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ABSTRACT:

This deliverable outlines how an easy-to-use psychological profile questionnaires for cancer patients (ALGA-C) has been developed and validated on a two different samples of healthy controls. These surveys will cover patients' psychological needs and provide information that will facilitate improved communication between the patient and the physician to enable a shared treatment decision-making process and improve patient empowerment. The deliverable outlines how a patient's quality of life is affected by their perceived health state and other psychological, psychosocial and cognitive factors, and how the ALGA-C questionnaire will be developed to investigate these areas.

KEYWORD LIST: Patient empowerment, psychological profile, patient questionnaires

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[1] **R**=Report, **P**=Prototype, **D**=Demonstrator, **O**=Other

[2] **PU**=Public, **PP**=Restricted to other programme participants (including the Commission Services), **RE**=Restricted to a group specified by the consortium (including the Commission Services), **CO**=Confidential, only for members of the consortium (including the Commission Services)

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1 Executive Summary

The main objective of this deliverable is to outline the psychological framework around which the p-medicine patient empowerment tools and services will be built. By developing an understanding of the factors affecting a patient's quality of life, the project can define a strategy for how the patient empowerment tools and services developed within p-medicine seek to affect the factors that influence this.

This deliverable defines the psychological, psychosocial and cognitive factors that influence quality of life and how these elements can be investigated and measured through a patient survey (ALGA-C).

The p-medicine environment will provide a series of patient empowerment tools that will provide information to empower the patient. This additional information, combined with heightened understanding of a patient's psychological needs, provided by the results of the ALGA-C questionnaires, will facilitate patient/doctor communication and ensure that treatment decisions are made jointly and that patients are empowered.

2. Introduction

The purpose of this document is to identify the processes needed to form a robust psychological framework for the patient empowerment tools developed within the p-medicine environment. Quality of life is obviously very important to a cancer patient, but quality of life can be affected by different factors in different patients. We will identify how to develop a framework in which the different psychological, psychosocial and cognitive that influence quality of life will be measured.

By measuring these factors through a unique, easy to use and short questionnaire, physicians can be given a heightened insight into the psychological profile of a patient and how best to take these factors into account. Through this process, patient-doctor communication will be influenced to ensure that patients are fully involved informed and empowered to be involved in the treatment decision making process.

3. Questionnaires (e.g. specific CRFs) for patients enrolled in clinical research and daily clinical care

3.1 Background

The increasing incidence of cancer, as well as the increasing number of people surviving the disease, means that there are approximately 12 million cancer survivors around the world (www.seer.cancer.gov) require both the search for new and effective cures for various types of cancer and the understanding and improvement of survivors' health status, impacting on patient care in general. We thus need better medical treatments and optimized therapies on the one hand, and instruments to monitor changes in the patient's health-related quality of life on the other hand. While the former is addressed by the recently emerging and promising field of personalized medicine, the latter is approached by the use of patient-reported outcome measures (PROMs). PROMs are reports that are directly coming from the patient, providing patient-based information about health condition, illness and the effects of treatment. This information is related to the quality of life of a patient and is therefore reasoned to benefit patient care in multiple ways. PROMs were shown to facilitate communication between the physician and the patient through heightening health care providers' awareness of patient issues, thereby increasing the possibility of identifying and prioritizing patients' problems and considerations. Improved communication is thought to promote shared decision making and patient empowerment which, in turn, is hoped to affect patient outcomes. However, research found the impact on health outcomes to be less evident. The transformation of changes in the process of care to changes in patient outcomes poses a major challenge for future considerations. Limitations to a successful and wide implementation of PROMs in clinical practice might constitute one explanation for the missing impact on health outcomes in patients. Practical, attitudinal and methodological barriers to the successful adoption of PROMs in daily clinical practice must first be overcome before optimizing their use with the aim of influencing patient outcomes in a desired way. One of the most important first steps in overcoming these barriers is the development of a sound measure investigating the most important dimensions related to patients' quality of life. In developing such a measure, special attention should be paid to the format and length of the measure as well as potential IT support facilitating the administration, scoring and interpretation of patient data. In conclusion, PROMs offer a promising first step into this direction, though instruments must be continuously improved and the impact on patient outcomes optimized.

As much effort as possible should be taken to improve both the personalized medicine approach, and the approach including PROMs, we feel that it is of utmost importance to combine these two approaches. In our view it is essential to combine the medical and the psychological perspective in cancer care in order to optimize general health care delivery. Therefore, we developed a multi-dimensional, short, easy-to-use and acceptable psychological profile questionnaire specific for cancer patients (ALGA-C) that is aimed to monitor patients' quality of life and, at the same time, support the physician in his/her treatment decision-making process.

Once the questionnaire was developed (see below for details), in order to provide preliminary proof for the effectiveness of the instrument, to adjust for cultural differences and to calculate norm scores, the psychometric properties of a slightly adjusted version of the ALGA-C, the ALGA, were examined in two large population representative samples.

3.2 Quality of Life Assessment in Patients

Contemporary enhanced awareness of the strong correlation between quality of life aspects and the process of cure have led to recent attempts of finding reasonable and successful ways of including quality of life measures into the clinical process. Quality of life is commonly assessed by patient-reported outcome measures (PROMs) including health-related quality of life (HRQL) information. PROMs can be defined as “reports coming directly from patients about how they function or feel in relation to a health condition and its therapy, without interpretation of the patients’ responses by physician or anyone else” (Valderas et al., 2008).

Such measures can thus be described as instruments which provide patient-based information about health, illness and the effects of treatment. A large number of measures providing HRQL information is currently available. These instruments embrace a broad range of health dimensions such as physical, psychological and social functioning (Greenalgh, 1999). In addition to these aspects which are directly related to the quality of life of a patient, PROMs sometimes investigate broader constructs such as impairment, disability and handicap, also influencing quality of life to a substantial degree.

Addressing the rationale behind quality of life assessment in the clinical context, the use of PROMs is reasoned to benefit patient care in multiple ways. First, it increases physicians’ and nurses’ awareness of patients’ HRQL and thereby eases the discussion of these aspects.

Second, it has the potential of identifying and prioritizing problems such as physical or psychosocial problems that otherwise might have been overlooked and remain unrecognized. Since these problems might interfere with treatment, their detection is essential.

Third, patients’ preferences among outcome goals can be identified. This is important because physicians’ and patients’ priorities often differ substantially concerning the aims of treatment, the impact of the disease on patients’ lives and the values of possible outcomes. Additionally, the investigation of patients’ preferences enables an anticipation of benefits regarding patients’ adherence to treatment.

Fourth, PROMs allow for the monitoring of disease progression and treatment that may not be revealed via clinical testing.

Fifth, PROMs can be used as screening instruments investigating unmet needs that require referral.

Sixth, as a result of including PROMs into the treatment process, the patient might feel better cared for which positively influence his/her emotional functioning.

A last, and probably one of the most important, advantages of using PROMs in clinical practice is the fact that it was found to facilitate and improve the communication between the physician and the patient. Despite the interconnectedness between the different advantages, improved communication may result from other just-discussed advantages such as heightened awareness of quality of life aspects on the side of the physician which facilitates communication of these aspects. In general, all these advantages resulting from the use of HRQL information are reasoned to promote shared decision making and patient empowerment which, in turn, is hoped to affect patient outcomes.

3.2.1 Shared decision-making and patient empowerment (through quality of life assessment)

It is essential for the patient to be actively involved and to participate in the decision making process concerning treatment in order to assure that decisions are consistent with the patient's values, preferences and general considerations. Shared decision making based on patient centered medicine involves a bi-directional information exchange between the physician and the patient (Neuman, Charlson, & Temple, 2007). For shared decision making to be effective, the content of communication in a medical consultation should include both factual data and patients' considerations. While the former is derived from clinical tools providing information about genetics and treatments, the latter is provided by PROMs providing HRQL information. Barnato et al. (2007) noted that "in an ideal world […] patients would come to a cancer consultation armed with sufficient knowledge, clarity about their personal value, and the ability to engage in a thoughtful discussion about the pros and cons of treatment options. Providers, in turn, would be prepared to support their patients, armed with an understanding of the patient's knowledge gaps, personal values about possible outcomes and treatment preferences." (p.627). However, clinical consultations take place under conditions of limited time where physician talk sometimes overwhelms patient's preferences and considerations. This gap between an optimal and many actual encounters could be reduced by implementing PROMs that raise awareness of patient considerations, facilitate the discussion of these aspects and thereby actively involve the patient into the medical decision process. This shared decision making process empowers the patient because it provides him/her with the chance of making his/her own, well-discussed and well-informed, choice concerning the treatment.

By fostering a shared decision making process and by generally empowering the patient, the use of PROMs in clinical practice is reasoned to improve generally delivery of care, to lead to better patient outcomes manifested in reduced symptoms, improved HRQL and patient satisfaction.
Despite the proposed positive impact of the integration of PROMs in daily clinical practice, the main question is whether the rationales behind the assessment of HRQL information turn out to manifest themselves in reality. To answer this question, the following paragraph includes research that is available to date examining the rationales behind the use of PROMs.

