UNIVERZITA KARLOVA V PRAZE

1. lékařská fakulta

Studijní program: Psychologie

Studijní obor: Lékařská psychologie a psychopatologie

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Prognostic awareness in advanced cancer patients

Prognostické uvědomování u pacientů s pokročilým onkologickým onemocněním

Disertační práce

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Praha 2022

PROHLÁŠENÍ

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Identifikační záznam:

VLČKOVÁ, Karolína. *Prognostic awareness in advanced cancer patients [Prognostické uvědomování u pacientů s pokročilým onkologickým onemocněním]*. Praha, 2022. 99 stran, 0 příloh. Disertační práce (PhD.). Univerzita Karlova v Praze, 1. lékařská fakulta, Psychiatrická klinika. Školitel: PhDr. Martin Loučka, PhD.

ACKNOWLEDGEMENTS

I would not have been able to finish my PhD without the help from a lot of people around me.

I would like to express my sincere gratitude to my supervisor, Dr Martin Loučka, for his encouragement, trust in me and patient leadership. I would like to also thank all my colleagues from the Center for Palliative Care Kristýna Poláková, Anna Tučková, Eva Gurná and Adam Houska who helped me a lot during my PhD in many ways.

I am also very grateful to all patients and their relatives who despite their difficult situation and serious condition took part in our study and could contribute to a science.

My thanks also go to my parents and my whole family, who supported me during my whole studies and always trust me.

Finally, I would like to thank my daughter Rozalie and my partner Matěj, who have been with me all the time and patiently survived all my studies.

Abstract:

Being aware of the severity of their medical condition is a key precondition for patients with advanced disease to be involved in advance care planning. This thesis aims to describe the phenomenon of prognostic awareness and identify factors that are related to prognostic awareness in patients with advanced cancer. The author of this dissertation thesis participated in a three-year project, which was supported by the Czech Science Foundation (IMPAC study, grant number 17-26722Y), which aims to map the preferences of patients with advanced disease and further describe factors related to prognostic awareness and assess its stability over time. The secondary goal was also to describe how patients with a serious diagnosis and their loved ones evaluate their participation in a research study.

In the introductory chapter of this thesis, we describe the concept of prognostic awareness, methods of measuring it and the goals of this work. The dissertation thesis includes 4 publications that are focused on this topic and 1 publication that responds to the secondary goal of this dissertation thesis. The publications are followed by a discussion in which we deal with all our findings in the context of the latest evidence available on this topic.

Our results prove that prognostic awareness is a complex phenomenon and identify several factors that can influence it. In addition, we have also shown that the level of prognostic awareness does not change over time and therefore, it is probably a stable phenomenon. Our data also showed that patients and their loved ones do not mind participating in the research study, with almost half of them even considering it an interesting experience. Our results prove that when delivering bad news, it is necessary to know the preferences and wishes of the patient and apply an individual approach.

Key words: prognostic awareness, communication, delivering bad news, quality of life, cancer

Abstrakt:

Být si vědom závažnosti svého zdravotního stavu je klíčový předpoklad pro to, aby pacienti mohli být zapojeni do plánování své budoucí péči. Tento předpoklad se v literatuře označuje pojmem prognostické uvědomování a dobrá komunikace s lékaři je jedním z faktorů, který jej významně ovlivňuje. Tato disertační práce se zabývá tímto tématem prognostického uvědomování u pacientů s pokročilým onkologickým onemocněním. Jejím cílem je popsat tento fenomén a identifikovat další faktory, které ovlivňují porozumění vlastní prognóze u pacientů s pokročilým onkologickým onemocněním. Autorka této disertační práce se podílela na tříletém projektu, který byl podpořen Grantovou agenturou ČR (IMPAC study, číslo grantu 17-26722Y)), jejímž cílem zmapovat preference pacientů s vážným onkologickým onemocnění a dále popsat faktory, které souvisí s prognostickým uvědomováním a prozkoumat jeho stabilitu v čase. Vedlejším cílem bylo také zmapovat, jaké je pro pacienty s vážnou diagnózou a jejich blízké účastnit se výzkumné studie.

V úvodní kapitole této disertační práce popisujeme koncept prognostického uvědomování, způsoby jeho měření a cíle této práce. Součástí disertační práce jsou 4 publikace, které se tímto tématem zabývají a 1 publikace, která reaguje na vedlejší cíl této disertační práce. Publikace jsou následovány diskusí, v níž se zabýváme všemi našimi zjištěnými poznatky v kontextu nejnovějších evidence, která je na toto téma dostupná.

Tato práce prokazuje, že prognostické uvědomování je komplexní fenomén a přináší výčet faktorů, které ho mohou ovlivňovat. Vedle toho jsme také ukázali, že míra prognostického uvědomování se s časem nemění a jedná se pravděpodobně o stabilní fenomén. Naše práce také rovněž ukázala, že pacientům ani jejich blízkým nevadí účast ve výzkumné studii, dokonce téměř polovina z nich to považovala za zajímavou zkušenost. Naše výsledky dokazují, že při sdělování závažných zpráv je nutné znát preference a přání pacienta a uplatňovat individuální přístup.

Klíčová slova: prognostické uvědomování, komunikace, sdělování závažných zpráv, kvalita života, onkologické onemocnění

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1 Introduction

´Communication between physicians and patients is a fundamental aspect of cancer care, yet most physicians have had little training in communication. The aspects of communication most valued by patients are those that help patients and their families feel guided, build trust, and support hope,´ (Back et al. 2005).

Physicians are well trained in medical interviewing which has the aim of taking a complete medical history of their patients. However, delivering bad news requires different communication skills which are not always part of the curriculum at medical schools (Back et al. 2005). Bad news in this context mean situations which are threatening for the mental or physical health of patients (Ptacek and Eberhardt 1996). These communication situations are difficult and require from physicians to maintain frankness but also sensitivity. Patients, on the other hand, deal with the emotional impact of life-limiting illness (Back et al. 2008). New therapeutic possibilities which are available enable patients with advanced cancer to live longer than ever before but it also brings more possibilities in care and requires more involvement of patients in the decision making process.

This requires from health care providers to respect the autonomy of patients, respect their values and choices and individualized approach. This is an important shift from the paternalistic approach which has been the norm in health care in the last century. Modern medicine emphasizes partner approach which empowers patients to participate in their care, especially in the decision making process (Breeze 1998).

One important indicator of this partner approach to patients is whether physicians disclose patients their diagnosis and prognosis. We can see a developing trend in this area when in the 1960s' not telling the truth was rather a norm (Oken 1961) but 20 years later this trend was significantly shifted towards a more honest approach (Novack et al. 1979). However, physicians still fear the consequences of delivering bad news such as causing emotional distress, loss of hope or disruption of patient-physician relationship or fragile emotional state of patients and their caregivers (Enzinger et al. 2015; Hancock et al. 2007; Saracino et al. 2021; Yun et al. 2010).

However, these assumptions are not supported by available evidence because when patients and their caregivers are asked what is important at the end of life, they agree on being informed and having a sense of control as one of the most important factors (Singer, Martin, & Kelner, 1999, Steinhauser et al., 2000, Harding et al., 2013). On the other hand, a recent study by Schoenborn et al (2018) showed that older persons might struggle with the idea of being offered a discussion about their prognosis which means this problem does not have one simple solution. Therefore, we should not avoid delivering bad news even though we should always assess the values and beliefs of our patients and ask them if they want to be informed and if they want someone else to be present during delivering bad news (Epstein et al. 2019; Rosenzweig 2012). This is also supported by the main results of one systematic review on this topic – that all patients want some information but they want to negotiate the content, timing and the extent of the information (Parker et al. 2007). Based on these results, we might say that patients prefer a realistic and individualized approach (Hagerty et al. 2005). Making choices and decisions is an important way of expressing patients´ autonomy that enable them to take an active part in their medical decision making process which is a good way how to support their dignity (Houska and Loučka 2019).

In situations when the primary goal is not to cure the disease anymore, balancing the patients' values and their future treatment options is not possible without adequate communication and a shared view on the disease trajectory. Moreover, a systematic review by Belanger et al. showed that patients want this active role and prefer to be active in the decision making process (Bélanger, Rodríguez, and Groleau 2011).

Therefore, the patients' and relatives' involvement in those decisions is desirable as a key feature of patient-centred care (Frank 2009). To ensure that patients can make medical decisions, which truly reflect their preferences and wishes, improving patients' understanding of their healthcare status is a fundamental task for all healthcare providers. Facilitating understanding of the prognostic of patients lies at the centre of these efforts.

The overall goal of this thesis is to focus on how patients with advanced cancer understand their prognosis and which factors influence this process of the development of prognostic awareness.

This thesis is based on a monothematic compilation of 5 peer-reviewed articles. The content of this introductory chapter is as follows: Firstly, we will describe the concept of prognostic awareness (section 1.1) and the current methodological strategies on how to measure this concept (section 1.2). Secondly, we will present our hypotheses (1.3) and describe the IMPAC project (1.4) that which this thesis was a part. In section 1.5. we will explain the outline of the main chapters that follow.

1.1 Concept of prognostic awareness

In the Introduction, we have explained that when we want to involve patients in decision making about their health status, they must understand their condition (Franssen et al. 2009). The ability to understand the disease, its seriousness and potential future trajectory is behind the concept of *prognostic awareness* which is central to this thesis. The concept of prognostic awareness has been discussed and studied a lot for the last two decades. Even though there are studies published before 2000 assessing whether patients know about their prognosis (Centeno-Cort and Nunez-Olarte 1994; Chandra et al. 1998), the term ´prognostic awareness‘ appeared probably for the first time in the paper by Chochinov and his colleagues in 2000 (Chochinov et al. 2000). In their study, this concept meant that patients acknowledged the advanced medical diagnosis and its terminal status (Chochinov et al. 2000).

Since 2000 many more studies were conducted on this topic, however, the operational definitions of prognostic awareness differ a lot across the studies. Some of the authors define it as illness understanding (Chow et al. 2001; Epstein et al. 2016; Sivendran et al. 2017), understanding prognosis (Barnett 2006; El-Jawahri et al. 2014; Enzinger et al. 2015), understanding goals of care (Lennes et al. 2013; Mitera et al. 2012; Soylu et al. 2016) which is very close to the knowledge of treatment intent (Craft et al. 2005), understanding life-limiting illness (Wagner et al. 2010), understanding of cancer stage (Kavradim, Özer, and Bozcuk 2013; Shin et al. 2018), or perceptions of prognosis (Temel et al. 2011), life expectancy estimates (Trevino et al. 2017), beliefs about curability (Duberstein et al. 2018), patients ´expectations about effects of chemotherapy (Weeks et al. 2012) perception of health status (Greer et al. 2014; Kurita et al. 2018), patients beliefs that chemotherapy may be curative (Mack et al. 2015).

From a theoretical perspective, prognostic awareness is very much related to the concept of illness representation which is based on patients' beliefs and expectations about their illness (Leventhal, Leventhal, and Contrada 1997). Development of illness representation takes place on both the cognitive and emotional levels, but it seems that these two levels work separately (Leventhal, Diefenbach, and Leventhal 1992). Illness representation is a part of self-regulation theory which postulates that person´s behaviour and attitude toward illness might be explained by their illness representation and coping strategies (Leventhal 1970; Leventhal et al. 1997). Illness representation has several different dimensions:

1) Identity or label of threat; timeline or believed time trajectory (acute, chronic, progressive)
2) Timeline or believed trajectory of threat
3) Believed consequences that might be expected (minor or major, fatal)
4) Cause or causal mechanism of threat (hereditary, multifactorial)
5) Control/cure or whether we can control threat or heal it
6) Illness coherence means whether patients think about the threat in a coherent way (Weinman et al. 2007).

When we look back at our different definitions of prognostic awareness it is possible to connect it with some of the dimensions of illness representation, e.g. label might be connected with perceptions of health status or illness understanding, and timelines seem to be similar to life expectancy estimates, the cure is related to treatment intent or goals of care or stage of the disease.

From the above, it seems that there is some overlap between these two concepts mostly and prognostic awareness might become a part of this concept as a specific component of the timeline dimension. Even though it was so far regarded and used as an independent construct because it is seen to be distinct from some aspects of illness representations. Illness representation is much more related to health behaviour, coping strategies, adherence to treatment and compliance, on the other hand, prognostic awareness is much more connected to health information needs and also prognostic acceptance (Hinton 1999; Justo Roll, Simms, and Harding 2009; Tang, Chang, et al. 2016; Thompson et al. 2009). It is also not clear whether it is only a cognitive process or how emotions influence the development of accurate prognostic awareness (Tang et al. 2021). Compared to illness representation, which is related to any disease at any stage, prognostic awareness is related only to serious diagnosis when conditions get worse which is a plausible argument for the distinction between these two concepts. It would be also interesting to assess the discriminant validity of these two concepts compared to each other and we are not aware that this has been done so far.

The growing number of articles and increasing interest in this topic led to a systematic review which was published in 2014 and included studies till 2012 (Applebaum et al. 2014). The main aim of this review was to look at how prognostic awareness is measured in different studies. It was found that there is a lot of variation in the conceptualization of prognostic awareness, and it may be seen also as a unidimensional construct, as well multidimensional construct (Applebaum et al. 2014). This review was recently updated, and a concept analysis was done to provide an evidence-based definition of prognostic awareness (Kühne et al. 2021). This recent systematic review brought conceptualization of this concept using content analysis and define it as:

'PA (prognostic awareness) *primarily comprises the appropriate estimation of chances for recovery (i.e., incurable disease), knowledge of limited time to live and the appropriate estimation of shortened life expectancy, and secondarily, the appropriate estimation of therapy goals as well as knowledge of the course of a disease, '*(page 3, Kühne et al. 2021).

This operational definition highlight different way how we can look at this phenomenon and how we can measure it. We can ask patients whether they think that their disease could be still cured, or what is their life expectancy or what is the goal of their therapy. But this brings very important questions are these aspects of prognostic awareness the same thing? Or should we assess all of them? Will patients answer all these questions in the same way? Do they can replace each other or are they three different components of prognostic awareness? So far, we do not have answers to this question. Definition of prognostic awareness should be also discussed from the perspective of patients. This could help because so far, there are differences in the methodological conceptualization of prognostic awareness which make understanding this phenomenon difficult (Finlayson, Chen, and Fu 2015; Laakso and Paunonen-Ilmonen 2001).

A recent large meta-analysis showed that a very low number of advanced cancer patients understand their prognosis well, the mean prevalence of accurate prognostic awareness was 49.1% (95% CI: 42.7%–55.5%, range: 5.4%–85.7%) (Chen, S. Kuo, and Tang 2017). This means that only half of the patients, at the best in included studies understood their prognosis and had an accurate understanding of how serious is their condition. The average accuracy of prognostic awareness varies across countries, which might be related to cultural factors: a slightly lower prevalence of prognostic awareness was identified in countries in Europe (Italy, Spain, and the United Kingdom were included in the review), the highest was in Australia (67. 7%) and East Asia (Chen, S. Kuo, et al. 2017). There was not any study from the Czech Republic included in the review.

