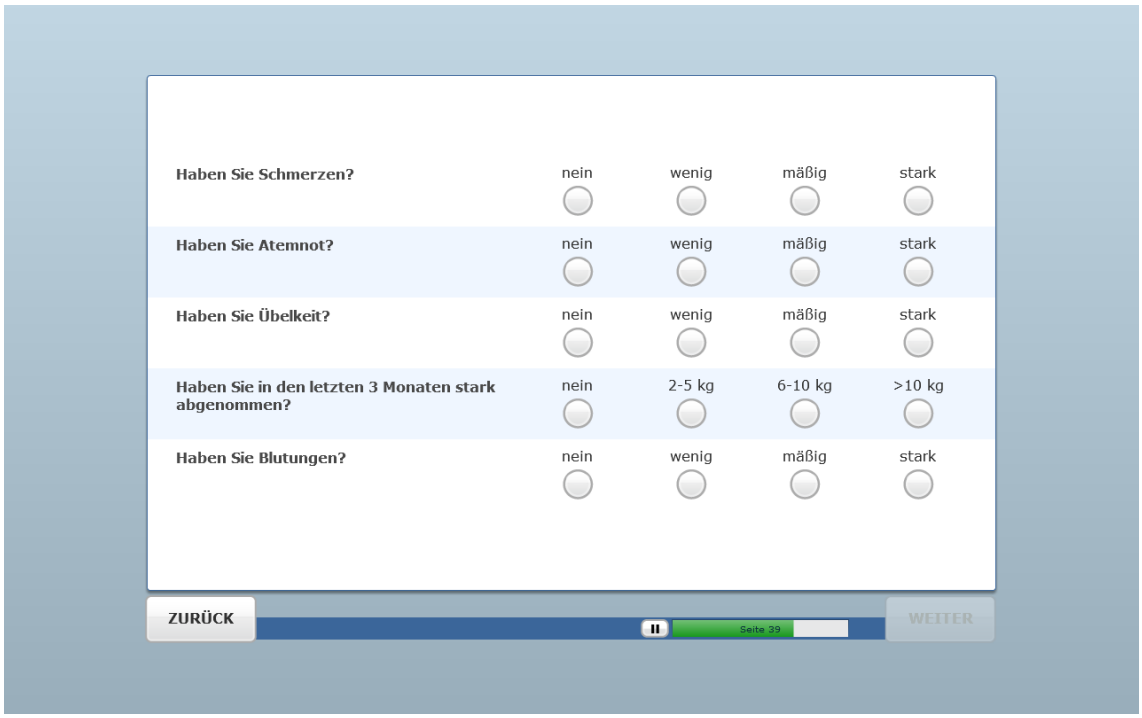

trifft nicht zu
trifft zu und belastet mich
kaum ..... sehr stark
Ich habe Schlafstörungen.
Ich kann meinen Hobbies (u.a. Sport) jetzt weniger nachgehen als vor der Erkrankung.
Ich fühle mich nicht gut über meine Erkrankung/ Behandlung informiert.
Ich bin angespannt bzw. nervös.
ZURÜCK
Seite 34
WEITER

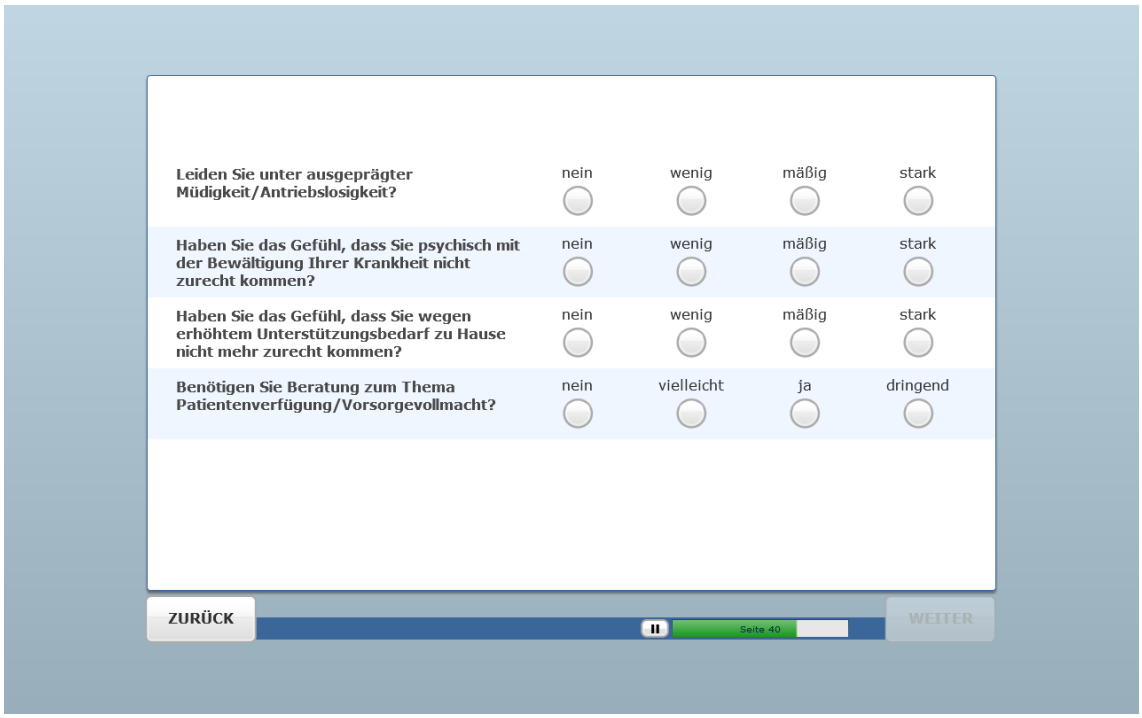

Im Folgenden finden Sie eine Reihe von Aussagen, die sich alle auf Ihre Erkrankung und mögliche **Zukunftssorgen** beziehen. Bitte kreuzen Sie bei jeder Aussage an, was für Sie zutrifft.
Sie können wählen zwischen »nie«, »selten«, »manchmal«, »oft« und »sehr oft«.
Sie werden sehen, dass einige Fragen nicht auf Sie zutreffen. Wenn Sie beispielsweise keine Familie haben, können Sie Fragen zur Familie nicht beantworten. Wir bitten Sie, in diesen Fällen ein Kreuz bei »nie« zu machen.
ZURÜCK
Seite 35
WEITER