3.2.2 Evidence for the effectiveness of quality of life assessment in patients

A great amount of research evaluated the efficacy of routinely integrating HRQL measures in daily clinical practice. Many of these studies include cancer patients. In general, the majority of these studies investigated patient-physician communication as an outcome measure. This is reasonable given that effective communication is an early step in the care process (Detmar, 2002). In case no effect of communication is found, it seems rather unlikely that results will show effects on more distal outcomes such as quality of life or patient satisfaction.
One study asked patients to complete standard health related quality of life measures that were transformed into a graphical summary and provided to the physician and patient prior to the medical consultation (Detmar, 2002). In contrast to most other studies that only use patients' self-reported data, this study sought to confirm self-report data by behavioral measures. Through audiotaping and content analyzing of the consultation patient-physician was analyzed. Results reveal that issues related to quality of life were discussed significantly more often compared to the control group. Consistent with this observation, all physicians and the majority of patients (87%) reported the intervention to facilitate communication. A similar study, additionally including nurses, found similar results (Hilarius et al., 2008). Although not containing behavioral measures, results indicate better awareness of patients' quality of life aspects on the side of health professionals. Again, this led to facilitated communication and more frequent discussion of HRQL issues. However, only modest effects were found with regard to patients' satisfaction and changes in quality of life over time.
Correspondingly, the majority of studies investigating the effect of PROMs on patient care and patient outcomes are rather disappointing. Despite most studies finding PROMs to be effective in facilitating patient-physician communication and problem detection, the impact on health outcomes has been less evident. Luckett et al. (2009) undertook a detailed, critical review of randomized controlled trials in oncology in order to find future suggestions for interventions to impact on patient outcomes. Six random controlled trials were found to investigate the effects of the implementation of PROMs on patient outcomes. A detailed analysis of these trials led the authors to conclude that PROM data is not optimally used because it is used only intermittently and then to an undetermined purpose by physicians. Furthermore, it seems very implausible that screening for quality of life aspects alone can improve patient outcomes (Jacobsen et al., 2007). Therefore, if a physician is provided with information about a patient's considerations such as, for example, heightened distress, this information should be accompanied by recommendations for specific actions because otherwise the investigation of patients' quality of life will not make a difference (Boyes et al, 2006; McLachlan et al., 2001). It can be concluded that the transformation of changes in the process of care, manifested in better patient-physician communication, to changes in patient outcomes poses a major challenge for future considerations. In the following section, additional future directions will be discussed.

3.2.3 Future directions in the assessment of quality of life – challenges and opportunities

Some governmental and professional organizations have advised routine screening for the presence of heightened psychological distress in cancer patients (NICE, Rebalance Action Focus Group). However, there are several

barriers preventing the routine use of screening or PROMs in clinical practice. These barriers can be classified in practical, attitudinal and methodological barriers (Greenalgh, 1999).The practical barriers include a lack of IT support concerning storing and retrieval of data, a lack of time and money needed to collect, analyze and appropriately use data as well as physicians' lack of familiarity and knowledge in the field of HRQL measures. Additionally, the format and length of most existing tools is a barrier to the adoption in clinical practice because a considerable amount of time is required for administering, scoring and interpreting the self-report measures (Jacobsen et al., 2007). Next to these practical barriers, there are attitudinal barriers most of which are referring to physicians' skeptical attitude towards these measures. Many clinicians underestimate the value and relevance of these measures and therefore prefer an informal assessment of quality of life which they regard as superior given their skeptical opinion about the validity of existing measures. A study confirming the fact that physicians seem reluctant to use screening tools found that although approximately two third of physicians regularly attempted to detect mood disorder during consultations, only less than 10% used validated questionnaires for their purposes (Mitchell et al., 2008). Main barriers mentioned in this context were again lack of time, lack of knowledge or familiarity and low levels of confidence. Barriers related to methodology include aspects such as the nature and design of the instruments themselves and in particular their psychometric properties. A meaningful interpretation of the scores and changes in scores is also problematic and should be addressed by future considerations. In our view, methodological barriers pose a major challenge and should be addressed first before trying to overcome other barriers because they lie at the very heart of the whole concept and approach. However, in developing sound measures investigating the most important dimensions related to patients' quality of life, several other challenges such as format and length of the measure and IT support should be taken into account, while others such as physician familiarity and confidence, which are already influences by changes in methodological and practical barriers, should be addressed with equal importance immediately afterwards.

3.2.4 The need for a new tool for the quality of life evaluation

As previously mentioned, many approaches to personalized medicine include medical relevant data such as genetic and bimolecular information that are used to predict the best treatment choice including predictions about adverse effects. However, we claim that these approaches neglect the unique influence of psychological dimensions and cognitive style. Through identifying a variety of biological and medical information physicians are able to predict the best treatment choice which leads to an increased life expectancy on the side of the patient, approaches that exclusively rely on biological and medical information miss a substantial part of the human being: psychology. By neglecting unique psychological information, these approaches limit their own effectiveness since psychological dimensions impact on treatment effectiveness to a considerable extent. Psychological influences limit the predictability of treatment effectiveness and thereby undermine the potential benefit of an approach that solely relies on biological and medical information. To illustrate the power of psychology regarding treatment effectiveness, we refer to the hypothesized example of a patient who is very anxious and possesses a moderate through high level of depression. A treatment that was predicted to yield good results because it was perfectly determined by analyzing bimolecular, genetic and imaging data, may turn out to be ineffective for the anxious and depressed

patient. This patient might be unresponsive to the treatment due to noncompliance to the treatment caused by the patient's heightened psychological distress. Given these important psychological influences, we suppose that current approaches to personalized medicine relying exclusively on biological and medical information, lack consideration of the psychological component that contributes to human uniqueness in the same way genetic information does. A human being can not be considered as unique by only referring to him/her as a biological and genetic entity. Instead, what makes a human being unique is also his/her specific needs and value, habits and behaviors, hopes and fears, beliefs and cognitive dispositions.

We therefore claim that the integration of psychological and personal variables into multiscale data systems containing heterogeneous data from a patient will greatly improve the predictive power of decision support systems developed on the basis of these data systems. This will lead to better and more efficient decision support tools for physicians.

The assessment of psychological and personal variables serves the additional purpose of monitoring the patient's perceived health status and general quality of life.

Different measures for the assessment of health-related quality of life of patients have been developed. However, most of them measure only one broad area, for example, psychological distress including depression and anxiety, psycho-social problems including dimensions such as social abilities, body image and financial problems, or health status in general including symptoms resembling pain, fatigue and physical problems. We claim that there is an urgent need for an instrument that measures all these different areas in order to represent a broad picture of the patient without missing essential information. Additionally, to our knowledge, there is no single measure including cognitive aspects of the patient such as memory and attention, rumination, or self-efficacy. One of the biggest problems in developing an instrument that measures all these broad areas is the fact that such an instrument needs to be very short and easy to fill out otherwise patients are not willing to comply. It is thus a major challenge to construct an instrument that measures all these areas and that is short and easy to fill out at the same time. The present study tackles this problem through the development of a short and easy to fill out questionnaire measuring four broad areas, perceived health state, psychological aspects, psycho-social as well as cognitive aspects, all investigated by different sub-dimensions. In the following, these four broad areas and their sub-dimensions included in the present instrument will be discussed by giving empirical support concerning their relation to quality of life, thus justifying their inclusion in the ALGA-C.

3.2.5 Quality of life and perceived health state

The way a patient perceives his/her own health state determines his/her quality of life to a large degree. Symptoms such as pain, sleep problems, fatigue, general physical problems and diminished appetite limit an individual's functioning, his/her perceived well-being and therefore his/her quality of life. Investigating these symptoms is essential as many cancer patients experience these problems to a heightened degree compared to healthy individuals.

Among the most common and feared side effects of cancer and treatments for cancer are pain and fatigue. Many patients have more than one type of pain and usually experience fluctuations in pain intensity (Portenoy, 1997). While estimates of pain range from 14% to 100%, estimates of fatigue range from 4%

to 91% (National Institutes of Health State-of-the-Science Panel, 2002). A lack of uniformity in measurement and methodology is responsible for these large ranges in the estimation of pain and fatigue. There is a lack of consistency in the conceptualization of these symptoms. For example, fatigue can be described as a subjective and multidimensional concept with several modes of expression (Servaes, Verhagen, & Bleijenberg, 2002). It can be measured at a physical level referring to diminished energy and the need to rest, at an affective level considering lack of motivation and interest or at a cognitive level when diminished memory capacity and attention are of main interest. Although all these different levels of investigation are expected to correlate, they measure different dimensions leading to different numbers of prevalence. The problem of conceptualization is closely related to the lack of consensus regarding the criteria to define the different symptoms. Furthermore, weaknesses in research methodology also include the lack of appropriate comparison group(s) to investigate whether the prevalence of the symptoms is in fact higher in cancer patients compared to healthy control subjects and a lack of well-defined study populations. Daily pain in elderly people was, for example, found to be especially untreated which may be the result of increased cognitive and sensory impairment that lead elderly people to report pain less frequently. However, a study found that among elderly people, 25% to 40% experience daily pain. Although the lack of uniformity in measurement and methodology needs to be addressed in future research, the exact number of prevalence for symptoms are not important for our current purpose. Instead, for the purpose of the present study, it is important to acknowledge that the majority of cancer patients suffer from pain and fatigue as a result of their illness and treatment and that the assessment of these symptoms is therefore essential. Related to experienced pain and fatigue are problems in general physical functioning and physical abilities which diminish a patient's quality of life. Another symptom often related to impaired physical functioning is the loss of appetite in cancer patients as a result of chemotherapy or other treatments. In general, these illness- and treatment-related symptoms often interfere with the daily activities of a patient, lowering his/her general quality of life. Therefore, the assessment of these symptoms is of great importance in order to discover them, treat them where necessary and thereby improve patients' quality of life.