It is also important to mention that this concept has been mainly studied discussed and observed in conversations with patients with advanced cancer so far. However, it might be relevant also for other diseases. For example, in the treatment of most advanced chronic diseases such as COPD, heart failure o dementia, patients and their families also face the challenges of balancing their values, priorities and worries on one side and the potential treatment options and medical interventions on the other. If we use the case of heart failure, which is the leading cause of death worldwide (WHO 2019). Only a few studies assessed prognostic awareness in this group so far with some showing a slightly higher accurate awareness in this group (51%-78%) compared to the results in cancer patients (Gelfman et al. 2020; Ozdemir et al. 2021). However, this might be again influenced by the conceptualization of prognostic awareness as other studies with heart failure patients found worse results in this population (Horan et al. 2000). Even though patients should have and would like to have clear information and discuss their prognosis (Boyd et al. 2004; Jaarsma et al. 2009), only around 10 % of patients with heart failure reported having such a conversation (Kramer et al. 2017). This is probably caused by clinicians' uncertainty in prognostication, differences in disease trajectory and also a variety of treatment options (Murray and Sheikh 2008; Siouta et al. 2016) and it might be similar for other diseases such as dementia, HIV, ALS or diabetes.

Few studies also assessed family caregivers ´prognostic awareness (Chandra et al. 1998; Gray et al. 2021; Tang et al. 2021) using different definitions of prognostic awareness which copied the definitions of prognostic awareness of patients. This means that caregivers were asked what is the goal of the treatment of their relatives (Chandra et al. 1998) or about the curability of the disease of their relatives (Tang et al. 2021). A more recent study used The Prognosis and Treatment Perception Questionnaire to define caregivers 'awareness (Gray et al. 2021). A very interesting contribution to this topic was brought by Tang and her colleagues – who found that emotional preparedness for death and prognostic awareness often does not agree (Tang et al. 2020, 2021). Their results suggest that prognostic awareness is rather a cognitive process and emotional acceptance of the situation is much more complicated and would require special support from staff in some situations (Tang et al. 2021).

1.2 How to measure prognostic awareness

The conceptualization of prognostic awareness is also very much related to the process of measuring it. The most used method for assessing prognostic awareness is Terminal Illness Acknowledgment (TIA) which was developed by Prigerson (Prigerson 1992) and was used by most of the studies that are identified in Applebaum´s review (Applebaum et al. 2014). This method uses the question: ´How would you describe your current health status' and offers the following response options: ´relatively healthy´, ´seriously but not terminally ill,´ and ´seriously and terminally ill, ' (Prigerson 1992). This method measures the accuracy of prognostic awareness with the question of the severity of the illness. This approach was used in other studies (Chan and Woodruff 1997; Yun et al. 2010) even though it was sometimes used as a question during unstructured interviews and patients were not offered the answers (Chittem, Norman, and Harris 2013; Chochinov et al. 2000).

Close to this method are many others which assessed whether patients know their stage of cancer (Lee et al. 2013). One of the structured methods that work with that is LSIU (Late-stage illness understanding) (Cohen et al. 2018). This method was also validated and had a mild correlation with the question about the terminal condition of patients (Cohen et al. 2018). Similarly, to that, prognostic awareness was sometimes measured with the question of whether patients knew that they had metastasis (Caruso et al. 2000).

Very close to understanding the nature of the disease is also the acknowledgement of the limited life expectancy. In some studies, patients were asked an open-ended question about their estimation of remaining time (Fried and Bradley 2006; Liu et al. 2014) or asking how probable is that they will live after two or six months (Haidet et al. 1998). Most studies work with patients' (or clinicians') estimates, although for example, Trevino et al. followed patients longitudinally to compare their estimation with the real length of survival (Trevino et al. 2017).

Other methods assess the accuracy of prognostic awareness with questions that were focused on the probability of being cured. Some studies used a visual analogue scale asking patients to indicate their chances of being cured in percentages (IGEO 1999; Shin et al. 2016) or using pre-specified answers with percentages (Costantini et al. 2015; Robinson et al. 2008; Weeks et al. 1998). Tang et al. developed their method of assessing how patients feel about the curability of their disease (Tang et al. 2006, 2008, 2014, 2021). Their method was based on asking patients to choose between three options describing their condition: (1) was curable; (2) might recur in the future, but their life was not currently in danger; and (3) could not be cured, or they would probably die soon (Tang et al. 2006). How patients perceived the curability of their disease was also assessed by asking them to choose between 2 options curable or incurable (Yanwei et al. 2017; Yennurajalingam et al. 2018).

The second part of the definition of prognostic awareness by Kühne and her colleagues (Kühne et al. 2021) is related to patients´ understanding of the goal of their treatment. Therapy goals were assessed with interviews with patients (Gough et al. 2019; Lennes et al. 2013; Soylu et al. 2016) and achieving the accurate prognostic awareness usually meant that patients understood the non-curative goal of their current treatment (Craft et al. 2005; Kao et al. 2013).

Other ways how the perceived goal of therapy was measured are to ask patients to choose between different options – whether the goal of their treatment is to cure, prolong life or relieve symptoms (Mitera et al. 2012; Shin et al. 2016) or whether the goals of treatment were to monitor illness, to improve quality of life, to control illness, or to cure the disease (Burns et al. 2007).

Some authors used questions from questionnaires that are originally meant to assess other concepts than prognostic awareness itself. One study used the Decisional Conflict scale (Baek et al. 2012) which is a scale that was developed to assess patients' uncertainty around their health-related decisions and how they perceive deciding their health condition (O'connor 1995). Another measurement that was also used to assess the accuracy of prognostic awareness was the Support Team Assessment Scale which was originally developed for assessing outcomes of palliative care and was intended to use by the palliative care team (McCarthy and Higginson 2016). One of the items in this scale is related to patients' insight into the seriousness of their condition (McCarthy and Higginson 2016). It was also confirmed that ratings between staff and patients are similar to each other using this method (Higginson and McCarthy 1993). In one study it was used and completed by nurses after clinical interviews with patients (Chan 2011).

As we mentioned above, prognostic awareness is somehow related to the concept of illness representation. Not surprisingly some studies used a questionnaire that assesses illness representation also for assessing patients' understanding of the severity of their illness. Price et al. (2012) used an established measure – the Brief Illness Perception Questionnaire (IPQ) which is a nine-item scale developed to rapidly assess a patient´s representation of illness (Broadbent et al. 2006). These questionnaires asked patients about their perceptions of the health threat, including beliefs about their life expectancy (Price et al. 2012).

In some situations, using the items from other measures might work well but we should keep in mind that the original aim of the questionnaire is different, and we should assess the psychometric properties of these items to confirm the validity of the item and provide information how strong is the connection between the item and the concept of prognostic awareness.

Several studies used more complex questionnaires to capture more aspects of prognostic awareness (El-Jawahri et al. 2014; Gray et al. 2021; Nipp et al. 2017). Prognosis and Treatment Perceptions Questionnaire consists of several methods mentioned above – patients are asked about primary treatment goal, curability of their disease, current medical status and it also includes TIA question developed by Prigerson (El-Jawahri et al. 2014; Nipp et al. 2017). All answers were combined and patients' perception was assessed as considering their status to be terminally ill or not terminally ill (El-Jawahri et al. 2014; Nipp et al. 2017). However, this method has not been evaluated for its psychometric properties.

Applebaum and her colleagues also revealed that many studies did not report exact methods on how they define the accurateness of prognostic awareness in patients or it was very much based on the judgement of the researcher or clinician which they created during the conversation with patients (Applebaum et al. 2014). In this case, prognostic awareness was confirmed for example if patients expressed that their condition was serious during the conversation or mentioned that they had metastasis. Although this approach is very problematic as patients may know but may not want to express it loud and they may rather wait for their physician to mention that first. Moreover, a meta-analysis done by Chen and her colleagues showed that the prevalence of prognostic awareness was significantly higher when it was assessed by physicians than by patient self-report (Chen, Kuo, et al. 2017). This might indicate that physicians may tend to overestimate this or they might not be sensitive to the situation when they deliver bad news but patients deny them as part of psychological adaptation (Vos et al. 2011; Watson et al. 1984). These findings suggest that we should always use self-report to assess prognostic awareness in patients.

Applebaum and her colleague identified that prognostic awareness was assessed using structured, semi-structured and unstructured measurements (Applebaum et al. 2014). When we used semi-structured and unstructured manner there is always a problem with the objectivity and reliability of this assessment which is supported by the overestimation done by physicians which are mentioned above.

What is also problematic in the case of structured measures of prognostic awareness is the fact that almost all the instruments that were used in the studies had not had their psychometric properties evaluated, such as validity and reliability (Chen, Kuo, and Tang 2017). As the methods for assessing prognostic awareness were not validated therefore it is complicated to compare them to each other and to compare results from different studies. Moreover, the development of specific methods for assessing prognostic awareness was always based on the view of researchers or clinicians but in this case, it might be very helpful also to get the perspective of patients and their family caregivers.

Recently, another complex tool for assessing prognostic awareness has been developed in the United States at Harvard Medical School (Brenner et al. 2021). This tool is being prepared in 2 steps procedure. Firstly, a team consisting of oncology clinicians, psychologists, psychiatrists, palliative care physicians and psychometrists had prepared items for the questionnaire. Secondly, cognitive interviews with 39 patients were conducted to assure the understandability and relevance of included items (Brenner et al. 2021). The next step will be to evaluate the psychometric properties of this new tool. Complex tools such as this will bring more understanding toward the conceptualization and increase our ability to measure the multifaceted concept of prognostic awareness.

1.3 The aim of this thesis

As described in section 1.1, prognostic awareness is a phenomenon which has been rarely studied from a longitudinal perspective. Available studies on prognostic awareness are also predominantly from the United States or Asian countries and the evidence from Eastern European countries is missing. The goal of this thesis is to enrich the knowledge about this concept from several perspectives described below.

This thesis has 3 aims:

1) To describe factors that may be associated with prognostic awareness in cancer patients

The plausibility of this aim will be tested with a systematic review of studies exploring the associations between accurate prognostic awareness and various factors.

2) To assess the stability of prognostic awareness in patients with advanced cancer throughout their disease

Regarding this aim, we postulate the following hypothesis:

H0: There is no significant change in prognostic awareness in patients with advanced cancer throughout their disease.

This aim will be tested with the longitudinal assessment of prognostic awareness in advanced cancer patients.

3) To describe the experience of patients and their caregivers with palliative care research

The third aim will be assessed with this hypothesis:

H0: Patients with advanced cancer do not mind participating in the palliative care research.

Besides prognostic awareness, this thesis has a secondary goal which is methodological, and it is focused on the experience of patients with advanced cancer with participation in research. This goal will be achieved in two steps. In the first step, we will ask participants in a cross-sectional study about the end of life care preferences to evaluate their experience with this study and we will also ask them about their motivation to participate in the research. The second is to ask participants in a longitudinal cohort study to evaluate their experience.

1.3 IMPAC study

This thesis is a part of the project Integrative Model of Prognostic Awareness in Patients with Advanced Cancer (IMPAC study) (Loucka et al. 2017). This work was supported by Czech Science Foundation (grant number 17-26722Y). The principal investigator of this study was my supervisor Dr Martin Loučka and the study was conducted by the Center for Palliative Care where I have worked as a research fellow since 2017. This project aimed to explore factors that patients with advanced illnesses consider as important and develop an integrative model of prognostic awareness that would provide insight into the mechanism of the decision-making process in advance.

The IMPAC project had 3 stages. In Stage 1 we conducted semi-structured interviews with patients with advanced cancer and their relatives and focus groups with health care providers. The goal of this stage was to explore what factors they consider important at the end of life. In Stage 2 we developed a questionnaire based on the results from Stage 1 and in this questionnaire patients with chronic disease, their relatives and physicians were asked to rank the importance of presented factors. In Stage 3 we recruited a cohort of patients with advanced cancer and their relatives and over 9 months we collected data from them at least 3 times. Using a structured interview, we asked them about their prognostic awareness (using 3 different methods), information needs, and quality of life (using 2 different methods). Follow up measurements with patients as well as their caregivers were conducted either in person or by phone. Their treating physicians were asked the same questions about prognostic awareness and they also provided other clinical data about patients.

1.4 Outline the chapters

The core chapters of this thesis are represented by 5 articles presenting the results of our work which have been published in peer-reviewed journals. I am the first author in 4 of them and the second author in 1 of them. All of them I wrote with my supervisor. The second paper is co-authored with colleagues from the QED group who helped us with the psychometric analysis and the rest of the papers are co-authored with my colleagues from the Center for Palliative Care who worked on the IMPAC study. The fourth paper is also co-authored with two physicians from hospitals that were involved in the longitudinal cohort study. The content of each chapter will be briefly described below with a focus on the connection between them.

Chapter 2 Factors associated with prognostic awareness: A systematic review

This chapter presents the results of a complex systematic literature review that we conducted intending to explore the factors that are associated with accurate prognostic awareness in cancer patients. We identified 102 factors that were found to have a significant association with prognostic awareness. Using thematic analysis, we grouped them into 7 groups. Demographic factors, factors related to coping, health condition factors, psychological factors, factors associated with end-of-life care, factors related to communication and factors related to relatives. Some of the factors have negative associations with prognostic awareness, some of them have positive and for some of them we found mixed results. The most studied factors were depression, anxiety and quality of life and they were associated with accurate prognostic awareness and with inaccurate prognostic awareness. This article uncovered the vast complexity of prognostic awareness and the results suggest that this phenomenon is very difficult to interpret. Most of the reviewed studies also used the cross-sectional design that highlights the need for longitudinal assessments to validate our knowledge about the development of prognostic awareness. This article serves as the foundational knowledge base for this thesis, and it helped us in designing the data collection methods for the latter parts of the IMPAC study.

This systematic review was published on 13 April 2021 in Psycho-Oncology, 29(6), 990-1003, IF= 3.89, Q1.

Chapter 3 Psychometric properties of the Czech Integrated Palliative Outcome Scale: reliability and content validity analysis

One of the factors that were identified as having a significant association with prognostic awareness in Chapter 2 was quality of life. This relationship is not clear because mixed findings were found for this factor (suggesting both positive and negative associations with prognostic awareness), and it needs further research. As part of our IMPAC study, we decided to examine the relationship with quality of life in our sample as it presents one of the central concepts to guide the care for patients with advanced disease. Therefore, part of this thesis was also the adaptation and standardization of the tool for measuring the quality of life. We have decided to adopt a specific tool for measuring the quality of life in the general population of palliative care patients that would have wider use in future research. The Integrated Palliative Outcome Scale (IPOS) was developed at King's College London and has been translated and used widely across the world as one of the most reliable tools to measure the quality of life in palliative care patients (Sandham et al. 2019). Standardization of IPOS allowed us to measure the quality of life in the longitudinal cohort study with a robust tool. IPOS was found to be reliable, and the adaptation process was successful.

The article presenting the development of the Czech version of IPOS was published on 25 March 2020 in BMC Palliative Care, 19(1), 1.8, IF= 3.23, Q2.