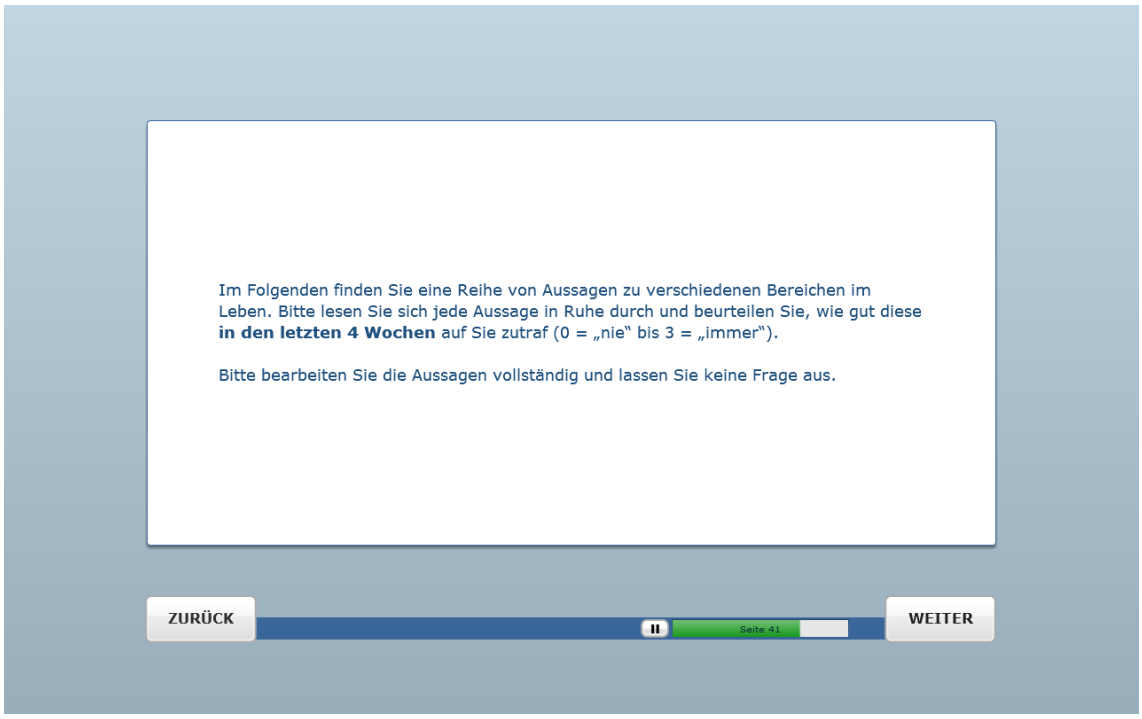

nie
selten
manchmal
oft
sehr oft
Wenn ich an den Verlauf meiner Erkrankung denke, bekomme ich Angst.
Vor Arztterminen oder Kontroll-untersuchungen bin ich ganz nervös.
Ich habe Angst vor Schmerzen.
Der Gedanke, ich könnte im Beruf nicht mehr so leistungsfähig sein, macht mir Angst.
ZURÜCK
Seite 36
WEITER

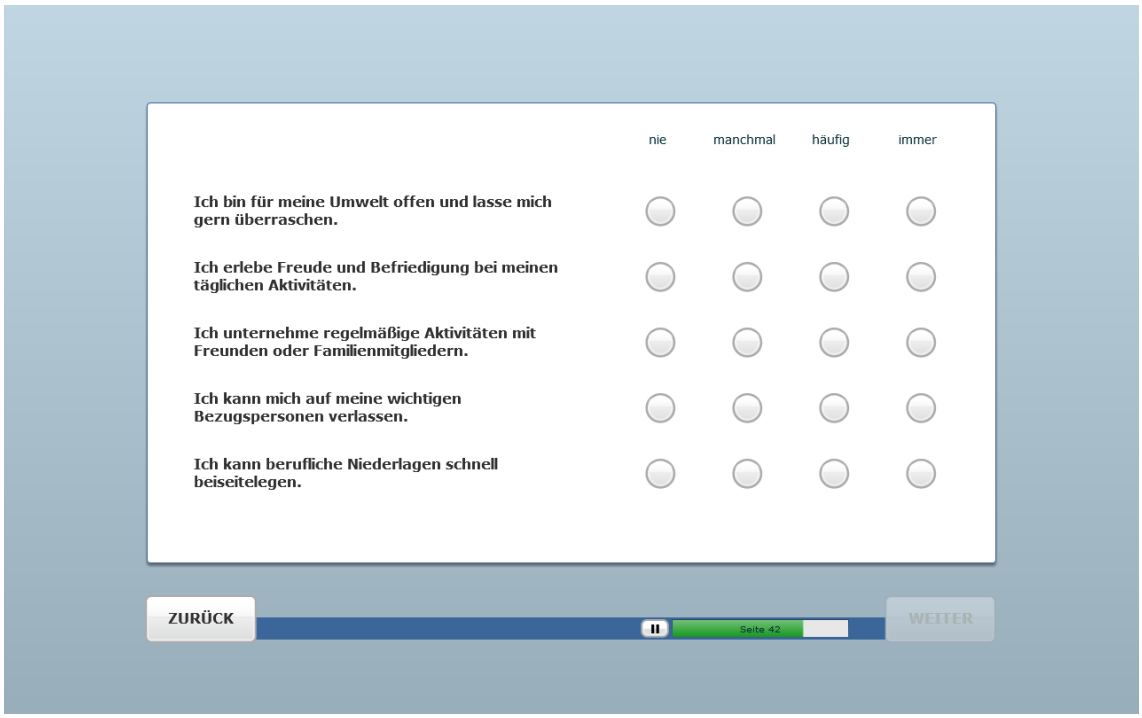

nie
selten
manchmal
oft
sehr oft
Wenn ich Angst habe, spüre ich das auch körperlich (z.B. Herzklopfen, Magenschmerzen, Verspannung).
Die Frage, ob meine Kinder meine Krankheit auch bekommen könnten, beunruhigt mich.
Es beunruhigt mich, dass ich im Alltag auf fremde Hilfe angewiesen sein könnte.
Ich habe Sorge, dass ich meinen Hobbys wegen meiner Erkrankung irgendwann nicht mehr nachgehen kann.
ZURÜCK
Seite 37
WEITER