3.2.6 Quality of life and psychological aspects

The most important psychological dimension related to quality of life is psychological distress which includes anxiety as well as depressive symptoms. A failure to detect and treat heightened levels of psychological distress limits the effectiveness of cancer treatments, decreases patients' quality of life, and negatively influences health care costs. Therefore, psychological distress is assessed by many instruments measuring patients' health-related quality of life since it was found to be a very common phenomenon in patients. In a large sample of 4496 cancer patients, more than one third (35.1%) of all patients was found to suffer from heightened distress (Zabora et al., 2001). Prevalence rates were different for diverse types of cancer, varying from 43.3% for lung cancer to 29.6% for gynecological cancers. Other studies investigating psychological distress found high prevalence rates in women with early stage breast cancer after diagnosis and also up to five years after diagnosis. Whereas Bleiker et al. (2000) found a prevalence rate around 20.0% two months after surgery and almost two years after diagnosis, in Burgess et al.'s (2005) study nearly 50.0%

of women had depression, anxiety, or both in the year after diagnosis, 25.0% in the second, third and fourth, and 15.0% in the fifth year. This result suggests that in women with breast cancer, the prevalence of depression, anxiety, or both during the year after the diagnosis is twice as large as the prevalence in the general female population. Regarding these high prevalence rates even years after diagnosis, it seems necessary to identify the best predictors or risk factors for depression and anxiety over time in order to enable the treatment of the respective factors. Bleiker et al. (2000) found patients who, on average, reported a larger number of intrusive thoughts about breast cancer, a larger number of health complaints, and/or sleeping problems to be at risk for experiencing elevated levels of distress two years after diagnosis. Previous life events and social support were not significantly associated with levels of distress. In contrast, Burgess et al. (2005) found that previous psychological treatment, the lack of an intimate confiding relationship and the experience of severe difficulties not related to cancer constituted the main risk factors for depression and anxiety over time. Although these studies found diverging results for the experience of severe non-cancer difficulties and social support, similar results were found regarding treatment and prognostic factors which were not associated with levels of distress. Furthermore, the finding that health complaints were predictive of psychological distress is consistent with other studies and can be explained by assuming that an increased number of health complaints leads to worries about a recurrence of cancer which results in a higher level of psychological distress. Indeed, Burgess et al. (2005) found that compared to 36.0% who experienced heightened distress in the three months after initial diagnosis, 45.0% of women suffered from elevated psychological distress in the three months after a diagnosis of recurrence. Depression and anxiety were thus more prevalent after recurrence of cancer than after initial diagnosis.

Another argument for including a measure of psychological distress in our instrument is evidence suggesting that heightened levels of anxiety and depression are associated with several negative outcomes containing patient noncompliance and non-adherence to treatment recommendations (Kennard et al., 2004) and decreased patient satisfaction concerning care (Von Essen et al., 2002). These negative outcomes, in turn, decrease a patient's quality of life.

Given the high prevalence rates of depression, anxiety, or both in cancer patients, and the increased chance for these symptoms to persist for years after diagnosis, their detection and treatment is essential. In order to optimize treatment, it is necessary to further investigate the main risk factors for continued psychological distress and clarify differences in results yielded by previously mentioned studies. In order to tackle this problem, we will, next to depression and anxiety, examine whether patients have intrusive thoughts, health complaints and/or sleeping problems as well as assess their social abilities and potential previous psychological treatment.

3.2.7 Quality of life and psychosocial aspects

Cancer treatment often leads to major changes in patients' physical appearance. It may, for example, result in alterations of body image through the loss of a body part, disfigurement, scars and skin changes (Hopwood et al., 2000). Whereas the effects of chemotherapy, such as hair loss, weight loss or weight gain, are rather transient and reversible to a certain degree, effects of surgery are often permanent. Also radiotherapy may have considerable effects since it may cause tissue damage with insidious changes over many years. Although differences in methodology and measurement have led to a wide

range of severity and frequency of body image outcomes reported by different studies, the vast majority of research indicates that body image is a key determinant of differences in quality of life. One study compared early-stage breast cancer patients who underwent different surgical interventions with respect to postoperative body image and quality of life (Pusic et al., 1999). Findings show that body image was poorest after mastectomy alone compared to mastectomy with breast reconstruction and lumpectomy with radiotherapy. The latter did not differ with regard to body image. These results are consistent with other studies which found that a higher degree of impairment of body image is reported in patients after mastectomy compared with patients who received breast conserving therapy (Poulson et al., 1997; Fobair et al., 2006). However, Pusic et al. (1999) also found that the impact of the type of surgery was related to the patient's age. Patients who received breast reconstruction therapy were found to be younger than patients who underwent lumpectomy and mastectomy. The relationship between postoperative quality of life and the type of surgery performed also varied by age. While among older women, there was no significant difference among different treatments, among younger women; mastectomy patients reported the poorest quality of life. A possible explanation for this finding may be the fact that for younger women, body image is generally a more important dimension related to quality of life compared to older women and therefore, mastectomy may be more disruptive for younger than for older women (Pusic et al., 1999).

In general, an extensive body of literature and studies regarding the effects of treatment on body image and other psycho-social aspects has mainly focused on breast cancer patients. However, a large number of patients across many disease groups and treatment types can be affected. The just discussed possibility that for younger women body image is a more important component of quality of life compared to older women, suggests that there might be age-related and possible other individual differences influencing the perceived effects of treatment on body image and other psycho-social aspects. Further support for the importance of investigating subjectively perceived changes in body image and related problems in cancer patients comes from research that found that the use of observer measures of cosmetics has not proved satisfactory because results of patient-observer ratings were often found to show poor concordance. This emphasizes the need of investigating patients' own views concerning the effects of treatment.

In the first month after treatment women diagnosed with breast cancer at the age of 50 or younger reported to experience a considerable amount of body image and sexual problems (Fobair et al., 2006). Half of the women experienced two or more body image problems some of the time, or at least one problem most of the time. When sexual problems or dysfunctions are reported, these most often include experiencing disturbances in sexual desire and the loss of sexual arousal. Other sexual dysfunctions contain reduced sexual pleasure, difficulties in achieving orgasm and pain during intercourse which might be related to vaginal dryness that often results as an effect of treatment. In general, only 67.0% of young women with breast cancer were found to be sexually active compared to 74.0%-81.0% of healthy young women (Fobair et al., 2006). Furthermore, findings of this study suggest that 57.0% of the breast cancer sample reported a lack of sexual interest compared to 38.0% of healthy women. While 48.0% of breast cancer patients, compared to 31.0% of healthy women, had difficulties in becoming sexually aroused, 40.0% of patients, compared to only 28.0% of healthy women, indicated an inability to relax and enjoy sex. These findings demonstrate that impairments in sexual functioning such as the loss of sexual interest and sexual enjoyment often

result after cancer treatment. In general, sexual functioning was found to be worse in women who received chemotherapy compared to those who did not (Ganz et al., 2004). Since body image and sexual problems were demonstrated to result from cancer treatment, especially chemotherapy, it is important to investigate these possible effects given their potential impact on mental health, partner relationships, social support and quality of life in general.

Social and interpersonal support was found to be critical for cancer patients after completing treatment. A lack of social support is reasoned to be a risk factor for the development of depressive symptoms. However, patients often experience that their physical conditions or other effects resulting from treatment interfere with the family life, their social activities and their working abilities. Such impairments might result in social problems leading to a limited social and interpersonal support which, in turn, negatively influence the patient's conditions and quality of life.

Next to social and interpersonal problems, financial problems might further impact on a patient's quality of life in a negative way. A study that examined differences in the quality of life of breast cancer survivors one year after diagnosis in comparison with women from the general population suggests that almost 40.0% of breast cancer survivors reported to have financial problems (Arndt et al., 2004). The difference compared with women from the general population was striking. Especially young women with breast cancer expressed psychosocial deficits and financial problems. Consistent with the finding, another study provided evidence for the fact that especially young women with breast cancer suffer from financial problems. Economic problems were reported in twice as many young breast cancer patients compared to older patients (Arndt et al., 2004). The fact that younger breast cancer patients perceive chemotherapy more frequently than do older breast cancer patients might be a possible explanation for this finding as more severe side effects resulting from this treatment might cause a loss of earnings. Furthermore, a loss of earnings might selectively affect women at pre-retirement age which might also account for the observed finding. In addition to financial problems, deficits in cognitive functioning were found to affect women with breast cancer. Potential problems in cognitive functioning and the most important cognitive dimensions that should be assessed in cancer patients will be discussed in the following.