Chapter 4 Association between quality of life and prognostic awareness in patients with advanced cancer

A systematic review in Chapter 2 showed that the association between quality of life and prognostic awareness is one of the most studied relationships but it is still unclear in terms of whether more accurate prognostic awareness leads to better or worse quality of life. We analysed this association in our study to further explore this relationship. We analysed data from the baseline measurement in the IMPAC study with a sample of 129 patients. We tested the association between the composite measure of prognostic awareness (using 3 different methods for assessing prognostic awareness) and quality of life using IPOS and a single-item quality of life scale. We found a negative association between accurate prognostic awareness and quality of life. However, detailed analysis that was allowed by using our validated IPOS tool showed the association was significant only for the physical domain of quality of life, not for the emotional and communication domain. These results suggest that the association between prognostic awareness and quality of life might be explained by the fact that patients aware of their diagnosis are usually in the advanced stage of their disease with a worse symptom burden. Therefore, prognostic awareness itself does not have to be related to emotional distress in patients which is often feared by clinicians.

This article was published on 4 February 2022 in Quality of Life Research, pp. 1-8, IF= 4.14, Q1.

Chapter 5 Prognostic awareness in advanced cancer patients and their caregivers: A longitudinal cohort study

This is the core chapter of this thesis which tested our second hypothesis. In this article, we analysed our data from the IMPAC study and assess the longitudinal stability of the prognostic awareness. We used 3 different measures for assessing prognostic awareness and as we were expecting different outcomes, we decided to develop a new composite measure, compiling the scores of all three questions with a potential outcome of 0 for no correct answers in any of the three questions (patient not aware), one point for at least one accurate answer (patient partially aware), and two points for all questions answered accurately (patients considered to be aware of their prognosis). We collected data three times over nine months from patients, caregivers and treating physicians. We also collected several factors that were identified as related to prognostic awareness in Chapter 2. We did not find any significant association between prognostic awareness and other factors such as gender, education, health information needs etc. Caregivers were slightly more aware of the prognosis of their loved ones than patients. Longitudinal analysis showed that prognostic awareness seems to be a stable concept over time, therefore it might be influenced by other aspects such as personality traits.

This article was published on 16 April 2021 in Psycho-Oncology 30(9), pp. 1449-1456, IF= 3.89, Q1.

Chapter 6 Views of patients with advanced disease and their relatives on participation in palliative care research

This chapter relates to the secondary aim of this study, the evaluation of participants' experience with palliative care research. The researchers in palliative care often face the problem of gatekeeping which is usually caused by treating staff or family members who are afraid of patients´ vulnerability and the burden caused by research participation and do not allow researchers to access the patients. There is still a lack of evidence on how patients evaluate their experience, especially from the Eastern European region. This article aimed to evaluate patients' and their caregivers' experiences with two parts of the IMPAC project. The first study was a cross-sectional questionnaire study assessing patients´ preferences and priorities regarding end-of-life care. Participants were asked to evaluate their experience on a five-point Likert scale and also use an open-ended question about their motivation to participate. The second evaluated experience was their participation in the longitudinal cohort study which is in detail described in Chapter 5. This study revealed that patients and their caregivers do not mind participating in research and about a half of the participants even rated their experience as interesting. These results imply that clinicians and staff do not have to be afraid to offer their patients and their caregivers the opportunity to engage in research, of course, while respecting and following the formal ethical procedures.

This article was published 5 June 2020 in BMC Palliative Care 2O(1), 1-7, IF= 3.23, Q2.

Chapter 7 Discussion

In this chapter, the results from previous chapters will be discussed in a wider context.

Chapter 8 Conclusion

In this last chapter, we conclude the findings from this thesis and suggest future directions for research work in this field.

Received: 9 December 2019 | Revised: 25 March 2020 | Accepted: 27 March 2020
DOI: 10.1002/pon.5385

REVIEW

WILEY

Factors associated with prognostic awareness in patients with cancer: A systematic review

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Abstract

Objectives: Prognostic awareness relates to patients' capacity to understand their prognosis and the likely illness trajectory. Based on the current evidence, accurate PA is associated with decrease in uncertainty, depresivity, and anxiety and with increase in quality of life. However, other studies found also negative associations of PA and quality of life and mental health. This systematic review synthesizes the available literature on factors associated with accurate prognostic awareness in patients with cancer.

Methods: Four databases were systematically searched for studies assessing prognostic awareness in patients with cancer. In these studies, we looked for factors positively or negatively associated with prognostic awareness. Included studies were critically appraised for methodological quality.

Results: We screened 28 078 studies and included 70. In these studies, 102 factors were found to be related to prognostic awareness positively or negatively. Identified factors were divided into seven groups: demographic factors, factors related to coping, health condition factors, psychological factors, factors associated with end-of-life care, factors related to communication, and factors related to relatives. Prognostic awareness differs according to age, personality, communication with doctor, disease stage, or being outpatient. For some factors such as depression, anxiety, or quality of life, higher level of these factors was found to be associated with accurate and inaccurate prognostic awareness.

Conclusions: Prognostic awareness is a complex phenomenon associated with various positive and negative associations for patients with cancer. Clinicians must consider individual preferences and values of patients and their families when discussing prognosis and must be prepared for potential adverse outcomes.

KEYWORDS
cancer, oncology, prognostic awareness, prognostic understanding

1 | INTRODUCTION

Prognostic awareness (PA) relates to patients' capacity to understand their prognosis, shortened life expectancy and the likely development of the disease.[1] Understanding diagnosis and prognosis was found to facilitate end-of-life care planning, discussion about life-prolonging treatment and establish do-not-resuscitate orders.[2-4] Based on the current evidence, accurate PA is associated with decrease in depresivity and anxiety and with increase in quality of life.[5,6] Moreover, prognostic awareness can be associated with less uncertainty

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from which patients' relatives suffer.[7] However, some studies also found prognostic awareness is associated with lower level of quality of life and worse mental health of patients with cancer.[8,9]

This inconsistency could be explained by different methodological conceptualization of prognostic awareness, such as using unidimensional or multidimensional approach as suggested by Applebaum et al.[1] Multidimensional approach consists of several factors such as being aware of the metastatic nature of disease, the purpose of treatment, shortened life expectancy and terminal stage of disease, while the unidimensional approach uses only one of these components.[1] Applebaum et al published a comprehensive systematic review focusing on the conceptualization of prognostic awareness in 2014 and reported different ways how PA can be measured. The level among cancer patients varied significantly across studies, from 0% to 75% which the authors explained by the different operationalization of PA.[1] The goal of this study is to expand our knowledge in this area by focusing on correlates of prognostic awareness. Our research question was: "What are the factors which are significantly associated with accurate or inaccurate prognostic awareness in adult patients with cancer?" This might bring important contribution to discussion about prognostic disclosure and clarify whether prognostic awareness is associated with positive or negative factors and identify personal and demographic factors which might be associated with prognostic awareness.

2 | METHOD

We conducted a systematic review following Preferred Reporting Items for Systematic Review and Meta-analysis Protocol (http://www.prisma-statement.org/). The PRISMA checklist is in Data S1. Heterogeneity of study designs and outcomes precluded meta-analysis. The search for this systematic review was conducted in four databases: MEDLINE, CINAHL, PsycINFO, and Embase. We searched for English, French, and Czech references, within the data range from January 1990 to December 2019, including studies reporting on adult patients with cancer (18+ years of age) and excluding case reports, editorials, letters to editor, and systematic reviews. For all databases, both controlled vocabulary and text word searches were performed. At the same time, we were conducting follow-up searches on citations found in included studies.

The research strategy started with preliminary search in MEDLINE database to identify relevant keywords using MeSH terms (see Data S2 for formula). The search terms had three components and all of them were combined using operator AND:

1 cancer; cancer staging;
2 awareness; health knowledge; attitudes; understanding;
3 prognosis; diagnosis; perception.

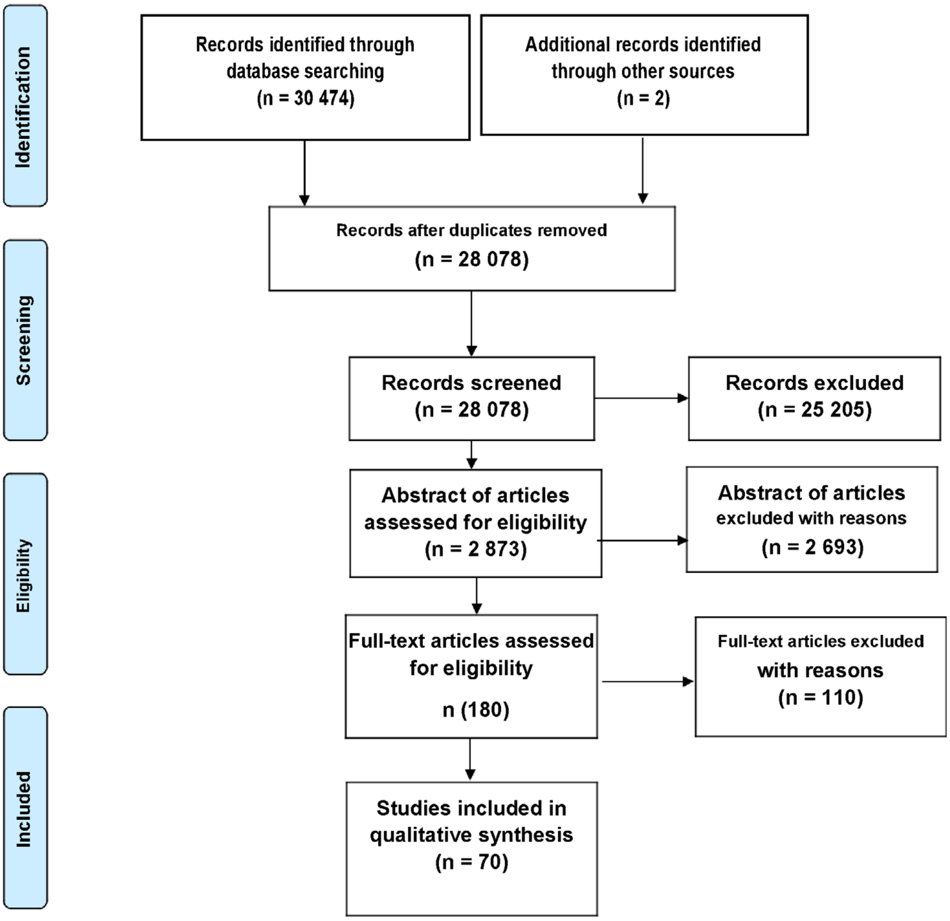

FIGURE 1 PRISMA flowchart

All search results were combined in a bibliographic management tool Mendeley and duplicates were eliminated both electronically and manually. In the first phase, we screened all articles and excluded most of them based on the title. This was followed by a second phase when two reviewers (KV, AT) independently checked abstracts and full texts of articles which were nor excluded during the first phase against inclusion criteria. Discrepancies were resolved by the two reviewers through discussion or with the assistance of third researcher. Out of 28 078 articles, 70 met the inclusion criteria (see Figure 1 for the PRISMA flowchart).

A data extraction form was created for consistent data extraction. Firstly, extracted data were divided into subgroups using theoretical thematic analysis.[10] We followed the process described by Braun and Clarke[10] using semantic coding. Themes were created by one of the author (KV) and checked again after completion of data extraction. Final defining and naming of the groups was done by two authors (KV, ML). Secondly, in every subgroup's articles were split based on their associations to accurate prognostic awareness. The association was identified to be either positive or negative (Tables 2-8 in Data S3). The positive relationship was defined as more accurate level of PA associated with statistically significantly higher incidence of those factors (eg. Positive association between PA and depression indicates that people with more accurate prognostic awareness feel more depressed than people with inadequate prognostic awareness. In contrary, negative association was associated with lover level of PA and higher prevalence of depression).

To prevent bias all included studies were assessed by two reviewers (KV, KP) for a methodological quality using critical appraisal tools developed by Joanna Brigs Institute (retrieved from: https://reviewersmanual.joannabriggs.org/). Discrepancies were solved through discussion. We used different checklists for cross-sectional studies, cohort studies, qualitative studies, and randomized-controlled trials. For every question in the appraisal tool the study could get from 0 to 2 points, two points for clear reporting, one point if it is not clearly reported, zero point if it is not stated at all. Beside the methodological quality we also assessed whether the measurement of prognostic awareness was clearly stated using 0 to 2 points assessment.

Because the maximum of points in checklists varied between the different types of studies we reported percentages instead of points.

2.1 | Statistical methods

Our review was limited by the heterogeneity of study designs to perform statistical analyses.

3 | RESULTS

Out of 28 078 articles identified by the search strategy, 70 met the inclusion criteria. Description of those studies is provided in Table 1. The majority of the studies used cross-sectional design, 13 studies used prospective cohort design, 4 had qualitative design, and one study was randomized controlled trial. The number of participants varied from eight participants to 6098, median was 231.5. Out of 70 articles 51 got 75% or more of maximum points, 19 studies had quality in range 74%-50%, only one study has less than 50% points. Detailed analysis of risk of bias is reported in Data S4. We did not exclude any study based on methodological quality. Most of the studies examined more than one factor associated with prognostic awareness.

3.1 | PA measurements

We identified several ways how PA was assessed. The most frequently used structured technique to measure prognostic awareness was Terminal Illness Acknowledgement tool.[73] This tool asks the patient following question: “How would you describe your current health status?” Patient can choose from three answers: (a) relatively healthy; (b) seriously but not terminally ill; (c) seriously and terminally ill.[26,73] The second most often used method was asking patients about the curability of their disease and offering three options to answer: (a) the disease is curable; (b) the disease might recur in the future; (c) the disease cannot be cured and they would probably die in future.[9] Cohen et al used question about the stage of the disease with five options (no evidence, early stage, middle stage, late stage, and end of cancer) and last two options were considered to be accurate.[15] In two studies, patients were asked about the stage of their disease and this information was compared to their medical records.[52] Similarly, in one study patients were asked if their cancer is stable, better, or worse and their ratings were compared with physician.[18] In two studies patients had to guess how long they might live and this estimation was retrospectively compared to their actual survival.[63] Three studies asked the patients to estimate their chance of curability by using either analogue scale, percentages, or Likert scale with options such as very likely, unlikely,[19,33,34,54] or dichotomous option yes/no.[69] In five studies participants were asked about the goal of treatment, but the options of answers differ across studies.[17,50,56,62] Three studies used questionnaires—Support Team Assessment Scale,[28] and Prognosis, Treatment Perception Scale[50] and Patients Illness Understanding Survey.[70] Most often the studies used semi-structured interview (12 studies), but the questions were not clearly stated in the published papers.[14,22,25] In eight studies the authors reported they developed their own questionnaire but the exact wording of the question on prognostic awareness was not specified in the paper.[66] Unstructured interview was used in six studies.[3,11,12,44,53,65] Two studies did not report the way of measuring PA.[35,37] Definition of accurate prognostic awareness is described for every study in Table 1.