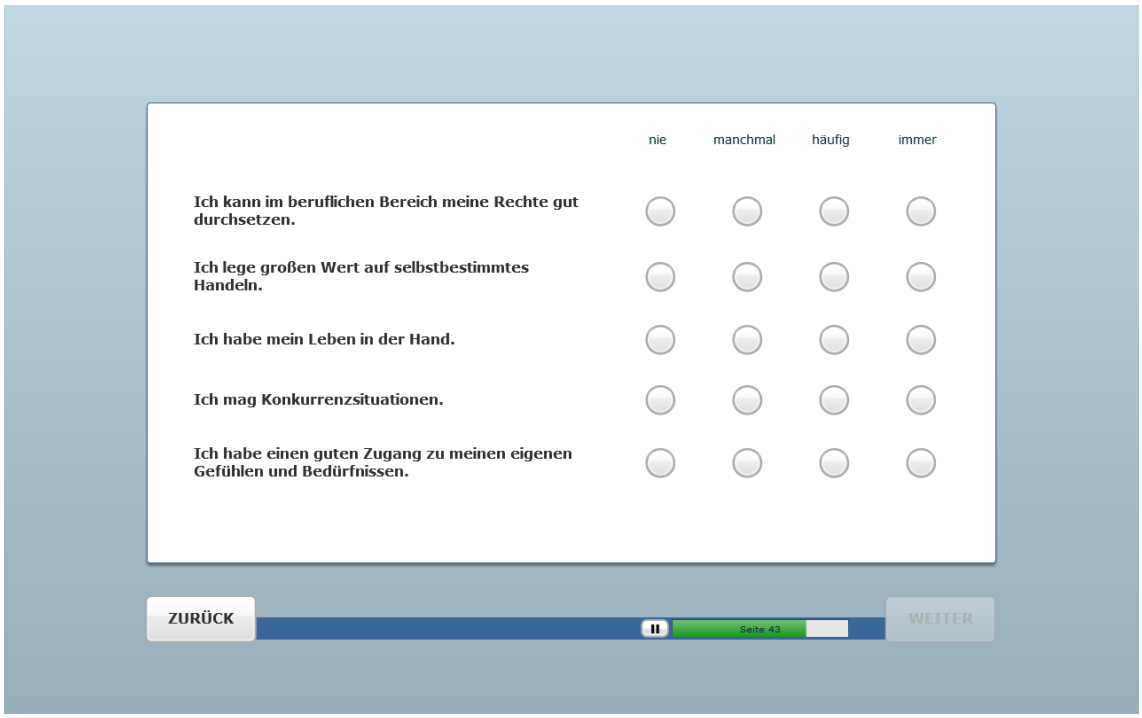

nie
selten
manchmal
oft
sehr oft
Ich habe Angst vor drastischen medizinischen Maßnahmen im Verlauf der Erkrankung.
Ich mache mir Sorgen, dass meine Medikamente meinem Körper schaden könnten.
Mich beunruhigt, was aus meiner Familie wird, wenn mir etwas passieren sollte.
Der Gedanke, ich könnte wegen Krankheit in der Arbeit ausfallen, beunruhigt mich.
ZURÜCK
Seite 38
WEITER

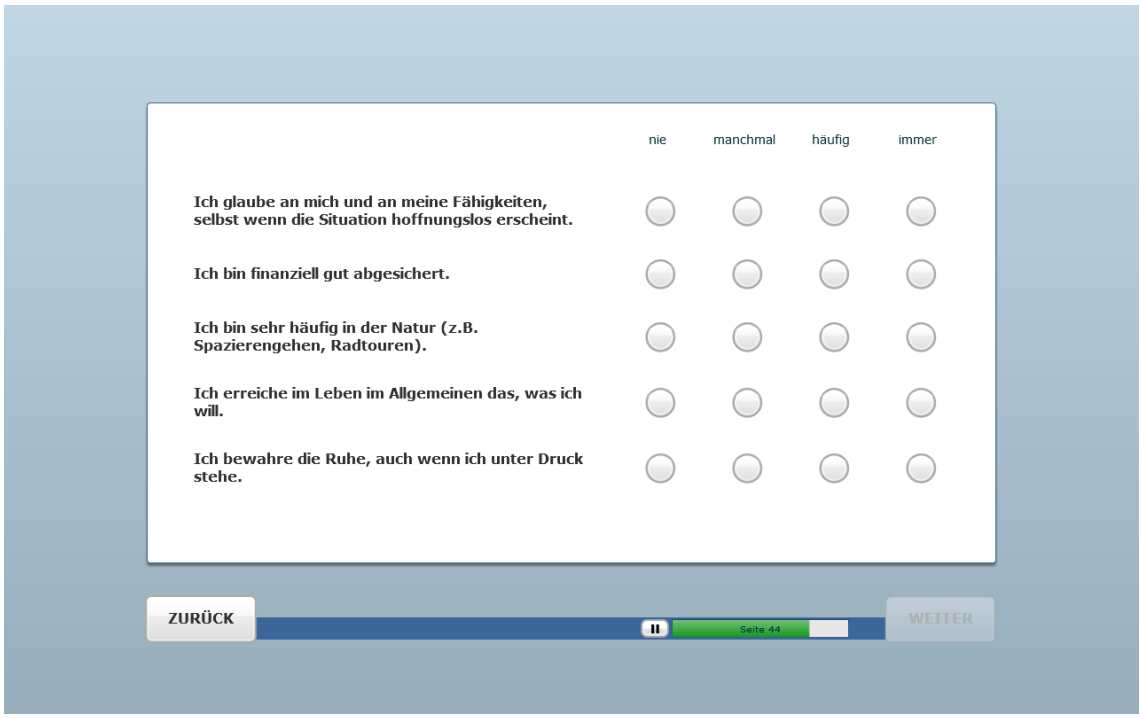

Haben Sie Schmerzen?
nein
wenig
mäßig
stark
Haben Sie Atemnot?
nein
wenig
mäßig
stark
Haben Sie Übelkeit?
nein
wenig
mäßig
stark
Haben Sie in den letzten 3 Monaten stark abgenommen?
nein
2-5 kg
6-10 kg
>10 kg
Haben Sie Blutungen?
nein
wenig
mäßig
stark
ZURÜCK
Seite 39
WEITER

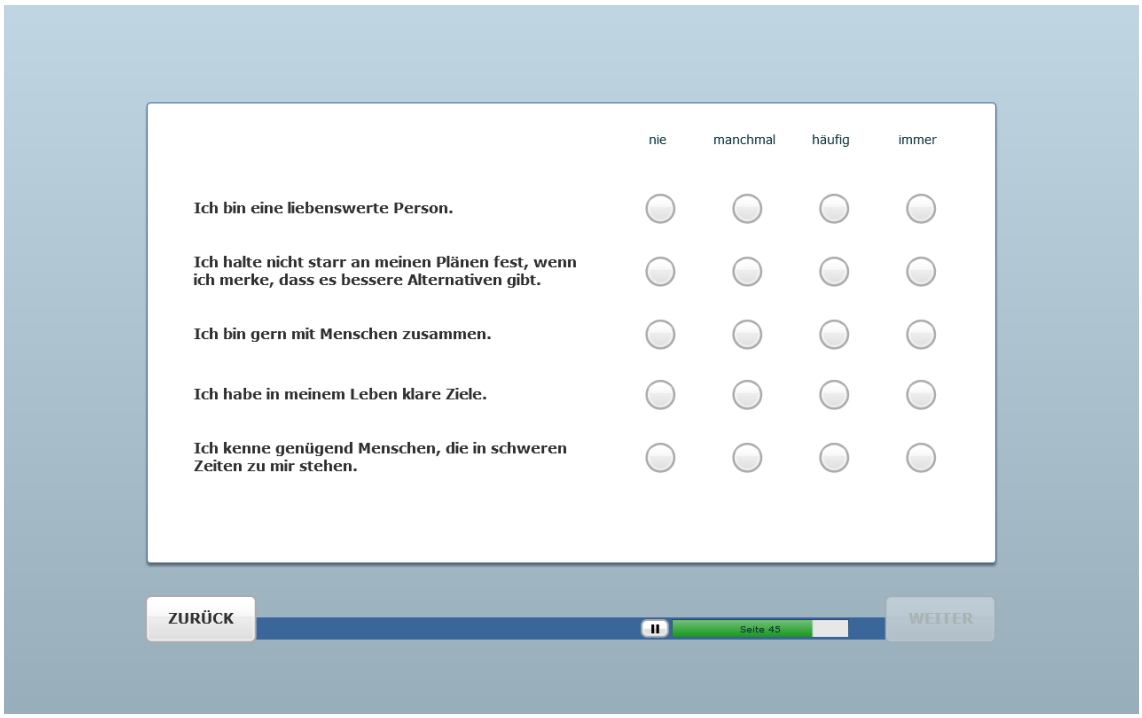

Leiden Sie unter ausgeprägter Müdigkeit/Antriebslosigkeit?
nein
wenig
mäßig
stark
Haben Sie das Gefühl, dass Sie psychisch mit der Bewältigung Ihrer Krankheit nicht zurecht kommen?
nein
wenig
mäßig
stark
Haben Sie das Gefühl, dass Sie wegen erhöhtem Unterstützungsbedarf zu Hause nicht mehr zurecht kommen?
nein
wenig
mäßig
stark
Benötigen Sie Beratung zum Thema Patientenverfügung/Vorsorgevollmacht?
nein
vielleicht
ja
dringend
ZURÜCK
Seite 40
WEITER