3.2.8 Quality of life and cognitive aspects

Potential health, psychological and psycho-social problems that result as side effects from cancer treatment might be most obvious and accordingly cared for in the first place. However, more subtle side effects, such as possible changes in cognitive functions, have received little attention, even though many patients report to suffer from subjective changes in memory and clear thinking during and after treatment (Brezden et al., 2000). Even small impairments in cognitive functioning are expected to influence a patient's ability to function, thereby negatively impacting his/her quality of life. The fact that subtle changes in cognitive abilities are sometimes difficult to detect might be a possible explanation for the lack of appropriate measures investigating cognitive dimensions in cancer patients. However, we claim that it is crucial to measure these dimensions in order to improve patients' quality of life and additionally support the physician in the medical decision-making process by taking into account patient's cognitive characteristics.

Difficulties in the ability to remember, think and concentrate are often reported by breast cancer patients receiving chemotherapy. Evidence supporting this

fact comes from a study that examined differences in cognitive functioning between breast cancer patients currently receiving chemotherapy and healthy control subjects (Brezden et al., 2000). In comparison to healthy women, breast cancer patients were found to have decreased cognitive functions, especially with regard to the memory domain. Furthermore, patients' cognitive functions were not only found to be impaired during the time of treatment but residual effects were detected even after completion of chemotherapy. Next to the immediate impact of impairments in memory on the quality of life in patients, memory and concentration problems might also result in a patient's lowered chance of actively participating in the medical and treatment decision process when cognitive problems are not appropriately cared for. Impairments in memory and attention might account for the well-observed fact that patients do not fully understand and remember what was discussed in the encounter with the physician. By previously informing the physician about memory and attention problems, he/she might be able to adjust his/her way of communicating with the patient, thus ensuring shared decision making and patient empowerment.

Another cognitive dimension crucial of investigation is rumination which can be defined as the tendency respond to distressing situations in a maladaptive manner including repetitively and passively focusing on symptoms of distress (Nolen-Hoeksema, 1991). The reason why the investigation of rumination is important in the context of cancer is the fact that it enhances the effects of depressed mood on thinking, it interferes with effective problem solving and it increases the chance of losing social support (Nolen-Hoeksema et al., 2008). Furthermore, through these possible consequences, rumination possesses the potential to maintain and exacerbate initial depressive symptoms, possibly turning them into episodes of major depression. There is thus an increased chance for people who engage in rumination to experience prolonged periods of depression and develop clinically significant depressive disorders. Next to the correlation between rumination and depression, studies found rumination to be positively related to coping styles that include suppression or avoidance as reaction to distressing feelings and thoughts. It seems likely that the application of these coping styles as well as further impairment in concentration and memory, that is likely to result from rumination, influence treatment and cure of cancer in an undesired way. Given the fact that several treatments such as behavioral activation interventions, mindfulness and acceptance based approaches as well as interpersonal therapies were found to be effective in treating rumination, it is reasonable to investigate this dimension in cancer patients. Detecting and, where necessary, treating, patients who have the tendency to ruminate, is reasoned to positively influence depressive symptoms, treatment, cure and patients' quality of life.

Self-efficacy which is one of the core aspects of Bandura's social-cognitive theory (Bandura, 1977, 1997, 2000, 2001) refers to an individual's belief of being able to control and adapt to a wide range of challenging and demanding situations. It is referred to as "a broad and stable sense of personal competence to deal effectively with a variety of stressful situations" (Scholz et al., 2002). Individuals possessing high levels of self-efficacy are optimistic and self-confident of their own coping abilities when confronted with life stressors such as a diagnosis of cancer. A strong sense of self-efficacy was found to be generally correlated with better health (Schwarzer, 1992; Bandura, 1997). The additional fact that a rather low sense of self-efficacy is associated with depression and anxiety turn the dimension self-efficacy to be of crucial in the context of cancer.

Cognitive closure is a dispositional construct that is referred to as a latent variable manifested through several different aspects including the desire for predictability, the discomfort with ambiguity and close-mindedness. We reason that cognitive closure is related to a patient's preferences for the amount of information he/she wishes to receive from the physician and might therefore impact on the patient's level of involvement in the clinical decision making process. The assessment of cognitive closure might thus assist the physician in his/her decision how much information should be best provided to the patient in order for the patient to make an informed choice. If greater levels of informed choice are associated with greater levels of patient satisfaction and compliance to treatment, we should seek to better understand and measure patients' preferences. When talking about patients' preferences, it is critical to distinguish between preferences for specific health states and utilities and preferences for specific treatments. The investigation of the latter involves the assessment of risk.

In general, better understanding of patients' preferences concerning different treatment choices is central to the concept of informed choice and shared decision making of the physician and the patient (Bowling, & Ebrahim, 2001). Preference based decision making involves the assessment of risks and benefits of the alternative options for action. Therefore, the investigation of patients' perceptions of risk is essential given that informed treatment decisions must be made at the individual level after consideration of perceived risks as well as benefits. Another reason for the assessment of risk perception in patients considers that the attainment of improved health care relies on patients participating in clinical trials. Research evidence suggests that educating patients about clinical trials has a low impact on their willingness to participate. Instead, patients' choice of participating in clinical trials was rather influences by their perception of risk (Ellis et al., 2002).

In conclusion, considering that problems related to these four broad areas will limit the daily activities of cancer patients and thus influence their overall quality of life, early detection is crucial because timely interventions are likely to improve treatment outcomes. Furthermore, with respect to the aim of integrating psychological data with medical information, assessment of these dimensions at an early point in the health care process is necessary.

3.2.9 The uniqueness of ALGA

Some attempts have been made in the past regarding the development and validation of short screening instruments for cancer patients applicable in the clinical consultation context (Bogaarts et al., 2011). However, most of these instruments focus on the assessment of one main area, for example, including questions measuring solely psychological, psycho-social or health related symptoms, respectively. To our knowledge, there is no instrument including psycho-cognitive dimensions. Although, a few studies reported the investigation of memory functioning in cancer patients, no tool has been developed to measure psycho-cognitive dimensions critical in the context of cancer care. In addition, most screening instruments that have been developed for the use in cancer patients mainly focus on the investigation of symptoms in a specific cancer population such as breast cancer patients.

Taking these issues into account, ALGA is the first multi-dimensional instrument including psycho-cognitive aspects next to three other main areas relevant in assessing cancer patients' quality of life. Besides developing a short and acceptable measure that covers all important areas to generate a

psychological profile of the patient, the psychometric properties of the ALGA-C are examined in a trans-cultural validation study. This means that reliability, validity and acceptability of the ALGA-C are investigated in two different cultural samples, one Italian sample and one German sample.
Given that the ALGA-C is not only developed to monitor and improve cancer patients' quality of life but also to generate data that can later be merged with medical data of the patients, it is necessary to proof the ALGA-C to be a reliable, valid, acceptable and overall sound tool for application in cancer patients.
The present study tested the preliminary reliability, validity and acceptability of the developed instrument in control subjects from the general population in an Italian as well as German sample. Investigating the psychometric properties in samples from the general population seemed necessary for several reasons. First, the context of medical consultations is characterized by time constraints and often stressful situations for the patient. Therefore, it is necessary when testing new instruments in patients to have as much proof for its effectiveness as possible. Although sufficient empirical evidence justified the inclusion of the dimensions in the first three broad areas of the ALGA-C, evidence related to the inclusion of psycho-cognitive dimensions is rather sparse in the literature. The validation of a new instrument often requires adjustment and refinement such as the reformulation or total exclusion of items included in the scale. Therefore, in order to provide some initial empirical proof for the psychometric properties of our instrument and allow for possible adjustment of the scale, it was provided to general population samples. Second, since the ALGA-C is aimed to provide a tool that can be applied in many different cultures, the examination of possible cultural differences and difficulties related to the translation of the instrument to different languages can be detected. A third reason for the preliminary testing in the general population is the fact that we developed a completely new instrument which makes it difficult to develop an appropriate referral system relying on an individual's scores on the subscales. As previously mentioned, instruments assessing patients' dimensions related to quality of life makes sense only when appropriate cut-off scores assist the physician in determining when a patient is in need for referral for certain symptoms and problems. The investigation of norm scores from the general population for the subscales included in the ALGA-C facilitates the specification of cut-off scores necessary for referral. Furthermore, the comparison of scores from healthy control subjects in the general population and cancer patients provides information about the discriminant power of the instrument concerning the detection of differences in scores of clinical and non-clinical individuals.

3.3 Methods

3.3.1 Participants

The study included samples from the general population of two different European countries. Participants were recruited by sending the online link of the questionnaire via email, posting the link on the webpage of the research group and on the community platform Facebook. Whereas 216 individuals from the Italian population responded and filled out the questionnaire, the German sample involved 162 individuals. No exclusion criteria were imposed to the study. However, demographic characteristics were investigated at the beginning of the questionnaire to screen for individuals that have ever been diagnosed with cancer. Compared to two participants (1,3%) in the German sample, eight participants (3,8%) in the Italian sample indicated to have ever

been diagnosed with cancer. These participants were included in the statistical analysis considering the fact that the general prevalence rate for cancer in Europe is estimated to range from 1% to 3%. The percentages found in our samples thus represent the general prevalence rates in Europe, although a slightly higher percentage was found in the Italian sample.