We identified 102 factors significantly associated positively or negatively with accurate PA which we divided in seven categories: demographic factors; factors related to coping; health condition factors; psychological factors; factors associated with end-of-life care;

TABLE 1 Characteristics of included studies (N = 70)

Study	JBI appraisal (%)	Year	Study design	N	Factors positively associated with accurate PA	Factors negatively associated with accurate PA	Definition of accurate PA
Alexander et al[11]	71	1993	Cross-sectional	60	Psychiatric morbidity		Unstructured interview about nature of illness, treatment outcome
Barnett[12]	72	2006	Cross-sectional	106	High autonomy in decision-making, anxiety	Depression, anxiety	Unstructured interview about history of illness and treatment
Bracci et al[13]	72	2008	Cross-sectional	560	Being outpatient, breast cancer	Satisfaction with information about disease, metastasis	Questionnaire—how serious is your illness? + What is your chance of recovering
Centeno-Cortés, & Nunez-Olarte[14]	73	1994	Cross-sectional	97	Better communication with relatives, physicians, nurses, comprehension of given information, positive attitude toward further information, relationship with physician, trust in the care		Semi-structured interview about nature of illness
Cohen et al[15]	93	2018	Prospective cohort	209	Presence of oncologist during scan results		LSIU—stage of cancer is late or end stage
Costantini et al[16]	100	2015	Cross-sectional	262	Role limitations	Quality of life	How much is your illness curable/severe—scale 1-10
Craft et al[17]	79	2005	Prospective cohort	122	Married status, time to death	Nonmetropolitan resident, undergoing chemotherapy, being outpatient	Goal of treatment = not curative
Derry et al[18]	86	2019	Prospective cohort	94		Disease progression, anxiety	Whether their cancer is worse, stable, better, or other and concordance with physicians' rating
Duberstein et al[19]	93	2018	Cross-sectional	977	Lung cancer, white race, higher education	Self-reported fatalism	How likely do you think would cure your cancer? Not likely at all
El-Jawahri et al[8]	86	2014	Cross-sectional	50		Quality of life, social and emotional well-being, anxiety	Chance to be cured—no chance or unlikely chance + if the illness is terminal
Enzinger et al[20]	100	2015	Cross-sectional	590	Prognostic disclosure by physician		TIA
Epstein et al[21]	86	2016	cross-sectional	178	Recent discussion of prognosis with oncologist		TIA
Fan et al[22]	93	2011	Cross-sectional	182		Physical QoL, emotional QoL	Semi-structured interview—nature of disease
Fried et al[23]	86	2006	Prospective cohort	218		Time to death	If you had to guess how long do you think that you might live?—Less than 1 year
Greer et al[24]	100	2014	Prospective cohort	283	Anxiety, depresivity	Quality of life, longer survival	TIA
Gough et al[25]	75	2019	Qualitative study	24		Rarity of diagnosis, being asymptomatic	Semi-structured interview about the aim of treatment and curability

TABLE 1 (Continued)

Study	JBI appraisal (%)	Year	Study design	N	Factors positively associated with accurate PA	Factors negatively associated with accurate PA	Definition of accurate PA
Hsiu Chen et al[26]	86	2017	Prospective cohort	247		Time to death	Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; and (c) could not be cured, and they would probably die in the near future
Hughes et al[27]	95	2015	Qualitative study	8	Palliative care consultation		Semi-structured interview—nature of disease
Chan[28]	71	2011	Cross-sectional	935		Anxiety, difficulty in communication with family	STAS
Chandra et al[29]	86	1998	Cross-sectional	194	Oral cancer, relatives' awareness of the illness	Refusal for treatment for psychological problem	Semi-structured interview—nature of disease
Chen et al[30]	100	2003	Cross-sectional	234	Hospice referral/being hospice patient, preference for life quality		Perception of disease course—cure, improvement, no change, progression, death, or other
Chittem et al[31]	93	2015	Cross-sectional	329		Anxiety, depression	Unstructured interview—nature of disease
Chittem et al[32]	93	2013	Cross-sectional	329	Higher education, involved in medical decision, breast cancer, received combination of treatment, higher income, longer treatment, personal control, treatment control, understanding illness	Anxiety, depression, negative illness perception, illness identity (attribute symptom to illness)	Unstructured interview—nature of disease
Chochinov et al[5]	71	2000	Cross-sectional	200		Depression	Semi-structured interview—nature of disease
IGEO[33]	64	1999	Cross-sectional	6098	Higher education, time since diagnosis, anxiety about follow-up results, body changes due to illness, lack of optimism, economic problems, difficulties with physical work, changes in work skills	Performance status	Visual analogue scale for severity and curability
Janssens et al[34]	64	2017	Cross-sectional	106	Care preferences focused on quality of life		I can be cured/my treatment can cure me—very likely, somewhat likely, little likely, not at all
Johnston & Abraham[35]	70	2000	Qualitative	16	Short-term plans, inner peace, positive reflections of life		N/A[a]
Justo Roll et al[36]	71	2009	Cross-sectional	91		Severity of physical symptoms, anxiety, information, support (measured by POS)	Semi-structured interview—nature of disease

(Continues)

TABLE 1 (Continued)

Study	JBI appraisal (%)	Year	Study design	N	Factors positively associated with accurate PA	Factors negatively associated with accurate PA	Definition of accurate PA
Kállay et al[37]	64	2016	Cross-sectional	1214		Depression	N/A[a]
Kao et al[7]	64	2013	Cross-sectional	90	DNR consent by themselves, more time between signing DNR consent and death, signing DNR consent before referral to hospice	Anxiety, uncertainty, receiving vasopressors	Semi-structured interview—aim of treatment (not curative)
Kao et al[3]	93	2014	Cross-sectional	2020	DNR		Semi-structured interview—limited time
Kavradim et al[38]	86	2012	Cross-sectional	178	Hope		Questionnaire—stage of cancer
Kim et al[39]	93	2013	Cross-sectional	262	Higher degree of education, younger age	QoL, survival	Questionnaire—awareness of disease status
Kurita et al[40]	100	2018	Cross-sectional	300		Physical well-being, cognitive functioning	TIA
Lai et al[41]	86	2017	Cross-sectional	100		Anxiety, depression	Unstructured interview
Lee et al[42]	100	2013	Cross-sectional	100	Quality of life, decreased fatigue	Appetite loss, constipation, financial difficulties, anxiety	Do you know your disease stage? “advanced,” “locally advanced,” “early,” and “I do not know.”
Lennes et al[43]	100	2013	Cross-sectional	137	Younger age, English as mother tongue		Questionnaire—aim of treatment, prognosis
Liu et al[44]	93	2014	Prospective cohort	686	Prognosis discussion with doctor	Survival	How long you might live? Open-ended answer
Mack et al[45]	79	2015	Prospective cohort	622	Hospice referral, symptom-directed care		Is your cancer curable? Yes/no
Mercadante et al[46]	71	2017	Cross-sectional	314	Being persistent smoker		Semi-structured interview—prognosis
Miljkovic et al[2]	64	2015	Cross-sectional	93	DNR orders		Is your illness terminal? Yes/no
Mitera et al[47]	100	2012	Cross-sectional	100	Consultation with PC team		Goal of treatment—cure cancer, relieve symptoms, prolong life, do not know
Montazeri et al[48]	93	2009	Cross-sectional	142	Younger age, higher degree of education, colon cancer, fatigue, financial difficulties	Physical, social, cognitive and emotional functioning	Semi-structured interview—nature of disease
Motlagh et al[49]	79	2014	Cross-sectional	1226	Female gender, breast cancer, age		Questionnaire—about malignant nature of disease
Nipp et al[50]	100	2017	Cross-sectional	350	Depression, anxiety, positive reframing, denial coping	Quality of life	TIA + goal of treatment
Papadopulos et al[9]	79	2011	Cross-sectional	197	Female gender, younger than 65 y, higher level of education, caregiver's QoL, mental health, emotional role, social functioning, vitality, physical functioning	Gastrointestinal cancer, physical status, mental health	Unstructured interview

TABLE 1 (Continued)

Study	JBI appraisal (%)	Year	Study design	N	Factors positively associated with accurate PA	Factors negatively associated with accurate PA	Definition of accurate PA
Ray et al[51]	86	2006	Prospective cohort	338	Feel sad, nervous, worried, terrified, wish to die, DNR orders, conversation with physician, complete living will	Quality of life, physically feeling well	TIA
Santoso et al[52]	71	2006	Cross-sectional	286		Higher age, lower income, male gender	Stage of cancer compared to medical records
Sato et al[53]	60	2012	Qualitative	91	Clarification of wishes	Hope	Unstructured interview
Shin et al[54]	71	2018	Cross-sectional	134	Young age, female gender, surgical oncologist	Depresivity	Treatment goal (cure, life-prolonging, and symptom relief), and chance of cure (0%-25%, 26%-50%, 51%-75%,75%-99%, and unsure)
Sivendran et al[55]	93	2017	Cross-sectional	208	Female gender, younger than 65 years, higher level of education		What is stage of your cancer? Stage 0–4
Soylu et al[56]	79	2016	Cross-sectional	55	High degree of education	Hope, optimism	What is the purpose of your treatment? Open-ended (accurate = reduce symptom or extend lifetime)
Tang et al[6]	86	2008	Cross-sectional	1108	Quality of life		Semi-structured interview—about curability, information from physician
Tang et al[4]	93	2014	Cross-sectional	2467	EoL care, discussion with physician		Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; or (c) could not be cured, and they would probably die soon
Tang et al[57]	86	2014	Cross-sectional	2467	EoL care, preferences (comfort-oriented care, preferences for hospice care), high school education, lung cancer diagnosis	Life-sustaining treatment, higher age, female gender	Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; or (c) could not be cured, and they would probably die soon
Tang et al[58]	86	2015	Prospective cohort	380	Post-traumatic growth		Knowing about prognosis—yes/no
Tang et al[59]	100	2016	Prospective cohort	380	Comfort-oriented care	ICU care, intubation, mechanical ventilation	Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; or (c) could not be cured, and they would probably die soon.
Tang et al[60]	100	2016	Prospective cohort	325	Self-perceived burden to others	Quality of life	Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; or (c) could not be cured, and they would probably die soon

(Continues)

TABLE 1 (Continued)

Study	JBI appraisal (%)	Year	Study design	N	Factors positively associated with accurate PA	Factors negatively associated with accurate PA	Definition of accurate PA
Tang et al[61]	100	2018	prospective Cohort	330	Subsequent EoL care discussion		Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; or (c) could not be cured, and they would probably die soon
Temel et al[62]	81	2011	Randomized controlled trial	151	Early palliative care (vs standard care)	Intravenous chemotherapy (only in group receiving EPC)	Curability—yes/no
Trevino et al[63]	100	2016	Cross-sectional	229		Personal belief-source of information about prognosis, black race, type of hospital	Life expectancy estimates compare to real survival time
Wagner et al[64]	71	2010	Cross-sectional	559	Communication about nature of illness, discussion of preferences with family		Can the illness shorten your life? Yes/no
Walden-Galuzsko[65]	43	1996	Cross-sectional	410	Adjustment disorder		Semi-structured interview—the nature of disease
Weeks et al[66]	93	2012	Cross-sectional	1193	Lung cancer, white race	Colorectal cancer, lower score of physician communication	Purpose of treatment: "Help you live longer, cure your cancer, or help you with problems you were having because of your cancer?"
Wen et al.[67]	100	2019	Prospective cohort	218	Having preferred received life-sustaining-treatment		Curability: (a) was curable; (b) might recur in the future, but their life was not currently in danger; or (c) could not be cured, and they would probably die soon
Yanwei et al[68]	79	2017	Cross-sectional	178	Quality of life, depression, anxiety		Curability—yes/no
Yennurajalingam et al[69]	100	2018	Cross-sectional	121	Passive decision control preference, longer time from diagnosis to referral to PC	ICU admission in last month of life	Curability—yes/no
Yennurajalingam et al[70]	93	2018	Cross-sectional	1390	Female gender, higher education, unemployment status, living in France or South Africa	Better performance status, living in Brazil, Jordan, Philippines or India	Patients illness understanding survey
Yun et al[71]	93	2010	Cross-sectional	474	Positive attitude toward disclosure of diagnosis		Disease stage—early/advanced/terminal/other
Yun et al[72]	86	2011	Cross-sectional	480	Use of palliative care	Use of ICU	Awareness of terminal status—yes/no

Note: Extraction of the results.

Abbreviations: DNR, do-not-resuscitate; EOL, end-of-life care; EPC, early palliative care; ICU, intensive care unit; JBI, Joanna Brigs Institute; LSIU, late-stage illness understanding; PA, prognostic awareness; PC, palliative care; POS, palliative outcome scale; QoL, quality of life; STAS, support team assessment; TIA, terminal illness acknowledgment.

[a] Not available.

factors associated with communication; and factors related to relatives.

3.2 | Demographic factors

Studies in which demographic factors were significantly associated with PA are presented in Table 2 (Data S3). Results indicate that black race is factor which is associated with inaccurate prognostic awareness,[19,63,66] therefore higher education is associated with accurate prognostic awareness.[9,19,32,33,39,48,55-57,70] Most of these studies used education as categorical variable with three[9,19,32,33,48,55-57] or two categories.[39] Being women was also found to be associated with accurate prognostic awareness.[9,49,52,54,55,70] With increasing age the level of PA is getting worse.[9,39,43,48,49,52,54,55,57] Age was used as continuous variable[9,39,43,48,52,54] or categorical variable.[49,55,57] Lower income and economic problems are also associated with inaccurate level of PA.[32,42,52] However, two studies found that patients with accurate prognostic awareness more often reported having economic problems[33,48] or being unemployed.[70] We also identified one study in which the authors found positive association between being persistent smoker and more accurate PA.[46]

3.3 | Factors related to coping

In Table 3 (Data S3), we present factors which were found to be significantly associated with coping with life-limiting illness. It was found that some coping strategies such as positive reframing or denial coping can be connected to more accurate PA.[50] Patients with accurate PA have more positive attitude toward diagnosis disclosure and getting information and also have more trust in their health care providers.[14,71] Accurate PA is associated with positive feelings like inner peace, positive reflections of life[35] and less uncertainty.[7] However, two studies found that accurate PA is associated with lack of optimism.[33,56] For the level of hope we also found mixed results,[38,53,56] showing both positive and negative associations with PA. Inaccurate prognostic awareness was found to be associated with self-reported fatalism.[19] On the other hand, accurate PA was found to have associations with passive decision control preference.[69]

3.4 | Health condition

Third group is consisted of factors related to specific health conditions of patients with cancer (Table 4, Data S3). Several studies examined whether type of cancer is associated with accurate PA and found that breast cancer, oral and lung cancer were related to accurate PA.[13,19,29,32,49,66] In one study, gastrointestinal cancer was found to be related to less accurate PA than other types of cancer.[29] For colon cancer we found mixed results.[48,66] Rare type of cancer was found to be associated with inaccurate PA.[25] IGEO (1999) found that difficulties with performing physical work and adjusting to body changes were associated with more accurate level of prognostic awareness of cancer.[33] This is consistent with inaccurate prognostic awareness in patients who are asymptomatic.[25] On the other hand, some symptoms such as appetite loss or constipation was more prevalent or more severe with inaccurate PA.[36,42] We found mixed results about physical functioning, vitality or fatigue[9,42,48,51] and for cognitive functioning,[40,48] therefore, it is not clear whether accurate PA is associated with better functioning or not.