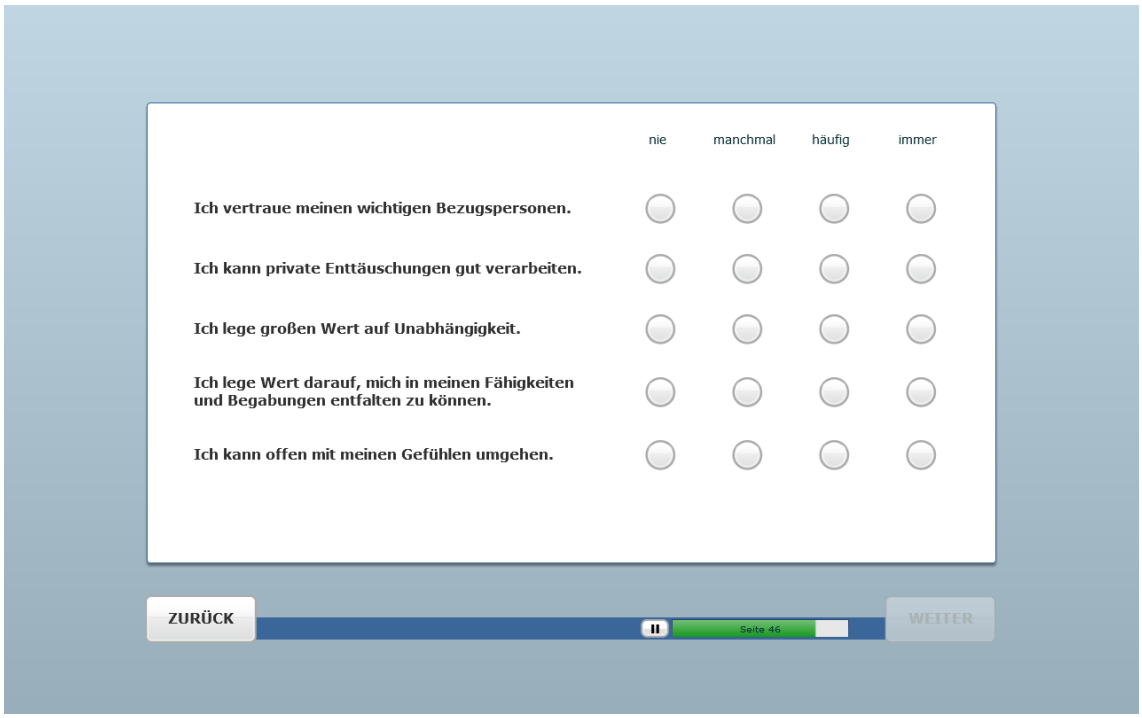

Im Folgenden finden Sie eine Reihe von Aussagen zu verschiedenen Bereichen im Leben. Bitte lesen Sie sich jede Aussage in Ruhe durch und beurteilen Sie, wie gut diese in den letzten 4 Wochen auf Sie zutraf (0 = „nie“ bis 3 = „immer“).
Bitte bearbeiten Sie die Aussagen vollständig und lassen Sie keine Frage aus.
ZURÜCK
Seite 41
WEITER

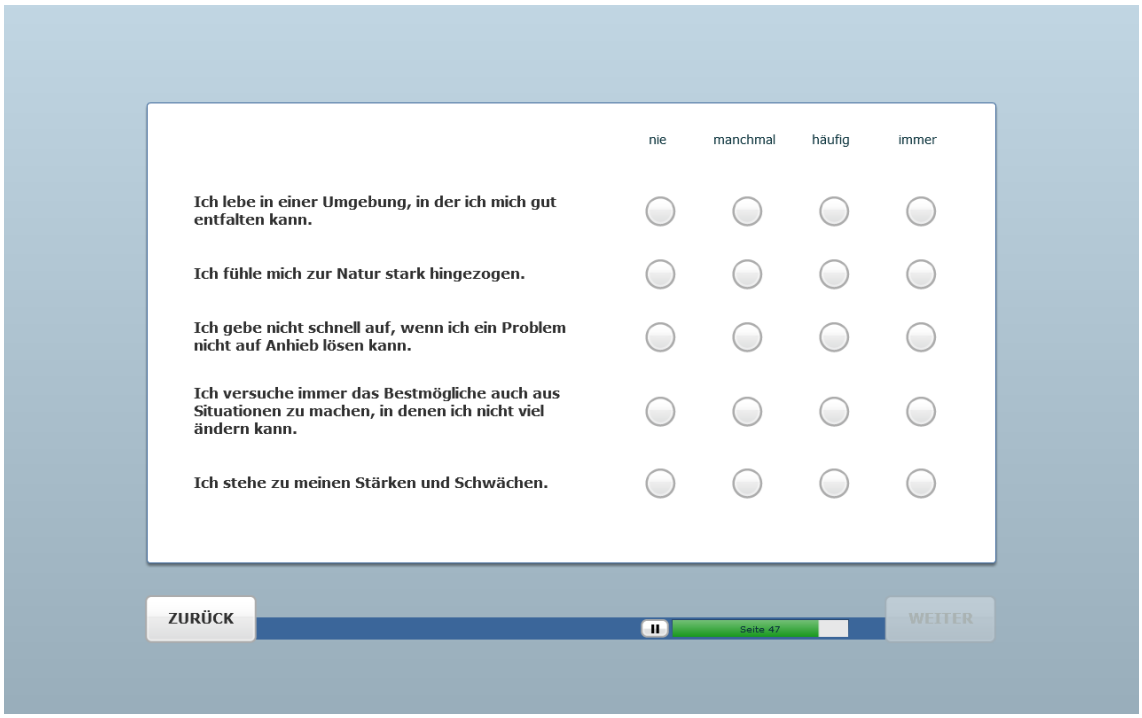

nie
manchmal
häufig
immer
Ich bin für meine Umwelt offen und lasse mich gern überraschen.
Ich erlebe Freude und Befriedigung bei meinen täglichen Aktivitäten.
Ich unternehme regelmäßige Aktivitäten mit Freunden oder Familienmitgliedern.
Ich kann mich auf meine wichtigen Bezugspersonen verlassen.
Ich kann berufliche Niederlagen schnell beiseitelegen.
ZURÜCK
Seite 42
WEITER