3.3.2 The development of the ALGA-C

The ALGA-C is a psychological profile questionnaire specific for cancer patients. It includes four broad areas (perceived health state, psychological aspects, psycho-social aspects, cognitive aspects), each composed of different subscales measuring dimensions related to the patient's quality of life. Next to the four broad areas, the ALGA-C includes a measure of personality.
The perceived health state of the patient is assessed by five different dimensions including general self-rated health (GSRH) (two questions), pain (two questions), sleep/ fatigue (three questions), physical abilities (4 questions) and appetite (one question).
Psychological aspects are measured by investigating anxiety (two questions), depressive symptoms (four questions) and self-efficacy (six questions).
The area of psycho-social aspects is composed of four subscales including social abilities (three questions), financial problems (one question), sexual problems (three questions) and body image (three questions).
Cognitive aspects of a patient are assessed by four different dimensions, being memory and attention (five questions), rumination (four questions), cognitive closure (five questions) and risk perception (six questions).
The four areas thus consist of 16 subscales assessed by 54 questions plus a 10-item measure of personality. The measure of personality is conceptualized as a separate subscale, though constituting a supplement measure to demographic characteristics of the patient rather than a psychological dimension related to quality of life.
Concerning personality as a separate subscale, the ALGA-C consists of 17 subscales composed of 64 questions of which 61 were selected, though mostly modified and reformulated, from existing and valid questionnaires: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core (EORTC QLQ-C30) (version 3.0), European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Breast (EORTC QLQ-BR23), Center of Epidemiologic Studies Depression Scale (CES-D), Everyday Memory Questionnaire – Revised (EMQ-R), Rumination Response Scale of the Response Style Questionnaire, General Self-Efficacy Scale (GSE), Need for Cognitive Closure Scale, Risk Perception, 10-Item Big Five Inventory (BFI-10).
The items of these various existing instruments differed greatly in the way they were formulated. Whereas some instruments used items that were formulated as statements, others used direct questions instead. Furthermore, some questions or statements were formulated using "I", others using "you". In order to design a uniform format of the ALGA-C, items were all formulated as questions including "you" except for risk perception and the personality inventory for which items were provided in form of statements. Similarly to differences in items, all existing measures used different response scales. The adoption of all these different response scales into the ALGA-C would have turned it into a very confusing and difficult to complete instrument. Therefore, we developed a uniform response scale for 44 of the questions included in the instrument. This uniform response scale included the following five response

options: *never, rarely, sometimes, often, always*. As previously described, for the items measuring GSRH and anxiety, a response scale in form of a 10 point Likert-like scale was chosen. For the six items measuring risk perception, the answering scale provided five options ranging from *extremely unlikely* to *extremely likely.* Since we included an already existing and valid tool for the assessment of personality (BFI-10), we adopted the five response options included in this scale (*disagree strongly, disagree a little, neither agree nor disagree, agree a little, agree strongly*).
In the following, by referring to every broad area assessed by the ALGA-C, we present some more detailed information about the existing measures from which the questions were chosen, providing information about psychometric properties where accessible. In addition, the investigation of demographic characteristics and evaluative information will be shortly discussed.

3.3.3 The investigation of perceived health state

Generated self-rated health (GSRH) was assessed by the two most widely used forms of the single-item GSRH questions which serve as summary measures (De Salvo et al., 2006). These two items include a “standard” version of GSRH and a “comparative” form of GSRH. Whereas the former asks participants to rate their health in general, the latter asks for an estimation of participants’ health in comparison to other individuals of their age. De Salvo et al. (2006) examined the psychometric properties of the two single-item questions about GSRH by assessing how well these two questions capture information in a validated, multi-item general health survey (SF-12V). Findings suggest the single-item GSRH questions to constitute a valuable substitute for longer instruments because they were shown to have good reproducibility, reliability, and strong concurrent and discriminant scale performance with the established multi-scale health status measure (De Salvo et al., 2006). While the original single-item GSRH questions asks patients to indicate their perceived health status on a five category response scale including the options of *Excellent, Very Good, Good, Fair,* and *Poor,* we modified the response scale into a 10 point Likert-like scale ranging from *1(very poor)* through 5*(moderate)* to *10(very good)* in order to provide a scale that is reasoned to be better able to detect small changes in GSRH over time.
The other four dimensions in the first broad area were all assessed by questions extracted from EORTC QLQ-C30 (version 3), except of one question included in the sleep/fatigue scale which was developed through discussion with the project group. The EORTC QLQ-C30 is a well-established instrument that is designed for the use with a wide range of cancer patient populations. It is a 30-item measure that incorporates nine multi-item scales. While five scales are functional scales assessing physical, role, cognitive, emotional and social functioning, three scales are considered symptom scales measuring problems related to fatigue, pain and nausea/vomiting. The final multi-item scale is a Global Health Status/QoL scale containing two items. Next to these multi-item scales, the instrument includes six single item scales investigating Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrhoea, and Financial Difficulties. Regarding psychometric properties, the instrument was shown to possess required standards such as validity, reliability and sensitivity by several different studies (Aaronson et al., 1993; Oscoba et al., 1994; Kaasa et al., 1995). Generally, EORTC QLQ-C30 can be regarded as an instrument applicable to patients with different forms of cancer. Therefore, it seems reasonable to extract questions from this valid instrument to measure symptoms and problems related to pain, sleeping problems, physical ability and appetite loss.

While discussing the selection of questions measuring sleep/fatigue, members of the project group decided to add a question asking whether fatigue interfered with the participant's general level of activity. The EORTC QLQ-C30 lacks a question measuring the impact of sleeping problems and fatigue on the general activity level which was considered valuable regarding its impact on quality of life. This decision was furthered justified by matching our choice of questions with other measures investigating fatigue such as the Fatigue Symptom Inventory (FSI) which is a 13-item self-report measure investigating intensity and duration of fatigue as well as its impact on quality of life. In total, we took nine from a total of 30 questions included in the EORTC QLQ-C30 in order to measure pain, sleep/fatigue, physical abilities and appetite and we added one question in to the sleep/fatigue subscale.

3.3.4 The investigation of psychological aspects

When measuring anxiety, a distinction is made between trait anxiety and state anxiety. Whereas trait anxiety is treated as a personality factor referring to how a person generally feels, state anxiety considers how a person feels at the moment. Trait anxiety thus constitutes a psychological risk factor as it is inherent to a person's personality. Furthermore, when measured in clinical settings, it is only measured once and not as state anxiety at consecutive points in time. State anxiety is not regarded as a disposition and can therefore be seen as a psychological problem rather than a psychological risk factor. Normally, these two types of anxiety are investigated by the Spiegelberger State Trait Anxiety Inventory (STAI) which is a 20-item measure. However, a study by Davey et al. (2007) showed that a single question measured with a Likert Scale or Visual Analog Scale (VAS) could be used in place of the state form of the STAI. Both the score on the question measured with a Likert Scale and the score on the question measured by the VAS were shown to strongly relate to the STAI score. Correlations between both of the single-item measures and the STAI were reasonably high depicting a strong relationship between the different measurement tools. By relying on evidence from this study, the project group developed two single-item measures, one investigating trait anxiety and the other measuring state anxiety. Even though the study by Davey et al. (2007) developed a single-item measure only for state anxiety, we reason that trait anxiety can be measured in the same way. The two questions thus ask the patient to indicate on a 10 points Likert-like scale how anxious he/she feels normally and how anxious he/she feels at the moment. The response scale consists of 10 evenly spaced numbers each anchored to a level of anxiety ranging from *1(extremely anxious)* through *5(moderately anxious)* to *10(not at all anxious)*.
The four items measuring depressive symptoms were selected from the CES-D, a 20-item self-report scale designed to assess the presence and degree of depressive symptoms. The Scale was developed by including items referring to symptoms associated with depression which have been used in previously validated longer scales. Concerning the psychometric properties of the scale, there is evidence showing that it has a very high internal consistency and adequate test-retest reliability. In the original CES-D, the items of the scale contain statements for which participants have to indicate how often they have felt the way described in the statement during the past week choosing between 4 different answering options: *rarely or none of the time (less than 1 day), some or a little of the time (1-2 days), occasionally or a moderate amount of time (3-4 days), most or all of the time (5-6 days)*. Again, for the sake of uniformity within

the ALGA-C, statements were reformulated into questions and the answer scale was adjusted. Furthermore, one of the items chosen from this scale was reversed-phrased and was therefore reversed-scored during the statistical analysis.