3.5 | Psychological factors

Psychological factors significantly associated with prognostic awareness are presented in Table 5 (Data S3) and it is the most often studied factors. For the three-key psychological factors (quality of life, depression, and anxiety) which are studied a lot, there are several studies with mixed results (see Table 5, Data S3). Our findings indicate that these psychological factors might be associated with both accurate PA or inaccurate PA. Patients who were aware of their prognosis more often reported that they feel to be a burden to their relatives,[60] they have the lack of emotional support[36] and worse overall well-being.[8,40,48] In one study, participants more frequently stated they feel sad and they wish to die.[51] Accurate PA was also found to be associated with more acceptance of psychological support.[29]

3.6 | Factors associated with end-of-life care

Factors associated with end-of-life care identified through this review are presented in Table 6 (Data S3). Patients with accurate PA were more likely to complete do-not-resuscitate orders (DNR),[2,3,7,51] use palliative care,[27,47,72] prefer treatment focused on comfort and quality of life,[30,34,45,57,59] and to use hospice care.[30,45,57] Patients with more accurate PA did not want to continue in life-sustaining treatment[57] and they were not likely to be hospitalized in intensive care unit in the last year of their life[59,72] or in the last month.[69] Accurate PA was also associated with less utilization of intravenous chemotherapy,[17,62] intubation, and mechanical ventilation.[59] Patients with accurate prognostic awareness received often preferred type of care.[67] On the other hand, patients with accurate PA tend to have shorter survival than patients with inaccurate PA.[17, 23, 24, 26, 39, 44] One study found that patients with accurate prognostic awareness waited longer from diagnosis for referral to palliative care.[69]

3.7 | Factors related to communication

In Table 7 (Data S3), we present factors which are related to communication. The results showed that patient-physician discussions about prognosis can lead to better PA.[20,21,44,51,64] This is consistent with findings that inaccurate PA was found in patients whose main source of information about their prognosis were more often their personal beliefs than their oncologist, other clinic staff or palliative care physician.[63] The evidence also showed that accurate PA was associated with frequent communication with family regarding patients' concerns about the illness[14,64] and with better clarification of their wishes and sharing those wishes with patients' relatives.[53,64] Prospective study also showed that accurate prognostic awareness was associated with subsequent EoL care discussion.[61] Surprisingly, in two studies inaccurate PA was associated with higher satisfaction with the amount of received information about disease.[13,36]

3.8 | Factors related to relatives

Last group of factors in Table 8 (Data S3) consists of factors which are related to relatives of patients. We identified two studies which examined associations between PA and relatives' prognostic awareness and their quality of life.[9,29] The association between relatives' awareness and patients PA was positive[29] and also the relatives' quality of life was better with more accurate PA.[73]

4 | DISCUSSION

The goal of this study was to identify factors which are significantly associated with accurate prognostic awareness in patients with cancer. Based on an extensive literature review, the results present a list of 102 factors, associated positively or negatively with prognostic awareness, divided into seven thematic groups. The high number of identified factors highlights the complexity of the studied phenomenon, which has several important implications for clinical practice. Firstly, when cultivating prognostic awareness with their patients, clinicians must take into account a large number of potentially intervening factors, which might influence the resulting level of prognostic understanding. As our results showed, although communication about prognosis and end of life care can be associated accurate prognostic awareness,[21,44] other factors that are not always known to clinicians, such as personal beliefs[63] or economic situation[32,52] might work against clinicians' efforts. The results of this review support advanced multidisciplinary assessment of patient's situation prior the actual prognosis disclosure, which might help clinicians to adequately tailor the conversation. Also, protocols for goals of care discussions, which use open-ended questions to cover the values and preferences of the patients, can be very useful in addressing individual mechanisms which patients use while work with their prognostication needs. Serious Illness Care Program (SICP), created by Bernacki et al[74] can be a good example of this approach.

The second striking outcome of this review is the high number of mixed results for several factors, especially for quality of life, depression and anxiety.[5,12,36,50,54,68] This inconsistency touches upon the crucial question—should doctors actually talk about the prognosis with patients or not? Our results indicate that from psychological point of view the answer to this question is not straightforward as some studies bring the evidence that patients with better prognostic awareness had lower quality of life and were more depressed and anxious.[24,50] On the other hand, these studies used cross-sectional design and only one used longitudinal measurement of these factors and prognostic awareness.[60] In this study, Tang et al found that association of anxiety and depression and prognostic awareness is not statistically significant if we added proximity to death as a confounder[60] which highlights the importance of prospective cohort studies. Accurate prognostic awareness was also found to be associated with negative feelings such as sadness, a wish to die or lack of hope.[33,51,53] Therefore, clinicians might be afraid of the consequences of prognosis disclosure, such as loss of hope, disruption of patient-physician relationship or fragile emotional state of patients.[75] Similarly, all six studies which assessed the association between survival and PA found negative relationship—patients with less accurate PA lived longer. This might be explained by the fact that patients who were sicker and closer to death became more aware about their poor prognosis just by their worsened health, or that clinicians used different communication strategies with patients in more advanced stages. However, there was limited information available in the studies to answer these hypotheses. The risk of negative impact of prognostic disclosure can be minimalized by specific interventions,[74,76,77] which was found to reduce anxiety and depression in patients after goals of care conversations.[74] On the other hand, this review also found associations of accurate PA with positive aspects such as better communication with family and health care providers,[14] feeling of having control[32] and inner peace.[35] Recent longitudinal studies showed that prognostic discussion can help in building therapeutic alliance[78] and patients with accurate prognostic awareness are more likely get the treatment which they prefer.[67] One potential solution for this dilemma of potential negative aspects of prognostic disclosure might be in tailoring communication about prognosis according to patients' preferences rather than focus on achieving accurate prognostic awareness itself while hoping that this will ease patients' suffering. Some of the studies included in this review showed that regardless their level of quality of life or depression, patients with better prognostic awareness more often make choices which can alleviate their suffering such as preferring comfort-oriented care,[30,59] choosing hospice care,[30,45,57] and completing DNR orders.[2,3,7,51]

Based on the result of this systematic review, for some groups of patients (less educated, male, or older persons) might be more difficult to accept and understand the prognosis correctly than for others. Recent study by Schoenborn et al[79] showed that older persons might even struggle with the idea of being offered the discussion about their prognosis. This might explain our results that younger age is associated with more accurate PA.[9,39,48,49,55,57] At the same time, a study analysing records from clinicians-family conferences showed that the conversations about goals of care and prognosis often lack communication about patients' values and preferences[80] which may explained the attitude of some older adults toward prognosis discussion in Schoenborn's study (2018). This once again highlights the need for effective, evidence-based guidelines on prognostic conversations.

5 | CONCLUSION AND FUTURE DIRECTIONS

A large body of literature showed that prognostic awareness is a very complex phenomenon associated with various positive and negative associations for patients and their relatives. Prognostic awareness might differ according to age, personality, type of cancer, disease stage, or being outpatient. The findings of this review suggest that patients with accurate prognostic awareness use ICU less often, are more likely to have DNR orders and prefer hospice care and comfort-oriented care. It is not clear if the prognostic disclosure can worsen or improve patients' quality of life and overall psychological well-being. The consequences of prognostic disclosure might be affected by the personality of the patient, type of cancer, severity of the disease.

To explore the causality and effects of prognosis disclosure on patients with cancer more research using longitudinal and randomized controlled trial design is necessary. Prospective studies which would include assessment of the actual prognostic disclosure and the level of PA would be helpful to understand better how important the communication is and what strategies are most effective in terms of improving patients' PA. Discussion about values could be led by nurses as suggested by 123 program[76] or by other members of the multidisciplinary team which would be feasible in busy oncology clinics and positively accepted by patients.[77] Future research might also benefit from more theoretical background from personality psychology, for example by considering the role of personality traits. Multidimensional analysis, evaluating more complex interactions between more factors would be also valuable contribution to further understanding of prognostic awareness.

5.1 | Study limitations

This study has several limitations. Despite using systematic literature search method, we might have missed some studies, especially unpublished ones. We included studies with different type of PA measurement which made the comparison difficult and from this reason we did not conduct meta-analytic assessment. Meta-analysis would be valuable approach especially for analyses of factors which have a good number of publications with mixed results, such as quality of life, depression and anxiety. Moreover, we only examined significant associations, therefore we cannot say anything about causality between identified factors and also did not analyse the nonsignificant associations.

In some of the included articles, information about the way of measuring PA was not mentioned or it was incomplete which makes our understanding of PA and related factors limited. Additionally, we included studies with cancer patient regardless the type of the cancer or the stage of the disease. Included studies were conducted in different countries but comprehensive evaluation of cultural differences was outside of the scope of this systematic review. Finally, the results may have been biased by the fact that we excluded studies published in different languages than English, Czech, or French.

5.2 | Clinical implications

This review shows that prognostic awareness is a very complex phenomenon which is difficult for interpretation. There is a strong view among clinicians that accurate prognosis should be at least partial aim of goals of care conversations, however, it might not be as straightforward as expected. Talking about prognosis is associated with some negative aspects for some patients such as anxiety, sadness, or lack of hope which might make doctors unsure about the benefits of prognostic disclosure. On the other hand, patients with accurate prognostic awareness often choose care which alleviates their suffering such as comfort-oriented care, DNR orders or they report having better communication with their family members. Therefore, it seems that there are many intervening factors which influence prognostic understanding as well as psychological well-being of patients. Negative consequences of prognostic disclosure might be reduced by using standardized protocols for goals of care discussion (such as SICP), asking about values and preferences of each patient and by individually tailoring communication about prognosis and advanced care planning. Clinicians should always focus on specific situation of their patients and should know their values and preferences before starting prognostic disclosure.

ACKNOWLEDGEMENTS

This work was supported by Czech Science Foundation (Grant No. 17-26722Y).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

PROSPERO REGISTRATION NUMBER

This systematic review was not registered at PROSPERO but protocol for the review is available from the corresponding author on request.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Vlckova K, Tuckova A, Polakova K, Loucka M. Factors associated with prognostic awareness in patients with cancer: A systematic review. *Psycho-Oncology*. 2020;1–14. https://doi.org/10.1002/pon.5385

Vlckova *et al. BMC Palliative Care* (2020) 19:39
https://doi.org/10.1186/s12904-020-00552-x

BMC Palliative Care

RESEARCH ARTICLE **Open Access**

Psychometric properties of the Czech Integrated Palliative Outcome Scale: reliability and content validity analysis

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Abstract

Background: Outcome measurement is an essential part of the evaluation of palliative care and the measurements need to be reliable, valid and adapted to the culture in which they are used. The Integrated Palliative Outcome Scale (IPOS) is a widely used tool for assessing personal-level outcomes in palliative care. The aim of this study was to provide Czech version of IPOS and assess its psychometric properties.

Methods: Patients receiving palliative care in hospice or hospitals completed the IPOS. The reliability of Czech IPOS was tested with Cronbach alpha (for internal consistency), the intraclass correlation coefficient for total IPOS score and weighted Kappa (for test-retest reliability of individual items). Factor analysis was used for elucidating the construct (Exploratory Factor Analysis). Convergent validity was tested with correlation analysis (Spearman correlation) in a part of the sample, who completed also the Edmonton Symptom Assessment System (ESAS) and the Palliative Performance Scale (PPS).

Results: The sample consisted of 140 patients (mean age 72; 90 women; 81% oncological disease). The Cronbach alpha was 0.789; intraclass correlation was 0.88. The correlations of IPOS with ESAS was $R = 0.4$ and PPS $R = -0.2$. Exploratory factor analysis revealed a 2-factor solution on our data. The first factor covers emotional and information needs and the second factor covers physical symptoms.

Conclusion: Czech IPOS has very good reliability regarding both internal consistency and test-retest reliability. Together with an item analysis results, we can conclude that the Czech adaptation of the tool was successful. The convergent validity needs to be assessed on the larger sample and the proposed 2-factor internal structure of the questionnaire has to be confirmed by using CFA.

Keywords: IPOS, Outcome measurement, Validity, Reliability, Patient-reported outcome measure, Palliative care, Symptom assessment, Psychometrics

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Background

The main goal of palliative care is to improve the quality of life of patients suffering from life-threatening illnesses and their families. Therefore, quality-of-life measurements are important for the evaluation of palliative care interventions and the needs of patients or quantifying the change in health status [1]. A wide variety of measurements currently exists and they differ in the number of measured domains, number of items, mode of administration (questionnaire/interview, patient/proxy) and also in the level of validity and reliability [2]. The Palliative Outcome Scale (POS) is one of the tools for comprehensive measurement of the patients´ main symptoms and concerns [3]. POS is widely used in clinical care, audit, research, and training and it was validated in several languages [4, 5]. The POS measures have been used in different patients populations such as patients with cancer, respiratory, heart, renal or liver failure, and neurological diseases [6–10]. POS-S was developed as an addition to POS to be used as a brief tool specifically focused on physical symptoms [11]. There are also specific variations of POS for dementia or renal failure patients, (POS S-Renal, POS S-Multiple Sclerosis, POS S-Parkinson Disease) [5]. IPOS is the youngest instrument from the POS family which merges questions from POS and POS-S as it was requested from clinicians [11]. IPOS consists of 10 questions which cover main symptoms, patient and family distress, well-being, sharing feelings with family, practical concerns and information needs [11].

IPOS was found to have excellent reliability [12–16] and face and content validity was also confirmed in several studies using cognitive interviews [11, 17, 18] Convergent validity has been confirmed for the original and German IPOS [13], Japanese version of IPOS [14] and French IPOS [16]. In many other countries the process of validation is ongoing and all language version which are currently available, such as Portuguese, Polish, Greek etc., can be found online (www.pos-pal.org).This study aims to provide a valid version of IPOS in Czech and to report the psychometric properties of IPOS from this first pilot Czech study. During the standardization, we followed the manual created by authors of POS [19].

Methods

This was a mixed-method multicenter study conducted in 6 organizations in the Czech Republic (1 home hospice care, 2 hospices facilities and 3 hospitals). Data were obtained by trained clinical staff - nurses or social workers during the inpatient admission or home visit. The inclusion criteria were: being patient of hospice or home hospice care or palliative care team/unit in the hospital and able to give consent to participate. We excluded patients who had cognitive impairment (judged by the clinical team) and who did not understand the Czech language. Patients completed IPOS and a demographic questionnaire on their own or with help from the staff member. When appropriate, patients were asked to complete IPOS twice for testing of reliability. The second measurement was done when it was possible and feasible from the clinical point of view, predominantly during the next appointment. The instructions were to do it after minimum of 3 days.