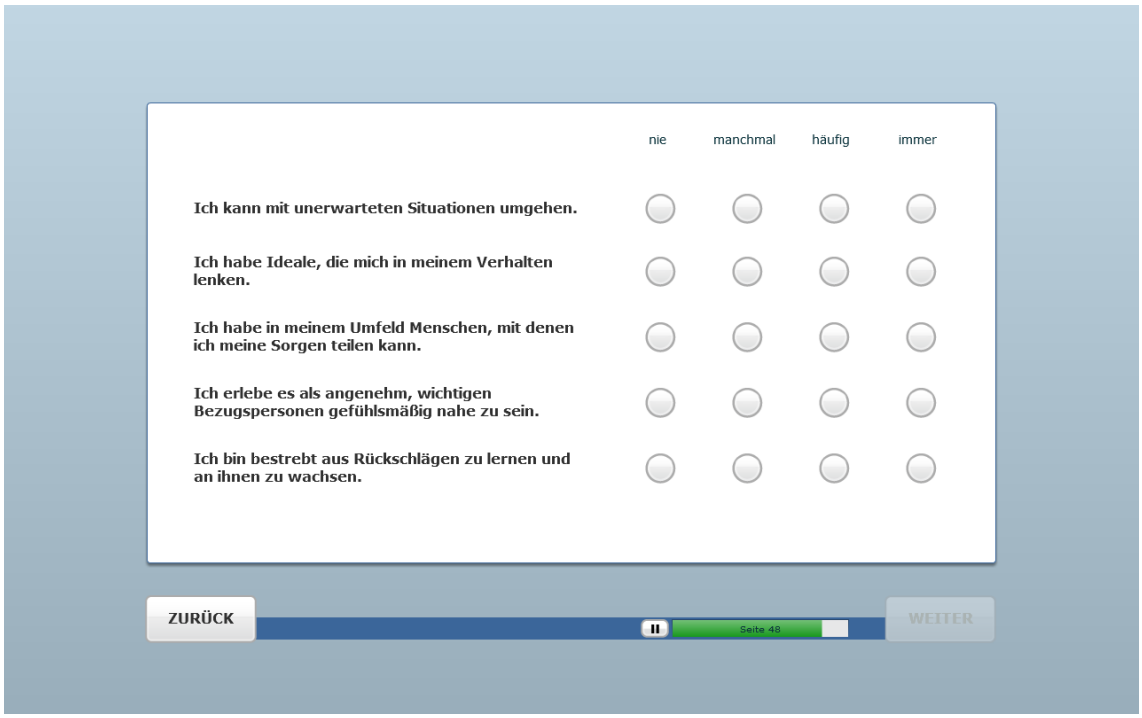

nie
manchmal
häufig
immer
Ich kann im beruflichen Bereich meine Rechte gut durchsetzen.
Ich lege großen Wert auf selbstbestimmtes Handeln.
Ich habe mein Leben in der Hand.
Ich mag Konkurrenzsituationen.
Ich habe einen guten Zugang zu meinen eigenen Gefühlen und Bedürfnissen.
ZURÜCK
Seite 43
WEITER

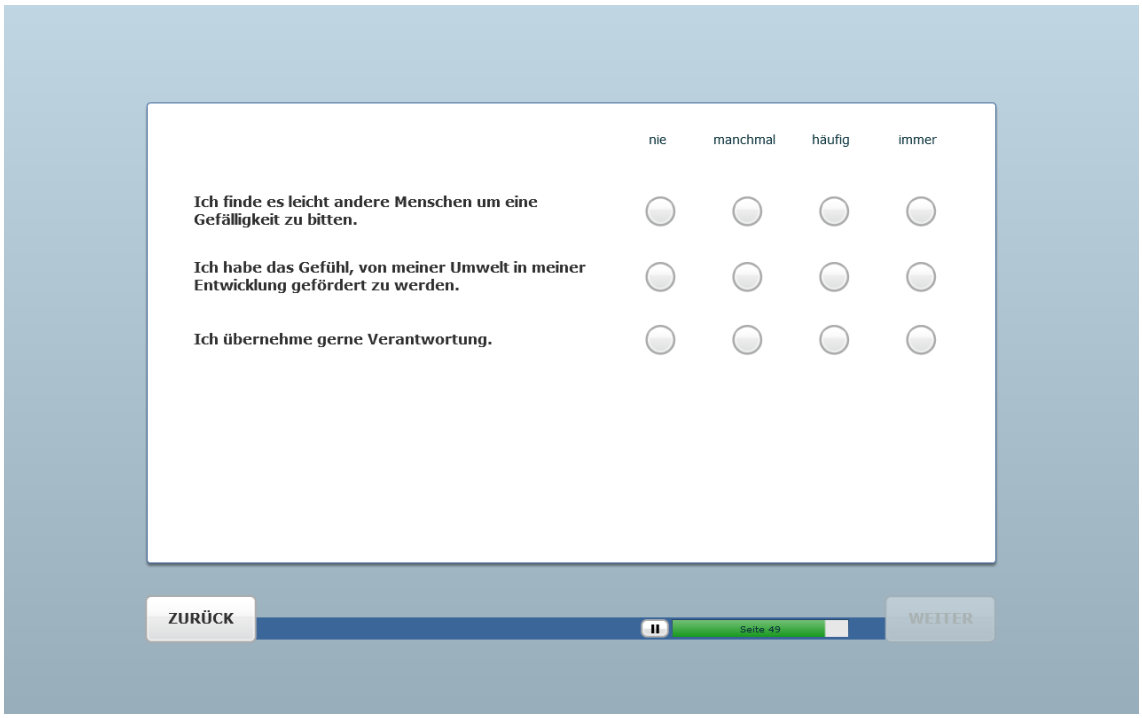

nie
manchmal
häufig
immer
Ich glaube an mich und an meine Fähigkeiten, selbst wenn die Situation hoffnungslos erscheint.
Ich bin finanziell gut abgesichert.
Ich bin sehr häufig in der Natur (z.B. Spazierengehen, Radtouren).
Ich erreiche im Leben im Allgemeinen das, was ich will.
Ich bewahre die Ruhe, auch wenn ich unter Druck stehe.
ZURÜCK
Seite 44
WEITER


nie
manchmal
häufig
immer
Ich bin eine liebenswerte Person.
Ich halte nicht starr an meinen Plänen fest, wenn ich merke, dass es bessere Alternativen gibt.
Ich bin gern mit Menschen zusammen.
Ich habe in meinem Leben klare Ziele.
Ich kenne genügend Menschen, die in schweren Zeiten zu mir stehen.
ZURÜCK
Seite 45
WEITER


nie
manchmal
häufig
immer
Ich vertraue meinen wichtigen Bezugspersonen.
Ich kann private Enttäuschungen gut verarbeiten.
Ich lege großen Wert auf Unabhängigkeit.
Ich lege Wert darauf, mich in meinen Fähigkeiten und Begabungen entfalten zu können.
Ich kann offen mit meinen Gefühlen umgehen.
ZURÜCK
Seite 46
WEITER