3.3.5 The investigation of psychosocial aspects

The single question on financial problems and the three questions on social abilities were also adapted from the EORTC QLQ-C30. Questions assessing body image and sexual problems were extracted from the EORTC QLQ-BR23 which is a reliable and valid supplementary measure that was developed for the specific use in breast cancer patients. After carefully examining the different items of this measure, the project group decided to extract three items for the body image subscale and the sexual problems subscale, respectively. Items chosen for the body image subscale measure the patient's perceived physical attractiveness, difficulties to look at oneself naked and overall satisfaction with the own body. The three questions on sexual problems ask for the general interest in sex, the extent to which patients have been sexually active and the extent to which sexually active patients enjoyed intercourse which. These three issues were previously shown to constitute the main sexual problems in cancer patients. Investigating body image and sexual problems might be especially important in breast cancer patients as these dimensions are strongly influenced by changes in female bodies resulting from surgery and chemotherapy. However, we regard these dimensions as also critical for other cancer populations since chemotherapy and other cancer treatments might result in body image and sexual problems, not only in breast cancer patients. The original answer scale of the EORTC QLQ-C30 and EORTC QLQ-BR23 includes 4 options ranging from *1(not at all) to 4(very much)*. However, this answer scale was not included in the ALGA-C for the sake of providing patients with a uniform answer scale, especially developed for the ALGA-C.

3.3.6 The investigation of cognitive aspects

Memory/Attention was measured by five questions chosen from the EMQ-R (Royle, & Lincoln, 2008). The EMQ-R is a shortened version of the Everyday Memory Questionnaire (EMQ), a subjective measure of memory failure in everyday life, which was initially constructed for survivors of head injury, but later refined for both non-clinical and clinical samples including populations suffering from Alzheimer's disease or multiple sclerosis. However, to our knowledge, it has never been tested in cancer patients. The EMQ-R includes 13 items and it was shown to be a valid and reliable tool that possesses good face validity (Royle, & Lincoln, 2008). Items in the EMQ-R are given in form of examples and things that happen to people in everyday life, asking participants to state how often these things happened to them. For the same reasons previously mentioned, statements were reformulated as questions.
Four questions measuring rumination were extracted from the Ruminative Response Scale of the Response Style Questionnaire (Nolen-Hoeksema, & Morrow, 1991). This scale examines participants' tendencies to respond to their own feelings and symptoms of dysphoria. By the selection of items from this scale, we relied on a study that conducted a principle component factor analysis on this scale resulting in 4 factors with eigenvalues greater than 1 (Roberts et al., 1998). Since the fourth factor was found to be uninterruptable, three factors remained. Whereas the majority of the 21 items in the original scale loaded on the first factor termed 'symptom-based rumination', less items

loaded on the second factor ('introspection/self-isolation') and third factor ('self-blame'). Taking this factor structure into account, we decided to take two items loading on the first factor and one item loading on the second and third factor, respectively.

Self-efficacy items were taken from the General Self-Efficacy (GSE) scale originally developed by Jerusalem and Schwarzer (1979). The GSE scale consists of 10 items containing statements for which participants have to indicate on a response scale from *1(not at all true)* to *4(exactly true)* to what extent each statement is perceived to apply to them. A study that assessed the psychometric properties of the GSE scale in 25 different samples found good internal consistency in the total sample (N = 19,120; Cronbach's α = .86) (Scholz, Dona, Sud, & Schwarzer, 2002). Next to good reliability, the scale was found to be homogeneous and unidmensional across 25 nations. Again, statements were reformulated as questions in order to suit in the format of the ALGA-C.

The five items measuring cognitive closure were chosen from the original Need for Cognitive Closure Scale of Webster and Kruglanski (1994). The scale includes 18 items in form of statements for which participants have to indicate to what extent each statement is characteristic for them (Cacioppo, Petty,, & Kao, 1984). One study that used an Italian version of this scale found the scale to be a reliable (Cronbach's α = .89) and valid instrument (Pierro et al., 1995).

Six items from the domain-specific risk-attitude scale (Weber, Blais, & Betz, 2002) were taken to measure risk perception. This original scale measure risk perception in five different decision domains: financial, health/safety, recreational, ethical, and social. Each domain is measured by 10 items, turning the whole scale into a 50-item instrument. Respondents are asked to rate the likelihood that they would engage in risky activities related to these five domains, answering options ranging from 1(extremely unlikely) to 5(extremely likely). For the PPQ-C we chose four items from the health/safety domain and two questions measuring risk perception in the financial domain.

3.3.7 The investigation of personality

Personality was assessed by the 10-item Big Five Inventory (BFI-10) which is an abbreviated version of the well established Big Five Inventory (BFI). The BFI-10 was developed by Rammstedt and John (2007) and it possesses psychometric properties that were shown to be comparable to those of the BFI in size and structure (Rammstedt, 2007). Several validation studies provided evidence for good reliability, construct validity and external validity of the BFI-10. This scale is especially useful for our purpose as it constitutes a personality inventory for settings such as a clinical environment characterized by extreme time constraints. The five personality dimensions are investigated by two items each, one coded in the positive and one in the negative direction. Scale scores are thus computed by recoding the item that is coded in the negative direction and then averaging both items assessing one dimension.

3.3.8 The investigation of demographic characteristics and evaluation information

In addition to the ALGA-C, a number of questions concerned demographic characteristics of the participants. Before completing the ALGA-C, participants were asked to indicate their gender, age, nationality, marital status, number of children and highest level of education. Moreover, they were asked to report whether they smoke, whether they exercise, whether they have ever received

psychological treatment and whether they have ever been diagnosed with cancer. In case they affirmatively answered these questions, they were provided with additional questions asking for more detailed information about the number of cigarettes they smoke, the number of hours they are physically active and the kind of psychological treatment they received. Participants who indicated to be previously diagnosed with cancer were additionally asked about the date of diagnosis, the main diagnosis, surgery and type of main treatment.
Upon the completion of these demographic questions and the ALGA-C, participants were asked to shortly evaluate the instrument. The first evaluation question asked participants to estimate the number of minutes it approximately took them to complete the questionnaire. The second evaluation question included five short statements for which participants had to indicate the extent to which the agreed on a response scale with five options (*completely disagree, slightly disagree, not sure, slightly agree, completely agree*).

3.4 Data collection

The original ALGA-C was developed in English and then translated to Italian and German by two independent, native-speaking persons, respectively. The two translated versions were compared and slight differences were adjusted through discussion with members from the project group. The ALGA-C, demographic and evaluation questions were then transformed into an online questionnaire for each language with support of SurveyMonkey, an online survey application. This software was especially useful for the dissemination of the ALGA-C for two reasons. Firstly, because it provides the opportunity to directly transform data into an SPSS-file and secondly because it enables the use of question logic, especially necessary for the investigation of demographic characteristics, though used in the subscales pain and sexual problems.
Before disseminating the link of the online questionnaire via email and by postings on the research group's website and Facebook, the ALGA-C was slightly modified and adopted to the use in the general population. Four items assessing financial problems and social abilities were excluded as they specifically referred to effects of physical condition or medical treatment not applicable to most individuals from the general population. In the slightly modified version of the ALGA-C for the use in the general population, four items were thus excluded. Additionally, we termed this modified version ALGA to discriminate it as slightly different from the ALGA-C. In the following, we will thus use ALGA to refer to the slightly modified version used for the investigation in the general population.

3.4.1 Statistical procedure

We are now starting the data analysis that will be performed separately for the German and the Italian sample due to the present study's aim of validating the ALGA in the general population of two different countries. The present study not only involves the validation of the ALGA in a German and an Italian sample from the general population, but also the comparison between data of these two samples. Such a comparison enables the detection of possible cultural differences that must be adjusted for before integrating the instrument in clinical practice.
In general, five analyses will be conducted.

The first analysis deals with demographic characteristics of the participants and therefore generates descriptive information that is compared for the two samples.
The second and third analyses are the main and most crucial analyses for the present study's purpose since they are performed to validate the ALGA. The second analysis includes the assessment of reliability for each of the different subscales of the ALGA that consists of more than one item. By investigating reliability, this analysis seeks to answer the question whether the different subscales consistently, and with sufficient precision, measure the construct or dimension they were supposed to measure. Reliability is assessed by Cronbach's alpha, the most prominent measure of internal consistency or scale reliability. According to Cohen (47), internal consistency of a scale is considered good when it is above 0.70. Although greatly discussed, the majority of the scientific community presently agrees that a value of 0.7 or 0.8 is an acceptable value for Cronbach's alpha. Before conducting reliability analysis, the two reversed-phrased items of the ALGA (question 42 and question 67_4) will be recoded. The assessment of scale reliability enables us to recognize the potential need for certain items to be removed from the scale in order to increase the value of Cronbach's alpha in the respective subscale. In order to include only the most important items and abandon those that were shown to decrease the value of Cronbach's alpha, we will first conduct the reliability analysis before performing the third analysis, an exploratory factor analysis (method PCA). This third analysis will be performed to examine whether each subscale constitutes exactly one factor, as hypothesized.
In the fourth analysis, a mean score for each subscale was calculated before investigating correlations between the different subscales. While mean scores are important with respect to the determination of cut-off scores, correlations can be compared to findings of previous studies investigating the correlation between different psychological dimensions. Well-established evidence from previous studies concerning correlations will serve as an initial anchor when comparing correlation data.
The fifth analysis investigates the acceptability of the ALGA by examining data provided in the evaluation questions that were added to the end of the questionnaire. These results, mostly being descriptive, assist us in drawing conclusions about participants' perception of the required time and ease to fill out the ALGA.
For all statistical calculations the Statistical Package for the Social Science (SPSS) 19.0 will be used.