IPOS consists of 10 questions with 17 items. Question 1 is about the main concerns and has open-ended options. Q2 addresses specific symptoms and there is also a place for adding any additional symptoms (Q2a-c). Q3-Q6 ask about psychological, spiritual, communication and practical concerns but Q6–8 address positive aspects and the direction of possible answers is opposite. Q10 is not scored and asks patients whether they filled IPOS with any help or by themselves. All questions except Q1 have a numerical scale from 0 to 4 and only one response is allowed for each question. The sum score can range from 0 to 68 and is computed from all items except Q1 and Q2a-c.

The Czech version was created clarifying conceptual definition equivalents in Czech followed by forward and backward translation which was done by independent translators as required by the Manual for the cross-cultural adaptation of the POS [19]. The initial Czech version of IPOS was piloted through cognitive interviews with 5 patients and 5 health care providers from hospice and the face validity of the Czech IPOS was confirmed. The final Czech version of IPOS can be found in Additional file 1.

Part of the sample completed the Edmonton Symptom Assessment System or the Palliative Performance Scale for testing the construct validity of IPOS. Only those data collection sites which use ESAS and PPS as part of routine care were asked to provide both data. The Edmonton Symptom Assessment System (ESAS) is another questionnaire assessing the key patients´ symptoms and concerns and is commonly used in Czech hospices. ESAS consists of 10 items measuring physical symptoms and well-being and patients are asked to rate the symptoms severity from 0 to 10 on a numerical scale [20].

Palliative Performance Scale (PPS) is a tool for measuring performance status of patients in palliative care and it is usually recorded by nurses or by physicians with good inter-rater agreement [21]. It was developed from the Karnofsky Performance Scale [22]. It is oriented on physical functions and activities and can be used for prognostication and planning care [23]. Patients' performance is scored by percentage in 11 categories from fully ambulatory and healthy (100%) to death (0%). The ratings are based on observation of 5 categories: ambulation, level of activity and evidence of disease, ability to self-care, food/fluid intake and state of consciousness [22].

The Ethical Committee of the General University Hospital in Prague approved the study (Protocol Number 51/18 S-IV) and all participants gave written informed consent.

Statistical analysis

Internal consistency of the IPOS total score was investigated by using Cronbach 's alfa. Item difficulty was calculated using item mean and converted to interval < 0;1 > using formula mean-scale min/(scale max-scale min). Part of the sample (13%) completed the IPOS in two different times for confirmation of temporal stability (T1 and T2) with an average range of 15.6 days between the measures (SD = 9.0). Test-retest reliability of the IPOS total score was evaluated for the part of the sample ($N = 14$, see Table 1) using the intraclass correlation coefficient (ICC). An ICC range of 0.4–0.7 was considered moderate and > 0.75 was considered to represent high test-retest reliability [24]. For each of 17 IPOS items, we also computed four metrics of test-retest reliability: level of agreement, level of agreement within one score, quadratic weighted kappa and Spearman correlation. A range of kappa from 0.41 to 0.60 was considered as moderate, 0.61–0.80 as substantial, and 0.81–1 as almost perfect [25, 26].

To test the influence of gender, place of care and age, we used parametric methods (t-test and Pearson correlation coefficient respectively) based on a sufficiently large sample and normal distribution of overall IPOS score.

Moreover, we used factor analysis to explore the possible dimensions of the Czech IPOS questionnaire and to elucidate the constructs. We applied Exploratory factor analysis (EFA) using principal axis factoring as the extraction method and Varimax rotations. The number of factors to be extracted derived from the combination of Kaiser's criterion and Cattell's scree plot method.

The Spearman correlations between the IPOS score and two other measures commonly used in palliative

Table 1 Characteristics of the final sample

	Number of patients (%)	Number of patients who completed IPOS twice (%)	Number of patients who completed IPOS and PPS (%)	Number of patients who completed IPOS and ESAS (%)
Age				
Range	27–95 years	55–88 years	49–92 years	49–89 years
Mean (SD)	72.1 (12.98)	70.0 (10.54)	71.4 (11.01)	70.4 (13.03)
18–55	14 (10)	1 (7.1)	5 (12.5)	2 (14.3)
56–65	23 (16.4)	3 (21.4)	7 (17.5)	4 (28.6)
66–75	44 (31.4)	7 (50)	14 (35)	3 (21.4)
76–85	36 (25.7)	2 (14.3)	9 (22.5)	2 (14.3)
> 85	23 (16.4)	1 (7.1)	5 (12.5)	3 (21.4)
Sex				
Men	50 (35.7)	4 (28.6)	12 (30)	1 (7.1)
Women	90 (64.3)	10 (71.4)	28 (70)	13 (92.9)
Marital status				
Single	16 (11.4)	2 (14.3)	2 (5)	1 (7.1)
Married	52 (37.1)	6 (42.9)	18 (45)	4 (28.6)
Divorced	17 (12.1)	2 (14.3)	5 (12.5)	1 (7.1)
Widowed	54 (38.6)	4 (28.6)	15 (37.5)	8 (57.1)
Registered (homosexual marriage)	1 (.7)	0	0	0
Diagnosis				
Cancer	113 (80.7)	13 (92,9)	39 (97.5)	14 (100)
Other	26 (18.6)	1 (7.1)	1 (2.5)	0
Not available	1 (.7)	0	0	0
Place of care				
Hospice	57 (40.7)	6 (42.9)	20 (50)	14 (100)
Home hospice care	23 (16.4)	5 (35.7)	20 (50)	0
Hospital	60 (42.9)	3 (21.4)	0	0
Total	**140**	**14**	**40**	**14**

care (ESAS and PPS) were assessed to report preliminary results of convergent validity. We expected mid-range correlation between total IPOS score and ESAS total score and PPS (0.5–0.7) because these methods do not cover spiritual, practical and family issues similarly like Murtagh and her colleagues [13]. The non-parametric method was chosen due to quite small sample sizes.

All missing values were excluded from the analysis. A significant *p*-value was set at 0.05. All analyses were conducted within SPSS v. 25.0 (IBM Corp., Armonk, NY, USA).

Results

Sample

From November 2017 until August 2018, we collected IPOS data from 144 patients. However, 4 patients had to be excluded from the final sample because they did not complete full IPOS. Most of them were inpatients, only in 16% of patients the place of care was at home provided by the home hospice. The number of patients from the hospital and hospice were similar (43% vs 57%). In the sample, there were few more women (64%) and most of the patients suffered from oncological disease (81%). The detailed description of the sample is in Table 1. Most of the patients (88.6%) needed help in the completion of IPOS.

Table 2 presents descriptive statistics of all 17 IPOS items for the whole sample. We used the short names in the description of items, similarly as Sakurai et al. [14] and Sandham et al. [15] [14, 15]. As a part of the item analysis, we evaluated each item's difficulty and correlation with the total IPOS score (item-total correlation). The minimum item difficulty was 0.13 (Vomiting), the maximum was 0.6 (Poor mobility). All item-total correlations were higher than 0.3, the highest predictor of the total score was item measuring Weakness with item-total correlation 0.66.

Influence of gender, age and place of care

The total IPOS score did not differ for men and women ($t = -1.537$, $p = 0.127$) nor did it correlate with the age of patients ($r = 0.141$, $p = 0.096$). However, we found a significant difference in the total IPOS score when comparing patients from hospices and patients from hospitals ($t = -3.613$, $p < 0.001$). More specifically, the average total IPOS score of patients from hospices was lower (38.75, $SD = 9.11$) than the average score of patients from hospitals (44.28, $SD = 8.77$).

Reliability

Cronbach's alpha for 17 IPOS items (which are used for calculation of the overall score) was 0.789. Temporal stability was evaluated for all items separately as well as for the overall score. A one-way intra-class correlation coefficient of IPOS total score indicated a high level of temporal stability (*ICC* = 0.88, *95% CI:* 0.56–0.94). Sufficient test-retest reliability was also supported by significant Spearman correlation between two total IPOS scores in

Table 2 Description of IPOS items

Item	% response for each value score					M	SD	Mo	Item Difficulty	Item-total correlation
	0	1	2	3	4					
Pain	22.1	25.7	28.6	20	3.6	1.6	1.1	2	0.39	0.48
Shortness of Breath	51.4	19.3	10.7	14.3	4.3	1.0	1.3	0	0.25	0.32
Weakness	10	12.9	32.1	38.6	6.4	2.2	1.1	3	0.55	0.66
Nausea	53.6	22.9	12.1	9.3	2.1	0.8	1.1	0	0.21	0.46
Vomiting	74.3	9.3	9.3	6.4	0.7	0.5	1.0	0	0.13	0.37
Poor Appetite	28.6	17.1	24.3	26.4	3.6	1.6	1.3	0	0.40	0.58
Constipation	46.4	17.9	13.6	20.7	1.4	1.1	1.2	0	0.28	0.44
Sore Mouth	26.4	23.6	21.4	26.4	2.1	1.5	1.2	0	0.39	0.33
Drowsiness	18.6	17.1	37.1	25	2.1	1.8	1.1	2	0.44	0.48
Poor Mobility	10.7	9.3	22.9	43.6	13.6	2.4	1.2	3	0.60	0.49
Anxiety	32.1	14.3	32.1	15.7	5.7	1.5	1.2	0	0.37	0.58
Family Anxiety	10.7	10	30.7	32.1	16.4	2.3	1.2	3	0.58	0.50
Depression	40.7	16.4	31.4	9.3	2.1	1.2	1.1	0	0.29	0.50
Feeling at Peace	15	36.4	28.6	15	5	1.6	1.1	1	0.40	0.59
Share Feelings	30.7	29.3	16.4	17.9	5.7	1.4	1.3	0	0.35	0.44
Information	51.4	28.6	12.1	5.7	2.1	0.8	1.0	0	0.20	0.48
Practical Problems	52.9	20	17.1	7.1	2.9	0.9	1.1	0	0.22	0.45

M mean, *SD* standard deviation, *Mo* modus.

T1 and T2 ($r = 0.88$, $p < 0.05$). For most of the items significant Spearman correlations were found as well as fair to good levels of weighted kappa, however, several items showed rather low temporal stability, mainly items called Family anxiety, Practical problems, Drowsiness or Anxiety. For more detailed results, please see Table 3.

Exploratory factor analysis

Both Kaiser-Meyer-Olkin Measure of Sampling Adequacy (0.696) and Bartlett's test of sphericity ($p < 0.001$) indicated that a factor analysis might be useful with our data. Based on the combination of Kaiser's criterion and Cattell's scree plot method, we decided to present the two-factor model (Table 4) as an output of EFA which explains 29.1% of the variance (*Factor 1:* 15.9%, *Factor 2*: 13.3%) and the factors showed a correlation of 0.316.

Convergent validity

Spearman's correlation of the sum score of IPOS and PPS was found to be weaker than was expected by our hypotheses and non-significant ($Rs(40) = -0.249$; $p = 0.121$), correlation with ESAS showed to be on a moderate level ($Rs(14) = 0.414$; $p = 0.141$), however, not significant due to a very small research sample. Data from PPS and ESAS were not available from many patients so these results have to be considered preliminary only.

Discussion

This study aimed to provide a valid version of the Czech IPOS and to report the psychometric properties of IPOS. Item analysis results showed that the Czech adaptation of the tool was successful. This study showed also that the Czech IPOS has very good reliability regarding internal consistency and we preliminary assessed the validity of the Czech IPOS and temporal stability.

Items analysis showed that all of the items in IPOS meet the requirements for item difficulty and item-total correlation. The lowest discriminant ability was found in item Vomiting because 75% of patients did not report this symptom. This is not consistent with previous results [15]. However, in Sandham et al. study only hospice patients were assessed which might have caused the difference [15]. Another study with patients from hospitals and home-based palliative services found similar results when Vomiting, Practical matters and Having enough information did not have full range of responses [13].

Regarding influence of place, age or gender, in our sample, we found significant differences in the total IPOS score according to the place of care which was also confirmed in other countries for POS [27, 28]. This might be explained by the fact that patients in hospices are usually in the terminal stage of disease with well-

Table 3 Temporal stability

	T1	T2	Agreement			
	Mean (SD)	Mean (SD)	Agreement (%)	Agreement within one score (%)	Weighted kappa (95% CI)	Spearman correlation
Pain	1.6 (1.3)	1.4 (1.0)	35.7	92.9	0.66 (0.40–0.92)	0.69[b]
Shortness of Breath	1.0 (1.2)	1.4 (1.5)	57.1	78.6	0.60 (0.21–0.99)	0.62[a]
Weakness	1.5 (1.0)	1.9 (1.2)	50.0	78.6	0.54 (0.18–0.91)	0.54[a]
Nausea	0.9 (1.1)	0.6 (0.9)	35.7	92.9	0.59 (0.41–0.77)	0.49
Vomiting	0.7 (1.1)	0.4 (0.8)	64.3	85.7	0.58 (0.29–0.86)	0.77[b]
Poor Appetite	1.1 (1.3)	1.6 (1.3)	42.9	92.9	0.65 (0.31–0.99)	0.67[b]
Constipation	0.9 (1.2)	0.9 (1.2)	71.4	71.4	0.46 (−0.02–0.93)	0.51
Sore Mouth	1.6 (1.3)	1.5 (1.0)	57.1	92.9	0.60 (0.15–1.05)	0.63[a]
Drowsiness	1.1 (1.1)	1.9 (0.9)	7.1	71.4	0.33 (0.06–0.60)	0.43
Poor Mobility	2.1 (1.2)	2.4 (0.9)	42.9	85.7	0.41 (0.03–0.79)	0.53
Anxiety	1.0 (1.3)	1.2 (1.1)	28.6	71.4	0.31 (−0.11–0.72)	0.35
Family Anxiety	2.1 (1.1)	2.6 (0.8)	42.9	71.4	0.02 (−0.33–0.37)	0.53
Depression	0.7 (1.1)	0.5 (0.9)	71.4	92.9	0.74 (0.48–1.01)	0.83[b]
Feeling at Peace	1.1 (0.9)	1.2 (1.1)	57.1	85.7	0.54 (0.12–0.96)	0.50
Share Feelings	1.1 (1.4)	1.2 (1.1)	50.0	92.9	0.77 (0.56–0.98)	0.80[b]
Information	0.2 (0.6)	0.2 (0.4)	71.4	100.0	0.40 (−0.08–0.89)	0.32
Practical Problems	0.1 (0.4)	0.4 (0.7)	71.4	92.9	0.27 (−0.23–0.77)	0.32
IPOS	18.9 (9.8)	21.1 (7.2)	–	–	0.83[c] (0.56–0.94)	0.88[b]

[a]. Correlation is significant at the 0.05 level (2-tailed)

[b]. Correlation is significant at the 0.01 level (2-tailed)

[c]. One-way Intraclass Correlation Coefficient (ICC)

Table 4 Factor loadings

	Factor 1	Factor 2
Anxiety	0.711	0.085
Feeling at peace	0.694	0.128
Depression	0.667	0.019
Information	0.531	0.066
Practical Problems	0.515	0.051
Share Feelings	0.431	0.109
Family Anxiety	0.374	0.258
Shortness of Breath	0.156	0.147
Nausea	0.017	0.607
Vomiting	−0.074	0.588
Poor Appetite	0.204	0.584
Weakness	0.403	0.513
Sore Mouth	−0.084	0.462
Drowsiness	0.173	0.429
Poor Mobility	0.220	0.381
Constipation	0.124	0.376
Pain	0.247	0.344

controlled symptoms as the median of the length of stay in Czech home hospices is around 10 days [29]. IPOS total score did not differ according to age or gender which is consistent with other studies [15].