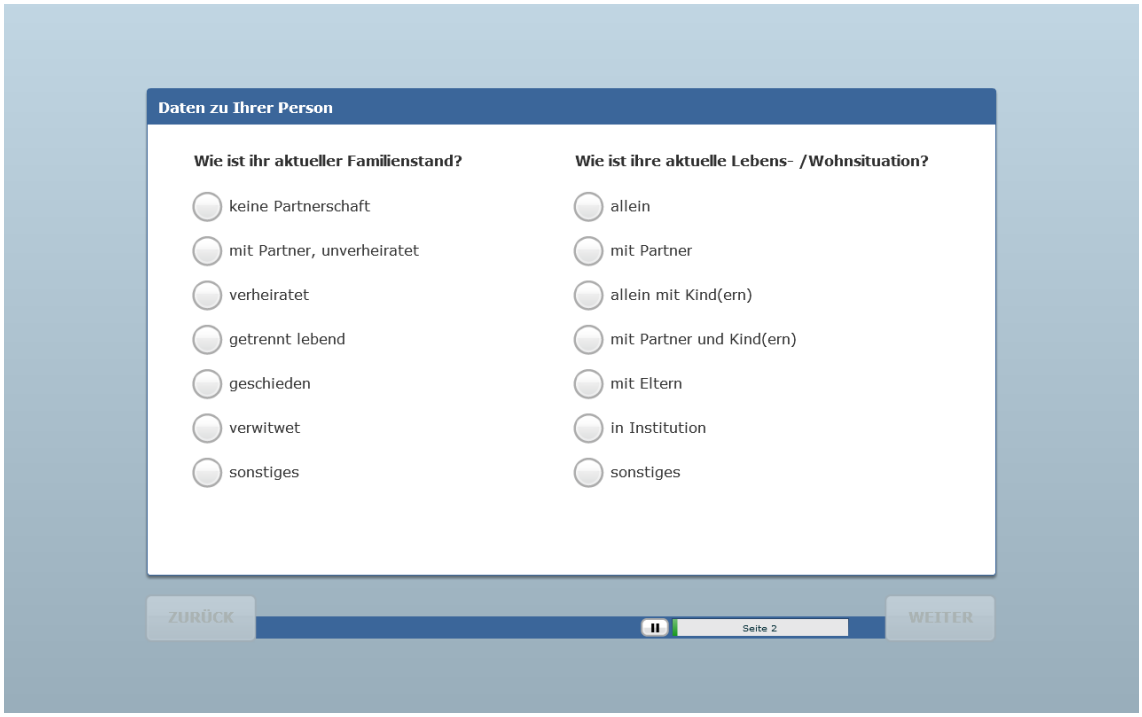

nie
manchmal
häufig
immer
Ich lebe in einer Umgebung, in der ich mich gut entfalten kann.
Ich fühle mich zur Natur stark hingezogen.
Ich gebe nicht schnell auf, wenn ich ein Problem nicht auf Anhieb lösen kann.
Ich versuche immer das Bestmögliche auch aus Situationen zu machen, in denen ich nicht viel ändern kann.
Ich stehe zu meinen Stärken und Schwächen.
ZURÜCK
Seite 47
WEITER

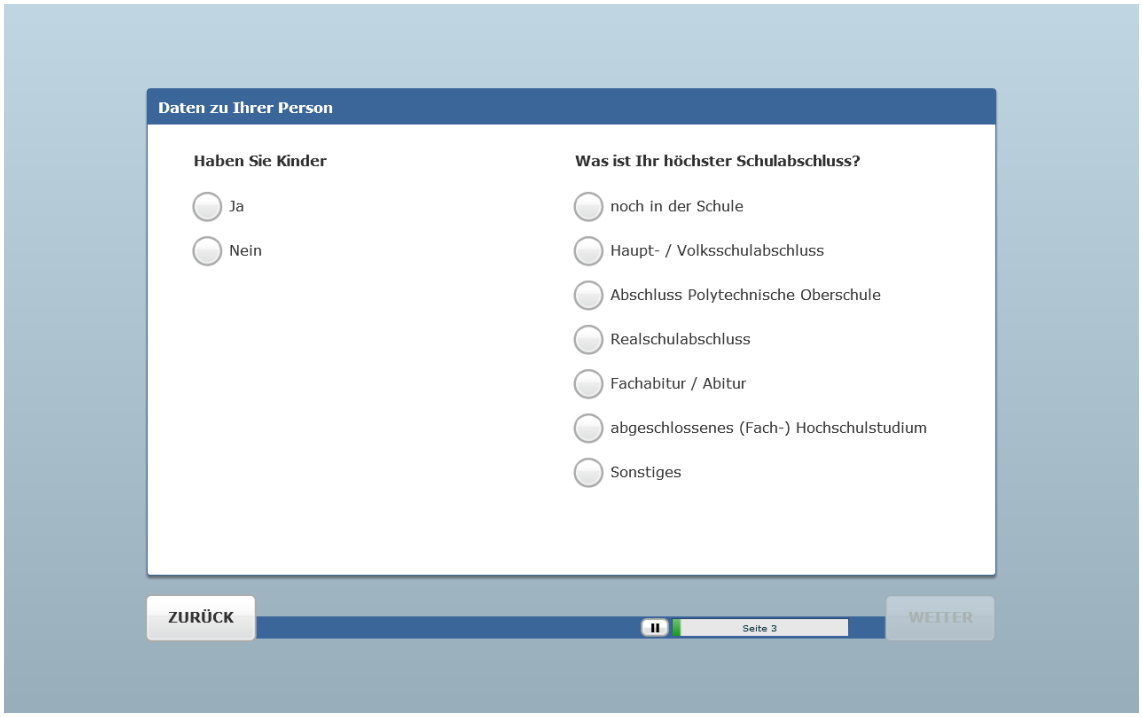

nie
manchmal
häufig
immer
Ich kann mit unerwarteten Situationen umgehen.
Ich habe Ideale, die mich in meinem Verhalten lenken.
Ich habe in meinem Umfeld Menschen, mit denen ich meine Sorgen teilen kann.
Ich erlebe es als angenehm, wichtigen Bezugspersonen gefühlsmäßig nahe zu sein.
Ich bin bestrebt aus Rückschlägen zu lernen und an ihnen zu wachsen.
ZURÜCK
Seite 48
WEITER

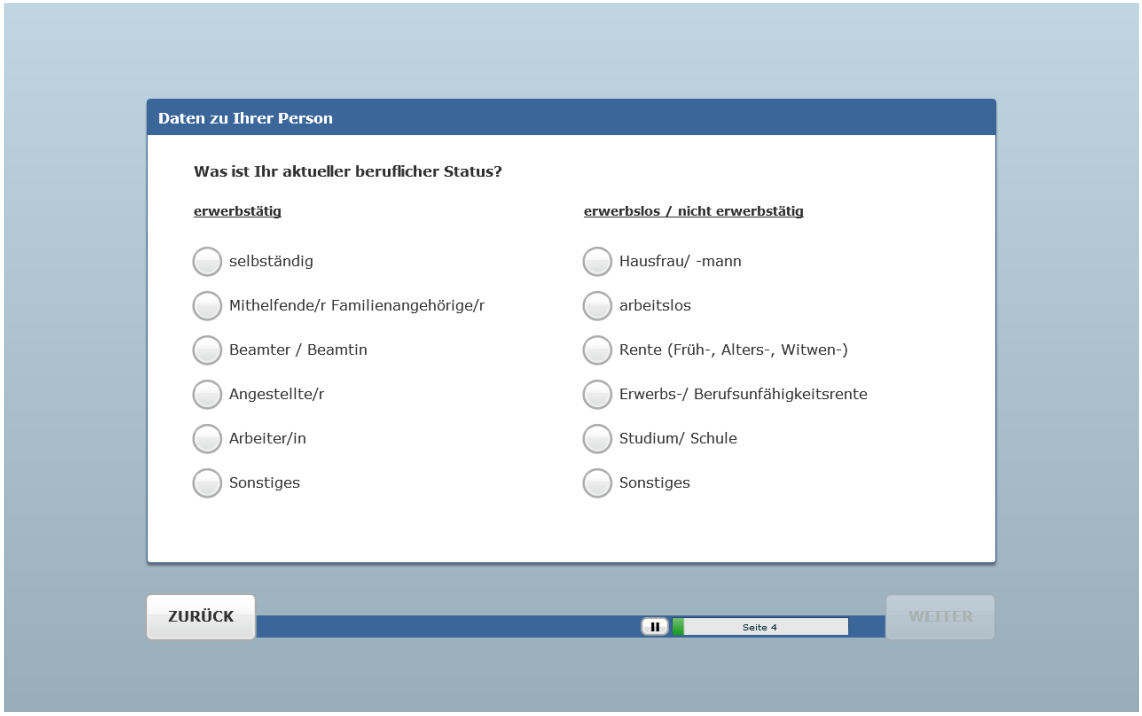

nie
manchmal
häufig
immer
Ich finde es leicht andere Menschen um eine Gefälligkeit zu bitten.
Ich habe das Gefühl, von meiner Umwelt in meiner Entwicklung gefördert zu werden.
Ich übernehme gerne Verantwortung.
ZURÜCK
Seite 49
WEITER