3.5 Next steps

- Validation of the questionnaire at least in another sample of healthy subjects (e.g. English);
- Once the statistical analyses described above are performed we will have normative data (at least on the Italians and Germans) that can be used to compared with data obtained from cancer patients;
- ALGA-C will be tested on patients;
- Data from patients will be analyzed following the same procedures we used for healthy subjects;
- Data obtained by the questionnaire will be used to create the patient's personal profile using the IT competences and to monitor the patient's quality of life, thereby facilitating the patients' involvement in the clinical decision process, finally leading to patient empowerment.

4. Patient Empowerment data scenarios

As defined in D2.2, the data scenarios for the different patient empowerment tools are below:

4.1 Search for running clinical trials in Europe

Item	Description
Identifier	PG_1 (IEmS_1)
Version	1.0
Name	Pathway scenario for patient empowerment: Clinical trials search
Description of the use case (end-user perspective)	Users will be able to search a database of clinical trials to determine which are available and whether they are eligible
Problem(s) to solve	The ability to search available clinical trials databases
Challenges	To display information on eligibility with possible autocomplete from patient records, compatible with all clinical trials databases. Eligibility criteria can change from trial to trial
Risks	Clinical trial databases could restrict access or change format.
Expected benefits	Increase the number of patients enrolling in clinical trials through increased awareness of availability of trials
Characterization	○ fundamental ◉ general ○ specific
If specific, please give the Domain	○ Acute lymphoblastic leukaemia ○ Breast Cancer ○ Nephroblastoma ○ other Cancer, please specify: ○ Non-Cancer Domain, please specify:
End-user	○ system ○ person ○ basic scientist ◉ clinician ○ computer scientist ○ regulatory body, lawyer, ethicist ◉ patient ○ other, please specify:

Pre-condition(s)/pre-requisite(s)	Access available to clinical trial databases	
Requisite(s)	Compatible with the Clinical Decision Support tools to ensure access for clinicians as well as patients. This will be regulated via the p-medicine portal.	
Post-condition(s)/post-requisite(s)	When used in conjunction with the Clinical Decision Support tools patient information on the available trials must be available for the patient to access at a later date.	
Constraints		
External sources needed from outside p-medicine	⊙ data, please specify: Eudract clinical trials database as a minimum (possibly other global clinical trials databases e.g. clinical trials.gov, WHO trials registry etc.) O tools, please specify: O services, please specify: O models, please specify: O other, please specify:	
Data used	⊙ personal O only non-personal O target population, please specify:	
Input data	⊙ internal database, please specify: personal health record system O external database, please specify: O online input	
Output data	O database, please specify: O variables for use, please specify: ⊙ structured document, please specify: Should list all available clinical trials with their eligibility criteria and rank them according to the best analogy to the patients individual clinical data O graphic, please specify:	
Data volume	As needed	
Dataflow	Please specify: From the database(s) to the users records, data should be stored in the data warehouse	
Data storage	Please specify: Pseudonymized personal data should be stored in the data warehouse	
Successful End Condition	Correct information on trials displayed in an understandable way to assist in decision making	
Fail End Condition	No trial data available	
Basic workflow	Actor Action	System response
	Basic search parameters set from patient data (possibly automatically)	Searching trials that fulfil this criteria

		Available trials displayed along with additional useful information. This information is different between patients and physicians in the amount and detail of content, references, and the language used.
	Import function used	Details of the available clinical trials imported into the personal health record if existing
Expected usage frequency	Regularly	
Needed for DSS	⊙ yes O no	
Needs HPC	O yes ⊙ no	
Needs Grid	O yes ⊙ no	
Priority for development	Moderate	
Responsible for development	Will be decided by the IT group	
Mock-up needed	O yes ⊙ no	
Responsible for Mock-up		
Who is building the tool	Will be decided by the IT group	
Open Source tool	⊙ yes O no, please specify why	

4.2 Consent and Re-consent Scenario

Informed Consent (Patient's Perspective)

Item	Description
Identifier	PG_2 (IEmS_2)
Version	1.0
Name	Pathway scenario for patient empowerment: Informed consent
Description of the use case (end-user perspective)	Patients will be able to provide, withdraw and manage consent for clinical trials online.
Problem(s) to solve	Management of informed consent
Challenges	Communicating with the trial management system for different trials and providing the correct informed consent information for each trial will be a challenge
Risks	Patient data is handled insecurely or inaccurately or the wrong information is given at the point of consent
Expected benefits	Increased transparency for clinical trials leading to great trust, understanding and involvement
Characterization	○ fundamental ◉ general ○ specific
If specific, please give the Domain	○ Acute lymphoblastic leukaemia ○ Breast Cancer ○ Nephroblastoma ○ other Cancer, please specify: ○ Non-Cancer Domain, please specify:
End-user	○ system ○ person ○ basic scientist ○ clinician ○ computer scientist ○ regulatory body, lawyer, ethicist ◉ patient ○ other, please specify:
Pre-condition(s)/pre-requisite(s)	Clinical trial identified using the clinical trial search tool and the relevant informed consent information is provided
Requisite(s)	
Post-condition(s)/post-requisite(s)	Patient must be able to re-access and alter their information
Constraints	Informed consent information varies from trial to trial. The

	correct informed consent must be identified for each trial	
External sources needed from outside p-medicine	⊙ data, please specify: Trial management information O tools, please specify: O services, please specify: O models, please specify: O other, please specify:	
Data used	⊙ personal O only non-personal O target population, please specify:	
Input data	⊙ internal database, please specify: Personal health record O external database, please specify: O online input	
Output data	O database, please specify: O variables for use, please specify: ⊙ structured document, please specify: Status of informed consent O graphic, please specify:	
Data volume	Mild	
Dataflow	Please specify: The data flow needs to be specified during development.	
Data storage	Please specify: Data should be stored in the data warehouse	
Successful End Condition	Patients are able understand “informed consent” and manage their status	
Fail End Condition	No access to informed consent status	
Basic workflow	Actor Action	Actor Action
	Clinical trial is identified from a list	Information and questions relevant to this trial are displayed
	User moves through the information and the questions providing the answers	The system checks that the user is eligible for the trial and is providing the correct consent. Once the final pieces of information are gathered and the user has shown to understand what they are agreeing to an electronic signature is required
	Electronic signature provided	
	User login	Access to current status of consent which can then be

		modified
Expected usage frequency	Moderate	
Needed for DSS	O yes ⊙ no	
Needs HPC	O yes ⊙ no	
Needs Grid	O yes ⊙ no	
Priority for development	Moderate	
Responsible for development	Will be decided by the IT group	
Mock-up needed	O yes ⊙ no	
Responsible for Mock-up		
Who is building the tool	Will be decided by the IT group	
Open Source tool	⊙ yes O no, please specify why	

4.3 Own Data Scenario

Item	Description
Identifier	PG_3 (IEmS_3)
Version	1.0
Name	Pathway scenario for patient empowerment: Own data
Description of the use case (end-user perspective)	Patients will be able to access the data stored on them with the data "translated" into a patient friendly format and language
Problem(s) to solve	Access to patient records within the p-medicine platform
Challenges	Displaying the information in a way that is suitable for all patients with differing levels of understanding and education, easy data transfer from existing patient records in p-medicine
Risks	Patient data stored in an insecure way, access granted to the wrong individual or hacked into
Expected benefits	Self-validation of data, greater transparency and patient empowerment
Characterization	○ fundamental ◉ general ○ specific
If specific, please give the Domain	○ Acute lymphoblastic leukaemia ○ Breast Cancer ○ Nephroblastoma ○ other Cancer, please specify: ○ Non-Cancer Domain, please specify:
End-user	○ system ○ person ○ basic scientist ◉ clinician ○ computer scientist ○ regulatory body, lawyer, ethicist ◉ patient ○ other, please specify:
Pre-condition(s)/pre-requisite(s)	Compatible with existing personal health record systems and existing patient records
Requisite(s)	
Post-condition(s)/post-requisite(s)	
Constraints	
External sources needed from outside p-medicine	○ data, please specify:

	○ tools, please specify: ○ services, please specify: ○ models, please specify: ○ other, please specify:	
Data used	◉ personal ○ only non-personal ○ target population, please specify:	
Input data	○ internal database, please specify: ◉ external database, please specify: Import from existing patient records ○ online input	
Output data	○ database, please specify: ○ variables for use, please specify: ○ structured document, please specify: ○ graphic, please specify:	
Data volume	High	
Dataflow	Please specify: The data flow needs to be specified during development.	
Data storage	Please specify: In the data warehouse	
Successful End Condition	Patients have access to their own data online in an easily understandable format	
Fail End Condition	Patients don't have access to their data	
Basic workflow	Actor Action	Actor Action
	Patient login	Available health data is displayed in an understandable format. If further information or information validation is required, a message is displayed with this information
	Patient inputs data	Patient record updated
Expected usage frequency	High	
Needed for DSS	◉ yes ○ no	
Needs HPC	○ yes For IT team to decide ○ no	
Needs Grid	○ yes For IT team to decide ○ no	
Priority for development	High	
Responsible for development	For IT team to decide	