The reliability of IPOS was measured in two ways with Cronbach alpha and test-rest reliability. The Cronbach alpha showed a high internal consistency of the Czech version of IPOS which is consistent with other studies [12, 13, 15]. IPOS was completed twice by 14 patients and test-retest reliability was confirmed by a sufficient intraclass-correlation coefficient. Some items showed low temporal stability, mainly items called Family anxiety, Practical problems, Drowsiness or Anxiety (0.02–0.33) which is not consistent with Japanese validation where items with the lowest temporal stability (0.522–0.622) were Share Feelings, Information and Practical Problems, for others items ICC was higher than 0.7 [14]. This study is missing independent global change rating which would confirm stability of patients´ health condition. Condition of patients in palliative care is fast-changing which makes the interpretation of our results more difficult. The low temporal stability of these items in Czech IPOS might be also explained by the fact that time between measurement was longer than in previous studies and varied ($M = 15.6$, $SD = 9$). In other studies retest was conducted the next day [14, 30]. Therefore, we need to confirm the retest reliability for Czech IPOS in a shorter period. On the other hand, the second measurement should be done later than the next day to avoid bias that respondents may recall their previous responses [14]. These results show that Practical Problems is an item on which we should focus our attention because it is unstable, and it can change even within 1 day.

The results of factor analysis showed the two-factor model could be applied to our data. The first factor consists of items associated with psychological concerns (Anxiety, Depression, Information etc.) and the second factor is composed of items assessing physical symptoms. Only the item Shortness of breath cannot be easily assigned to one of these factor groups because the loadings reached the low and almost equal level. Sandham and her colleagues identified unidimensionality in IPOS measuring palliative care needs of patients [15]. Even though our data showed the possibility of applying the two-factor model for Czech IPOS, there is a significant correlation between both factors ($R = 0.316$). In our study, we were limited by the size of the overall sample not sufficient to apply Confirmatory factor analysis (CFA). Murtagh and her colleagues identified three factors in IPOS using CFA – Physical Symptoms, Emotional Symptoms and Communication/Practical Issues [13]. This suggests that subscales could differ according to socio-cultural context or that we need more data for testing our two-factor model and the three-factor model using CFA and to compare which of these models is more precise for our population.

In terms of convergent validity, the overall score was correlated with PPS which is a tool measuring physical status [22] and the correlation was weaker than expected because this tool is only focused on physical symptoms. For correlation with ESAS, we found a moderate correlation which was not significant because of the small number of patients who completed IPOS and ESAS. Correlation with ESAS was also confirmed in other study [13]. Sakurai and his colleagues also confirmed validity of IPOS using other instruments (EORTC QLQ-30, FACIT-Sp12, and STAS) and found strong to moderate correlations, except for the item Information [14]. One possible explanation is that this item is rather unique as the only similar question from STAS is answered by a clinician [14]. Correlation of APCA African POS and MVQoLI were found to be weak to moderate for which the explanation might be that different measures of quality of life use different conceptualizations of this term [30].

Limitations

This study has several limitations. We found moderate but not significant correlation of IPOS and ESAS which means that we cannot confirm convergent of validity of Czech IPOS due to small sample who completed IPOS and ESAS. These results only imply trend which was confirmed in other studies. Due to logistical demand on participating staff it was not possible to get ESAS from every patient in the sample. Only those data collection sites which use ESAS and PPS provided both data. We also could not conduct confirmatory factor analysis on this data due to insufficient sample size. The interval of retest should be shorter with a low level of variability or instead of short time period we should use external criterion to judge stability of patients´ condition. The number of patients who completed the second measurement in this study was very low, therefore, more data for more precise retest reliability results are needed.

Conclusion

This study confirmed that the Czech version of IPOS might be used in the clinical setting and the cultural adaptation was successful. This study also further proved that IPOS is a reliable method for assessing the quality of life of patients in palliative care.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12904-020-00552-x.

Additional file 1. Czech version of IPOS

Abbreviations

POS: Palliative outcome scale; IPOS: Integrated palliative outcome scale; ESAS: Edmonton symptom assessment system; PPS: Palliative performance scale; ICC: Intraclass correlation coefficient; EFA: Exploratory factor analysis; CFA: Confirmatory factor analysis; APCA: African palliative outcome scale; MVQoLI: Missoula-Vitas quality of life index; EORTC QLQ-30: European organisation for research and treatment of cancer quality of life questionnaire; FACIT-Sp12: Functional assessment of chronic illness therapy – spiritual well-being; STAS: Support team assessment schedule

Acknowledgments

We thank all women and men who took part in this study. We also thank the staff from hospice "Cesta domů", Hospice of the Good Shepherd and Hospice of the St. Stephan and the staff from hospitals in Jihlava, General University Hospital in Prague and The Sisters of Mercy of St. Charles Borromeo who gave time helping recruit the participants and complete IPOS with them.

Authors' contributions

KV contributed to the investigation, data curation, and overall writing of the manuscript. EH and EC contributed to data analysis and EH contributed to the writing of the Methods, Results and Discussion and editing of the manuscript. ML contributed to conceptualization, funding acquisition, data curation and editing of the manuscript. The authors have read and approved the manuscript.

Funding

This study was supported by grant no. 17-26722Y Czech Science Foundation. The funder had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of data; the preparation, review, and approval of the manuscript; or the decision to submit the manuscript for publication.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Ethical Committee of the General University Hospital in Prague approved the study (Protocol Number 51/18 S-IV) and all participants gave written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 30 December 2019 Accepted: 20 March 2020

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Publisher's Note

Quality of Life Research
https://doi.org/10.1007/s11136-022-03097-z

Association between prognostic awareness and quality of life in patients with advanced cancer

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Accepted: 20 January 2022

Abstract

Purpose Despite the current guidelines supporting open communication about serious news, the evidence about the impact of prognostic awareness on the quality of life in cancer patients is not clear. The aim of this study was to assess the association between quality of life and prognostic awareness in patients with advanced cancer.

Methods This was a cross-sectional study which involved patients ($n=129$) with incurable advanced cancer (estimated by oncologist using 12-month surprise question). Data were collected at oncology departments at 3 hospitals using structured interview in which patients were asked about their quality of life (using Integrated Palliative Outcome Scale—IPOS and a single-item global measure), prognostic awareness, information needs and demographics.

Results Only 16% of the sample was completely aware of prognosis and 57% was partially aware. Accurate prognostic awareness was significantly associated ($p=0.02$) with lower level of quality of life between (when measured by both the IPOS and the single-item scale) patients with accurate prognostic awareness ($M=37.1$; 10.4) and partially aware ($M=31.9$; 9.1) and unaware patients ($M=30$; 7.4). Detailed analysis showed that significant difference between groups was found only for physical symptoms subscales ($p=0.002$), not for emotional and communication subscales.

Conclusion Prognostic awareness was found to be negatively associated with physical domain of quality of life, but not with emotional and communication domains. More research is needed on personality factors that might influence the development of prognostic awareness and quality of life.

Keywords Quality of life · Palliative care · Advanced cancer · Prognostic awareness · Prognostic · Understanding

Abbreviations

IPOS	Integrated Palliative Outcome Scale
PA	Prognostic awareness
SICP	Serious Illness Care Programme

Introduction

The majority of patients suffering from advanced cancer want to know their diagnosis and prognosis. However, their relatives and physicians' views on patients' informational needs may differ [1–3]. Relatives and physicians tend to underestimate patients' information needs, even though they acknowledge that patients have the right to be informed about their condition [1, 4]. Being informed about the prognosis means that patients can understand the seriousness of their current health condition [5], their shortened life expectancy and the incurability of their disease [6]. Accurate prognostic awareness can help patients receive goal-concordant end-of-life care [7], including a higher chance of completing advance directives and discussing treatment options with physicians [8–10]. Effective communication is an essential prerequisite for developing accurate prognostic awareness. However, many other factors such as age, education and patients' values also play an integral role [4, 11–13]. Available evidence suggests that despite the current

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communication standards in oncology, most patients with advanced cancer keep an inaccurate perception of the curability of their condition and the goal of their treatment even while receiving palliative care [6, 14–16].

Being truthfully informed about diagnosis and prognosis shall be considered as the fundamental right of patients [17, 18], and many studies have shown that more accurate prognostic awareness may be associated with the better quality of life and less depression and anxiety [19, 20] [21, 22]. However, other studies have reported that being aware of the terminal condition may cause patients psychological distress, decrease their quality of life, increase anxiety and depression, and even shorten their survival [16, 23–27]. Such contradictory findings may stem from the fact that the available studies used different and often non-standardised methods of how prognostic awareness shall be assessed, asking patients to identify their current health status or indicating the curability of their condition, using open- as well as close-ended questions or scales [6, 11]. In comparison, assessing the quality of life and psychological distress is less challenging as a wide range of standardised tools is available for patients with advanced health conditions, including cancer [28]. Nevertheless, the tools applied in palliative care differ in their measurement properties. Moreover, many instruments have issues with construct validity, reliability, responsiveness still require to be adequately evaluated [29].

The complexity of prognostic awareness (PA) and the wide range of research methods used in this field contribute to the unclear evidence of whether it is suitable for patients to know the truth about their prognosis. Given that it continues to be a significant challenge both clinically and research wise, this study aimed to investigate the association between PA and quality of life in patients with advanced cancer. This study aims to test the hypothesis of a negative association between accurate prognostic awareness and quality of life.

Methods

Study design and participants

The STROBE statement was used to guide the study's reporting; the STROBE checklist is available in Appendix 1. It was a cross-sectional study using data from patients with advanced cancer. Patients were recruited in oncology wards in three hospitals (one secondary hospital and two university hospitals) in the Czech Republic. All three hospitals are located in the capital city, and all provide care to patients with various types of cancer. Data were collected from September 2018 to February 2019. The study included patients with incurable, advanced cancer. Inclusion criteria for patients comprised a diagnosis of advanced cancer, limited prognosis and cognitive ability to participate in a structured interview. The limited prognosis was indicated by the attending oncologists using the 12-month surprise question, meaning that the physicians answered adversely to the question: "Would it surprise me if this patient dies in the next 12 months?" [30, 31]. Suitable patients were recruited by their treating physicians. Experienced researchers (KP, AT, AH) collected data, and in doing so, they followed a structured interview protocol. During the structured interview, the researchers asked patients three questions regarding their prognostic awareness, information needs, demographics and quality of life (see Appendix 2 for the structure of the interview protocol). The study was a part of a multi-centre longitudinal cohort IMPAC study, focussed on repeated measurement of prognostic awareness.

Study measures

Quality of life

Two different methods measured the quality of life. The first was a validated Czech version of the Integrated Palliative Outcome Scale (IPOS) [32], and the second was a single-item global quality of life scale [33]. The IPOS consists of ten questions and covers the following topics: physical symptoms, well-being, patient and family distress, practical concerns and information needs [32]. The total score range was 0–68 points, with higher scores indicating a worse quality of life. Confirmatory factor analysis of the IPOS has established a three-factor structure—physical, emotional and communication subscales [34]. The IPOS was explicitly developed for palliative care patients and has had excellent reliability and validity, as confirmed by several studies [32, 34–37].

In the single-item global quality of life scale, patients answer the following question: "How would you rate your overall quality of life during the past week?", rating their quality of life on a seven-point scale, where 1 means "very poor" and 7 means "excellent"; i. e., the higher the score, the better the quality of life [33]. The global measure has been reported to have good reliability and validity for measuring the quality of life [33, 38, 39]. In the present study, this scale was used for data triangulation.

Prognostic awareness

Prognostic awareness was measured using three different methods that have been used in previous research [5, 40, 41]. Patients were asked three close-ended questions, each focussing on a different aspect of prognostic awareness. First, they were asked to define the seriousness of their illness ("How would you describe your current health care status?", with the following options: "Relatively healthy", "Ill, but not seriously", "Seriously ill, but my life is not currently at risk", "Seriously and terminally ill"), followed by a question about their own perception of the curability of their illness ("What is the probability that your disease will be cured?", answering on a percentage scale of 0–100%). The last question focussed on the goal of their current treatment ("What is the primary goal of your cancer treatment?" with the following answer options: "To cure my disease", "To prolong my life although the disease can no longer be cured", and "To relieve symptoms".). The patients were considered as prognostically aware if they answered "I am seriously and terminally ill" to the first question if they indicated in their second answer that the probability of being cured was less than 10%. For the final question, patients were considered prognostically aware if they answered that their treatment goal was to prolong their life or relieve symptoms. (see Appendix 2 for a complete description of the methods applied.) Patients were considered prognostically aware if they answered all three questions using answers consistent with their actual health care status (incurable advanced cancer with a possible survival time of less than 12 months). If they used these answers only in one or two questions, we considered them as partially aware.

Statistical analysis

Frequencies and proportions were used for descriptive statistics. Differences in quality of life were assessed using ANOVA test with Fisher's LSD post hoc test in three groups of patients based on a composite measure of prognostic awareness with three groups (aware, partially aware, unaware). Correlations between demographics and quality of life were assessed using a *T*-test for independent sample (religiosity, gender), ANOVA (diagnosis, education) and Pearson correlation coefficient (age). The correlation between the three close-ended questions measuring prognostic awareness and quality of life was also assessed using the T-test for independent samples. In addition, multivariate regression was conducted to examine the associations of quality of life with prognostic awareness after controlling for confounding factors which was revealed using ANOVA. Multivariate regression was done for total IPOS score and IPOS physical subscale. Composite measure of prognostic awareness was entered into the model as dummy variables. Unaware group was set as a reference category. All analyses were performed using IMB SPSS 27 software.

Results

Demographics

The sample consisted of 137 patients; however, but for 8 patients data were missing, so the analysis was based on 129 patients. The demographics of the sample are indicated in Table 1.

Table 1 Demographics

Gender	59 women (46%)
	70 men (54%)
Age	M = 64.8 (SD = 9.2)*
Diagnosis	21% lung cancer
	21% gastrointestinal cancer
	11% breast cancer
	12% urinary tract cancer
	15% ovarian/prostate cancer
	20% other
Education	10% elementary school
	70% secondary school
	20% university
Religiosity	37% yes

*Age did not differ in men and women ($p = 0.08$)

Prognostic awareness

The majority of the sample (57%) was partially aware of their prognosis, 16% of patients had accurate prognostic awareness and 27% were unaware. Gender, age, hospital type, diagnosis, education, religiosity or having enough information about their condition had no significant association with the level of prognostic awareness.