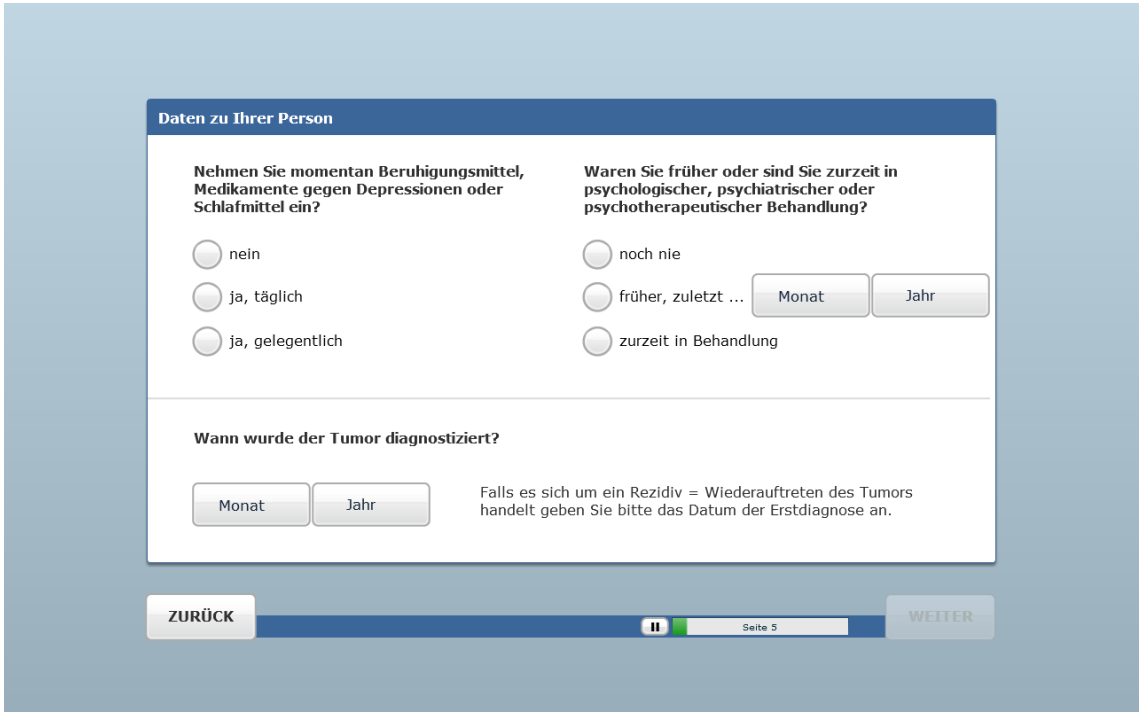
Appendix 9.

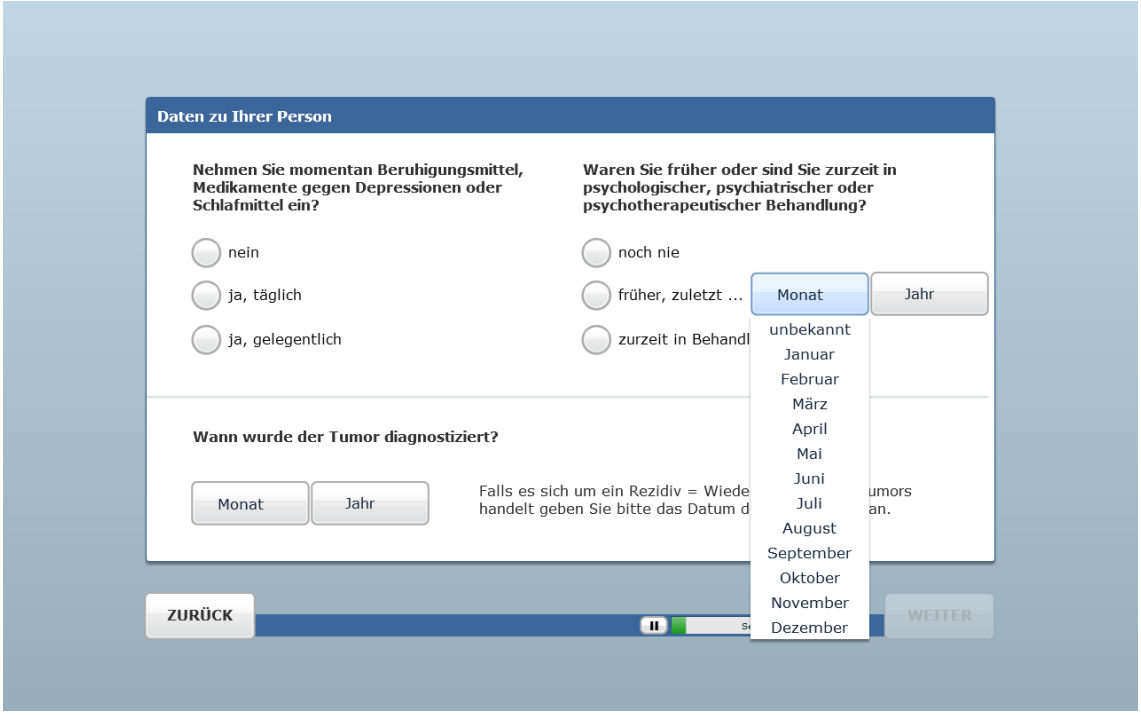
Sociodemographic and clinical data questionnaire in ePOS.