Mock-up needed	⊙ yes O no
Responsible for Mock-up	For IT team to decide
Who is building the tool	For IT team to decide
Open Source tool	⊙ yes O no, please specify why

4.4 Access to Biobanks Scenario

Item	Description
Identifier	PG_4 (IEmS_4)
Version	1.0
Name	Pathway scenario for patient empowerment: Access to biobanks
Description of the use case (end-user perspective)	Patients will be able to access the biobank data stored on them with the data "translated" into a patient friendly format and language
Problem(s) to solve	Giving appropriate meaning to the biobank data for patients
Challenges	Displaying the information in a way that is suitable for all patients with differing levels of understanding and education. Access to each of the biobank repositories
Risks	Patient data stored in an insecure way, access granted to the wrong individual or hacked into
Expected benefits	Greater transparency and patient empowerment
Characterization	○ fundamental ◉ general ○ specific
If specific, please give the Domain	○ Acute lymphoblastic leukaemia ○ Breast Cancer ○ Nephroblastoma ○ other Cancer, please specify: ○ Non-Cancer Domain, please specify:
End-user	○ system ○ person ○ basic scientist ◉ clinician ○ computer scientist ○ regulatory body, lawyer, ethicist ◉ patient ○ other, please specify:
Pre-condition(s)/pre-requisite(s)	Availability of biobank data and anonymization of personal data
Requisite(s)	If used in clinical decision support
Post-condition(s)/post-requisite(s)	If used as part of the clinical decision support, needs to be delivered promptly
Constraints	

External sources needed from outside p-medicine	⦿ data, please specify: Biobank data needed O tools, please specify: O services, please specify: O models, please specify: O other, please specify:	
Data used	⦿ personal O only non-personal O target population, please specify:	
Input data	O internal database, please specify: O external database, please specify: O online input	
Output data	O database, please specify: O variables for use, please specify: O structured document, please specify: O graphic, please specify: To be determined in development depending on patient understanding	
Data volume	Moderate	
Dataflow	Please specify: To be determined in development	
Data storage	Please specify: Data could be transferred to the warehouse if appropriate	
Successful End Condition	Patients able to see biobank data in a meaningful way	
Fail End Condition	No biobank data available	
Basic workflow	Actor Action	Actor Action
	Patient logs in	User recognised and biobank data found and converted into meaningful information for the patient
	Import function	If desired biobank data imported into the personal health record
Expected usage frequency	Moderate	
Needed for DSS	⦿ yes O no	
Needs HPC	O yes For IT team to decide O no	
Needs Grid	O yes For IT team to decide O no	
Priority for development	Medium	
Responsible for development	For IT team to decide	

Mock-up needed	O yes ⊙ no
Responsible for Mock-up	
Who is building the tool	For IT team to decide
Open Source tool	⊙ yes O no, please specify why

4.5 Summarize the history of the disease in an understandable way and increase patient-doctor understanding

Item	Description
Identifier	PG_5 (IEmS_5)
Version	1.0
Name	Pathway scenario for patient empowerment: Patient understanding
Description of the use case (end-user perspective)	Personalized medicine includes the analysis of the psychological and cognitive characteristics of each single patient. The analysis of the individual profile of the patient might serve to help physicians to evaluate how to inform the patients and which is the treatment that best fits with the personal profile of each patient. Such an approach will lead to an individualized treatment choice adjusted to the patient's needs. After a preliminary study (3 month – September/December 2011) in which ecancer will test the instruments (ipad or laptop-based questionnaires) to validate them and to verify their usability with patients, the IEmS tool will be developed. The tool will analyze the patient's answers in real time in order to provide an immediate visual feedback to the physician who will use this information to better understand the patient's needs and to propose him/her the treatment that best fits with the patient's profile. This first assessment will be followed by other periodical internet-based evaluations whose results will be accessible on-line both by physicians and patients. In this way physicians can monitor the psychological status of the patients as well as their perceived quality of life during the treatment, while patients can increase their level of empowerment having a more active role in the therapeutic process.
Problem(s) to solve	1. To help physicians to better understand the psychological and cognitive aspects of the patients so that they can find the best therapeutic approach giving them information and treatments personalized on their needs and values finding. 2. To increase the power of patients during the therapeutic process.
Challenges	1. To create a fast, easy-to-use tool to collect data from patients that can be easily interpreted by physicians. 2. To give patients the possibility to monitor their feelings and quality of life through the use of internet-based questionnaires.
Risks	Creating a personal psychological and cognitive profile through a relative small number of questions (no more than 50) can be very difficult. That's why it is necessary

	to conduct a preliminary study to test and validate the questionnaire.
Expected benefits	1. Obtaining a personal patient's profile will help physicians to better understand the patients and their needs. 2. Asking patients to answer the questionnaires will serve to increase their participation and their level of empowerment.
Characterization	O fundamental ⊙ general O specific
If specific, please give the Domain	O Acute lymphoblastic leukaemia O Breast Cancer O Nephroblastoma O other Cancer, please specify: O Non-Cancer Domain, please specify:
End-user	O system O person ⊙ basic scientist ⊙ clinician O computer scientist O regulatory body, lawyer, ethicist ⊙ patient O other, please specify:
Pre-condition(s)/pre-requisite(s)	Availability of patients' to answer the questionnaires before the first clinical encounter and from home during the therapeutic process.
Requisite(s)	On time analysis and delivering of data obtained from the first administration of the questionnaire to the physicians.
Post-condition(s)/post-requisite(s)	Possibility for the physician and the patient to access data obtained with the internet-based questionnaires.
Constraints	If used as DSS the patient's personal profile need to be available on time. These logistics have to be solved otherwise (if data are coming late) the patient and the physician will not benefit from this use case as a DSS.
External sources needed from outside p-medicine	O data, please specify: O tools, please specify: O services, please specify: O models, please specify: O other, please specify:
Data used	⊙ personal O only non-personal

	○ target population, please specify:	
Input data	○ internal database, please specify: ○ external database, please specify: ◉ online input (To be defined with IT experts)	
Output data	◉ database, please specify: Excel or SPSS ○ variables for use, please specify: ○ structured document, please specify: ◉ graphic, please specify: Graphic should clearly represent the values obtained by the patient on each evaluated dimension and the range of the minimum and maximum values for that dimension.	
Data volume	Large, depending on the number of cases	
Dataflow	Please specify: The data flow needs to be specified during the development of the tool. Data should be stored in the data warehouse.	
Data storage	Please specify: Data will be stored in the data warehouse.	
Successful End Condition	1. Helping physicians to understand the personal characteristics of each patient in a very short amount of time. 2. Delivering personalized information and treatments that are compatible with the personal profile of the patient. 3. Increasing the patient's participation in the therapeutic process. 4. Eventually defining subgroups of patients with similar psychological and cognitive characteristics to identify sets of intervention strategies.	
Fail End Condition	No personal profiles identified.	
Basic workflow	Actor Action	System response
		The registration mask appears
	The patient registers him/herself in the system	
		The mask for the epidemiological variables appears
	The patient records his/her epidemiological variables	
		The questionnaire appears

	The patient answers the questions	The system elaborates the answers and produces the output graphs
		Data are stored in an online database
	The physicians selects the patient	A view of the graphs indicating the patient's profile will be given
Expected usage frequency	Several times per week	
Needed for DSS	⊙ yes O no	
Needs HPC	⊙ yes To be determined by the IT team O no	
Needs Grid	⊙ yes To be determined by the IT team O no	
Priority for development	The first part of the tool (iPad or laptop-based application) should be available for the beginning of 2012, at least in a beta version.	
Responsible for development	To be determined by the IT team	
Mock-up needed	O yes ⊙ no	
Responsible for Mock-up		
Who is building the tool	To be determined by the IT team	
Open Source tool	⊙ yes O no, please specify why The software can be open source, while the questionnaires, for scientific reasons, will be proprietary as the majority of the existing psychological validated tests.	

5. Conclusion

By defining and understanding an individual patient's psychological profile the tools developed within the p-medicine project will be able to take the whole patient, their medical and psychological needs into account. By identifying the factors affecting a patient's quality of life and designing a questionnaire that will investigate these factors, the patient empowerment tools will provide a valuable tool to increase the understanding of patient's needs. Through the use of these tools, and the other tools developed within the p-medicine environment, doctors and patients will be able to make informed decisions regarding treatment choices. These decisions will be based on a patient's medical needs, but also their psychological profile, therefore ensuring that any treatment regime is truly personalized.

Appendix 1 - Abbreviations and acronyms

SOA	Service Oriented Architecture
PROMs	Patient recorded outcome measures
HRQL	Health related quality of life
EMQ	Everyday memory questionnaire
CES-D	Centre of epidemiological studies depression scale
GSE	General self-efficacy scale
BFI-10	10-item big five inventory
GSRH	Generated self-related health
STAI	State trait anxiety inventory
VAS	Visual analog scale
SPSS	Statistical package for social science
DSS	Decision support system