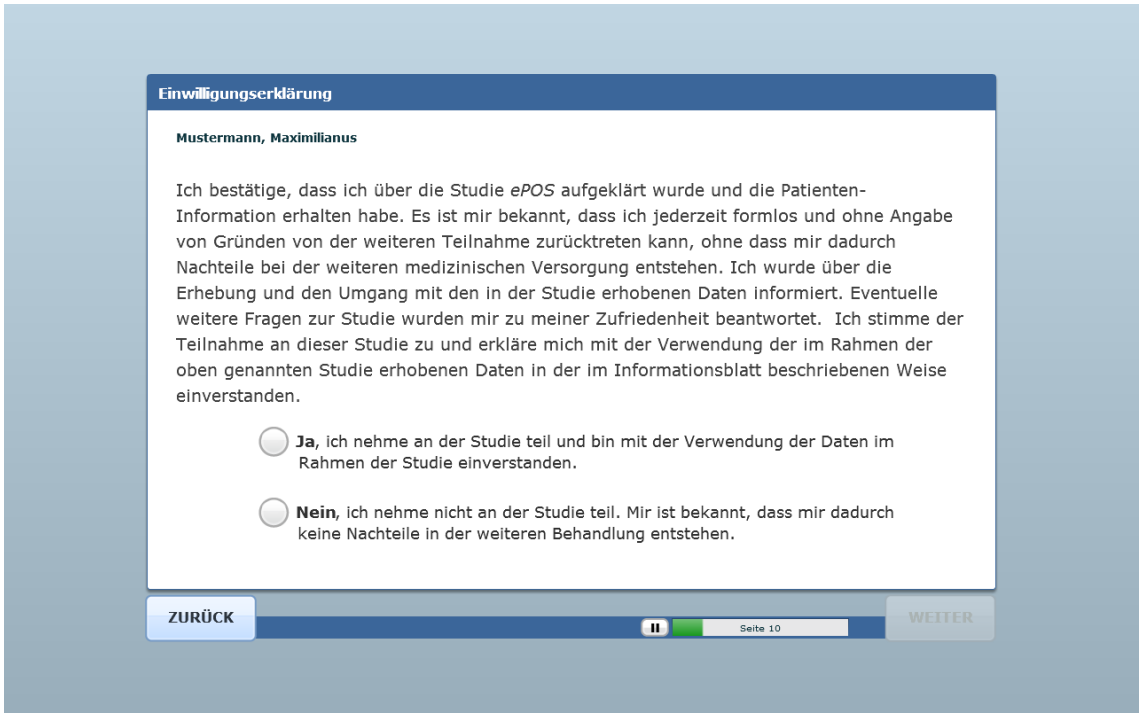

Daten zu Ihrer Person
Was ist Ihr aktueller beruflicher Status?
erwerbstätig
selbständig
Mithelfende/r Familienangehörige/r
Beamter / Beamtin
Angestellte/r
Arbeiter/in
Sonstiges
erwerbslos / nicht erwerbstätig
Hausfrau/ -mann
arbeitslos
Rente (Früh-, Alters-, Witwen-)
Erwerbs-/ Berufsunfähigkeitsrente
Studium/ Schule
Sonstiges
ZURÜCK
Seite 4
WEITER

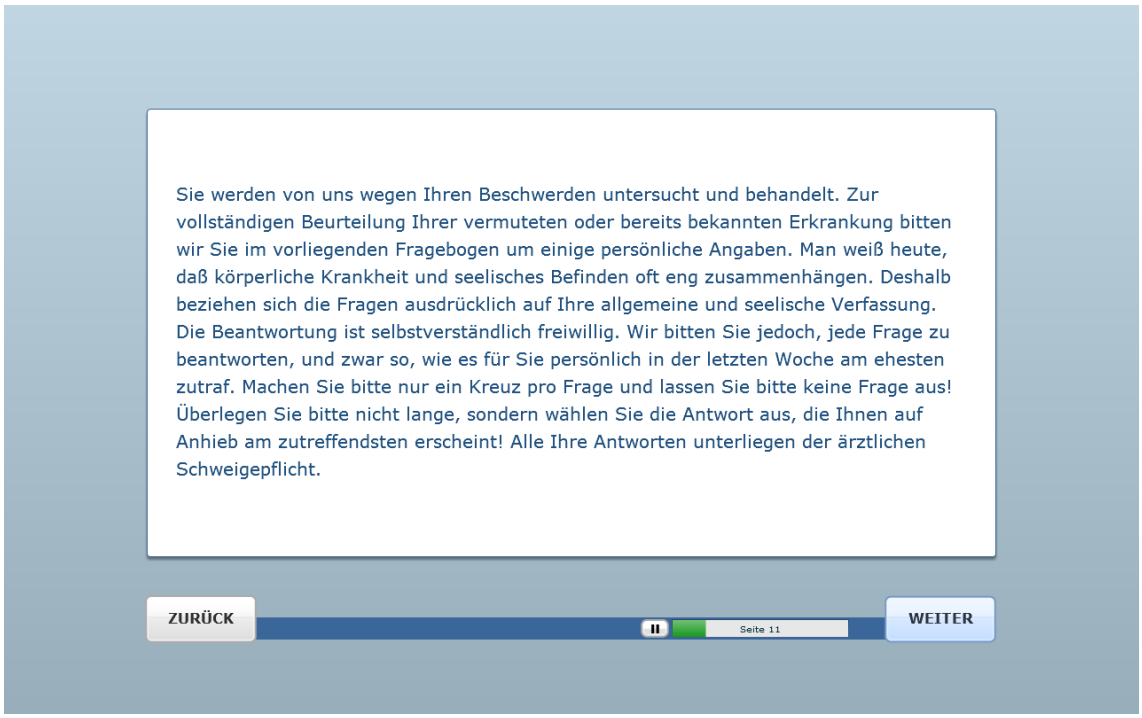

Daten zu Ihrer Person
Nehmen Sie momentan Beruhigungsmittel, Medikamente gegen Depressionen oder Schlafmittel ein?
nein
ja, täglich
ja, gelegentlich
Waren Sie früher oder sind Sie zurzeit in psychologischer, psychiatrischer oder psychotherapeutischer Behandlung?
noch nie
früher, zuletzt ...
Monat
Jahr
zurzeit in Behandlung
Wann wurde der Tumor diagnostiziert?
Monat
Jahr
Falls es sich um ein Rezidiv = Wiederauftreten des Tumors handelt geben Sie bitte das Datum der Erstdiagnose an.
ZURÜCK
Seite 5
WEITER


Daten zu Ihrer Person
Nehmen Sie momentan Beruhigungsmittel, Medikamente gegen Depressionen oder Schlafmittel ein?
nein
ja, täglich
ja, gelegentlich
Waren Sie früher oder sind Sie zurzeit in psychologischer, psychiatrischer oder psychotherapeutischer Behandlung?
noch nie
früher, zuletzt ...
zurzeit in Behandl
Monat
Jahr
unbekannt
Januar
Februar
März
April
Mai
Juni
Juli
August
September
Oktober
November
Dezember
Wann wurde der Tumor diagnostiziert?
Monat
Jahr
Falls es sich um ein Rezidiv = Wiede
handelt geben Sie bitte das Datum d
umors
an.
ZURÜCK
WEITER

Appendix 10.

Informed consent in ePOS.




Sie werden von uns wegen Ihren Beschwerden untersucht und behandelt. Zur vollständigen Beurteilung Ihrer vermuteten oder bereits bekannten Erkrankung bitten wir Sie im vorliegenden Fragebogen um einige persönliche Angaben. Man weiß heute, daß körperliche Krankheit und seelisches Befinden oft eng zusammenhängen. Deshalb beziehen sich die Fragen ausdrücklich auf Ihre allgemeine und seelische Verfassung. Die Beantwortung ist selbstverständlich freiwillig. Wir bitten Sie jedoch, jede Frage zu beantworten, und zwar so, wie es für Sie persönlich in der letzten Woche am ehesten zutraf. Machen Sie bitte nur ein Kreuz pro Frage und lassen Sie bitte keine Frage aus! Überlegen Sie bitte nicht lange, sondern wählen Sie die Antwort aus, die Ihnen auf Anhieb am zutreffendsten erscheint! Alle Ihre Antworten unterliegen der ärztlichen Schweigepflicht.
ZURÜCK
Seite 11
WEITER