Prognostic awareness vs quality of life

The mean of quality of life measured by the IPOS reached 32.2 (SD = 9.1), and $M = 4.7$ (SD = 1.5) using the single-item global measure. The quality of life measured by the IPOS differed significantly between groups ($p = 0.02$; $\omega^2 = 0.03$), and post hoc analysis showed unaware and partially aware patients had a significantly better quality of life compared to aware patients ($M = 30$; SD = 7.4 and $M = 31.9$; SD = 9.1 versus $M = 37.1$; SD = 10.4). The difference between unaware and partially aware patients was not significant. The difference in the score of more than five points can also be considered as a relevant difference, likely to indicate a significant change in patients' health condition [34]. The quality of life measured by single-item measure was also considerably higher ($p = 0.005$; $\omega^2 = 0.03$). Post hoc analysis showed major differences between all three groups of patients. Unaware patients experienced a better quality of life ($M = 5.2$; SD = 1.3) than partially aware patients ($M = 4.6$; SD = 1.3), who furthermore enjoyed a significantly better quality of life than aware patients ($M = 3.9$; SD = 1.8). Using three close-ended questions measuring prognostic awareness, we were able to identify a significant association with quality of life

Table 2 Quality of life and prognostic awareness

	Aware M(SD)	Partially aware M(SD)	Unaware M(SD)
IPOS total score	37.1 (10.4)	31.9 (9.1)	30 (7.4)
Single-item measure	3.9 (1.8)	4.6 (1.3)	5.2 (1.3)
IPOS physical subscale	21.1 (6.6)	18.3 (5.3)	15.9 (4.4)
IPOS emotional subscale	10.8 (4.9)	8.7 (3.6)	8.6 (3.5)
IPOS communication subscale	5.1 (2.9)	4.8 (2)	5.6 (2.2)

only for the question related to the patients' health status ($p=0.001$). Furthermore, this fact confirmed the assumption that unaware patients experienced a better quality of life ($M=30.1$; $SD=8.1$) compared to aware patients ($M=35.7$; $SD=9.8$).

IPOS subscales

We have analysed the association of IPOS subscales with prognostic awareness. It became evident that there was a significant difference between groups only for the physical symptoms subscale ($p=0.002$; $\omega^2=0.04$), but not for the emotional ($p=0.063$; $\omega^2=0.01$) and communication subscales ($p=0.281$; $\omega^2=0.002$) (see Table 2).

Demographics factors such as the diagnosis type ($p=0.7$), gender ($p=0.07$), religiosity ($p=0.25$), age ($R=0.04$) or education ($p=0.5$) had no significant association with quality of life.

Multiple regression

The results of multiple regression are presented in Table 3. We have determined that only prognostic awareness was a reliable predictor of quality of life. It was a slightly stronger predictor for the physical subscale than the IPOS total score (standardised B 0.33 versus 0.28).

Table 3 Multiple regression

	IPOS total score		IPOS physical subscale	
	Regressionβ coefficient (95% IC for B coefficient)	p value	Regression β coefficient (95% IC for B coefficient)	p value
PA	–		–	
Aware	0.28 (1.92 to 11.79)	0.007*	0.33 (2.03 to 7.9)	0.001*
Partially aware	0.13 (– 1.37 to 5.94)	0.218	0.23 (0.39 to 4.67)	0.021*
Unaware	Ref		Ref	
Age	– 0.08 (– 0.25 to 6.34)	0.386	– 0.04 (– 0.13 to 0.08)	0.617
Gender	0.17 (– 0.02 to 6.34)	0.052	0.13 (– 0.44 to 3.29)	0.134
Religiosity	0.09 (– 1.5 to 5.04)	0.286	0.11 (– 0.7 to 3.16)	0.210

Discussion

The study focussed on the association between prognostic awareness and quality of life among patients suffering from advanced cancer. Our findings indicate that accurate prognostic awareness in this population is significantly associated with worse quality of life. This fact was confirmed using two different methods for measuring patients' quality of life and a composite indicator of prognostic awareness based on the most commonly used tools for assessing this phenomenon. Compared with unaware and partially aware patients, the standard deviation of the quality-of-life measure scores was higher in patients with accurate prognostic awareness, suggesting more significant variation in this group of patients.

However, our analysis of the IPOS subscales has corroborated that the worse quality of life reported by patients aware of their prognosis relates only to worse physical symptoms, not to emotional distress or other aspects of quality of life.

Several studies have reported a negative relationship between accurate prognostic awareness and overall quality of life [16, 24, 26, 27, 42, 43]. Similar to our findings, at least one study [44] has shown that emotional aspects of quality of life did not significantly differ between prognostically aware and unaware patients. However, the total score and the scores for the other subscales (such as physical activities, role limitations, cognitive activities) differed. Indeed, findings from previous studies support these results, as they also determined that accurate prognostic awareness was related to shorter survival [15, 43], worse performance status [41, 45] or physical well-being [46], suggesting that patients with more severe health impairment at the end of their lives better understood their poor prognosis. While we did not identify a significant association between PA and emotional well-being in our study, the tendency was similar to several studies that contradicted our results by detecting a substantial negative correlation of accurate PA with emotional quality-of-life domains [24, 42]. Moreover, several studies identified a negative relationship between accurate PA and depression and anxiety [16, 23, 26, 41].

On the other hand, several studies have corroborated the correlation between accurate prognostic awareness and a better quality of life [9, 21, 47, 48]. Regarding the emotional quality-of-life sphere, it seems that such an association may be more complicated and possibly influenced by confounding factors. Ray and her colleagues [9] have determined that the association of PA and quality of life was affected by peacefulness. If patients were aware and peaceful, they were less sad and enjoyed a better quality of life. Other studies have corroborated that the emotional quality-of-life domain related to the patients' acceptance of diagnosis and prognosis [49] and their coping strategies [26]. On the other hand, Kim et al. [43] found that depression did not function as a confounding factor, as the significant association between worse quality of life and accurate prognostic awareness remained even when the level of depression was statistically controlled. This evidence suggests that patients' personality might be a crucial factor affecting the prognosis acceptance and playing a key role in the relationship between quality of life and PA. Another fundamental factor influencing the relation between prognostic awareness and quality of life is how the physicians convey diagnosis and prognosis [9, 11, 15]. However, only 8% of our participants recalled discussing hospice or end-of-life care, so the data did not allow us to examine the correlation between communication and prognostic awareness.

The different results regarding the association between quality of life and prognostic awareness may also be explained by the fact that the inclusion criteria for patients suffering from advanced cancer varied between different studies: some included all patients undergoing chemotherapy [50], patients at stage III or IV [24] or stage IV, unresponsive to current treatment [49], patients with metastases or first-line chemotherapy failure [9] or with metastases and low-performance status [16], or not receiving treatment with curative intent [26, 42]. Other studies have used prognosis estimation provided by physicians based on the surprise question [43]; such was the case in the present study. In addition, it is also important to note that the studies mentioned above [8, 9, 21, 22, 42–44, 48, 49] used different instruments to measure the quality of life, which means that the operationalisation of the domains differs and, thus, the comparability of the results is limited [51].

Limitations

There are several limitations of this study. First, its design was cross-sectional, preventing us from making any assumptions about the causal relationship between prognostic awareness and the quality of life. Randomised controlled trials using specific communication interventions to improve prognostic awareness (e. g., SICP [52] programme) and measure the quality of life would be needed to answer this question. Our sample was relatively small, and our results' effect is considered limited [53]. Another limitation of the study is the lack of information on other potential confounders, such as the patients' medical records, hospitalisation history or treatments specifications. Our results concerning the association between accurate prognostic awareness and worse physical quality of life could also be supported by measuring patients' functional condition using specific additional tools, such as the Palliative Performance Scale, which we did not apply. Similarly, emotional or informational needs could be measured by other additional tools. At the same time, the IPOS is a validated and widely used measure for assessing perceived symptom burden in all three domains. The burden of additional questionnaires and their impact on this vulnerable population should also be considered**.** The convenience sampling method applied in the study may have caused selection bias, as patients with higher emotional distress may not have wanted to participate in research. We also did not ask patients how long they were aware of their terminal prognosis, which might also affect their quality of life.

Conclusion

This study has corroborated that the physical domain of quality of life in patients suffering from advanced cancer is negatively related to accurate prognostic awareness. Such an association is not significant for the emotional and communication domains. Our findings suggest that accurate understanding of prognosis and reduced life expectancy do not necessarily correlate with a worse emotional status, and that the worse reported quality of life of prognostically aware patients is explicitly related to their worse physical condition. Therefore, the mere prognostic disclosure does not have to be associated with emotional distress of the patient, and physicians do not have to worry about that [4]. The relationship between patients' prognostic awareness, their quality of life and emotional well-being is highly complex. Therefore, a meta-analysis of the current evidence on specific factors, such as depression and anxiety, would be helpful in better understanding their mutual associations. Future research should also focus on personality traits, as they may constitute an overlooked key factor facilitating the development of prognostic awareness and quality of life in patients with advanced cancer.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11136-022-03097-z.

Acknowledgements We would like to thank all patients and relatives who took part in this study. We are grateful to the medical staff who helped us with patients recruitment and data collection from following hospitals: Thomayer Hospital, General University Hospital, Prague, Hospital at Bulovka.

Authors contribution KV contributed to the data collection, investigation, data analysis and overall writing of the manuscript. KP contributed to the data collection, investigation, data analysis and overall writing of the manuscript. AT and AH contributed to data collection and editing of the manuscript. ML contributed to conceptualisation, funding acquisition, data collection and editing of the manuscript. All authors have read and approved the manuscript.

Funding This study was supported by grant no. 17-26722Y Czech Science Foundation. The funder had no role in the design and conduct of the study; the collection, management, analysis and interpretation of data; the preparation, review and approval of the manuscript; or the decision to submit the manuscript for publication.

Availability of data and materials The datasets used during the study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest All authors declare that they have no conflict of interests related to submitted manuscript.

Ethical approval This study was approved by the Ethical Committee of Center for Palliative Care (ref. 1–2732015). The local ethical committees at all hospitals involved in the data collection also approved the study (Ethics Committee of the Institute for Clinical and Experimental Medicine and Thomayer Hospital, ref. G-18–57 13782/2018; Ethics Committee of the General University Hospital, Prague, ref. 1033/18 S; Ethics Committee of the Hospital at Bulovka, ref. 4.2.2019/9034/EK-Z).

Consent to participate Written consent was obtained from all participants.

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Received: 25 March 2021 | Revised: 13 April 2021 | Accepted: 13 April 2021
DOI: 10.1002/pon.5704

WILEY

ORIGINAL ARTICLE

Prognostic awareness in advanced cancer patients and their caregivers: A longitudinal cohort study

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Funding information
Grantová agentura České republiky

Abstract

Objective: The aim of this study was to analyse longitudinal development of prognostic awareness in advanced cancer patients and their families.

Methods: This was a longitudinal cohort study, involving 134 adult cancer patients, 91 primary family caregivers and 21 treating oncologists. Key eligibility criterion for patients was life expectancy less than 1 year (estimated by their oncologists using the 12-month surprised question). Structured interviews, including tools to measure prognostic awareness, health information needs, and demographics were conducted face to face or via phone three times over 9 months. Forty-four patients completed all three phases of data collection.

Results: Only 16% of patients reported accurate prognostic awareness, 58% being partially aware. Prognostic awareness of both patients and family caregivers remained stable over the course of the study, with only small non-significant changes. Gender, education, type of cancer, spirituality or health information needs were not associated with the level of prognostic awareness. Family caregivers reported more accurate prognostic awareness, which was not associated with patients' own prognostic awareness (agreement rate 59%, weighted kappa 0.348, CI = 0.185–0.510).

Conclusions: Prognostic awareness appears to be a stable concept over the course of the illness. Clinicians must focus on the initial patients' understanding of the disease and be able to communicate the prognostic information effectively from the early stages of patients' trajectory.

KEYWORDS
advance care planning, cancer, communication, family, oncology, patient care planning, prognosis, psycho-oncology

1 | BACKGROUND

Current guidelines on communication with patients with advanced cancer emphasize the focus on patients' autonomy and the shared decision making.[1–3] When the disease advances, patients must make decisions about their future care by taking into account both potential risks and benefits of another line of treatment as well as their limited life expectancy, using their values and preferences as the guiding tools.[4] Accurate information about prognosis and the expected trajectory of their disease is fundamental to ensure that patients are well positioned to make these difficult decisions.[5]

The concept of prognostic awareness refers to patients' level of understanding of the terminal nature of their disease. There is a number of methods how the prognostic awareness is measured, usually focussing on asking patients to indicate the likely chance that their cancer will be cured, estimating their life expectancy or assessing the seriousness of their illness.[6] The available evidence shows that strikingly low number of advanced cancer patients understand their prognosis well—the mean prevalence of accurate prognostic awareness in a recent large international meta-analysis was 49.1% (95% CI: 42.7%–55.5%, range: 5.4%–85.7%)[7]—and most of them usually see their situation as overoptimistic compared to their physicians. Accepting the bad news and being able to make decisions reflecting the poor prognosis is a very complex process, involving a number of factors such as the patients' coping style, doctor/patient relationship, clinicians' communication skills or the hope and ability to accept the stage of the illness in family members.[8,9] At the same time, the available evidence shows that most patients prefer to be informed about their diagnosis and prognosis, even if it is poor, and their preferences for health information are not related to their level of prognostic awareness.[10–12] Several studies also showed that accurate prognostic awareness can positively influence achieving goal-concordant care at the end of life.[13–15] Although we could expect some specific factors being associated with prognostic awareness of patients in the Eastern Europe, recent systematic reviews did not find any research published on prognostic awareness from this region.[6,7,9]

Family caregivers need reliable information about patients' status to emotionally, cognitively and behaviourally prepare for their role[16] and lack of prognostic awareness might negatively impact their quality of life.[17] Some studies found family caregivers reporting more accurate prognostic awareness compared to their patients,[11] suggesting that prognostic awareness in caregivers is not associated with their anxiety, depression or emotional preparedness for death.[18,19] On the other hand, Kang et al.[20] found that better prognostic awareness in family caregivers can positively impact the patients' quality of life but can also lead to worse quality of life and more depression in caregivers themselves.

As Jackson et al.[21] state in their landmark paper, "patients gradually develop prognostic awareness through an incremental cognitive and emotional process" (p. 894). With regard to this process and the gradual development of prognostic awareness, there is a striking lack of longitudinal research on prognostic awareness, with most studies reporting only cross-sectional data.[6,9] Therefore the primary aim of this study was to analyse the possible changes in prognostic awareness of advanced cancer patients over time. The secondary aim was to explore the association between prognostic awareness of patients and their family caregivers.

2 | METHODS

The Integrative Model of Prognostic Awareness in patients with advanced Cancer (IMPAC) study was researching factors influencing prognostic awareness in patients with advanced cancer. This paper reports the primary analyses of the project, a multi-centre longitudinal cohort study, involving patients and their caregivers. Data were collected in three university hospital oncology departments in Prague, Czech Republic, from September 2018 till September 2019 and ethics approval was granted by the research ethics committee at each of the three sites (for reference numbers see Supplementary Appendix 1). The STROBE checklist for cohort studies is attached in Supplementary Appendix 2.

Participants were recruited from September 2018 till February 2019 to allow at least two follow-up measurements over 9 months after recruitment. The study included patients with advanced cancer and their relatives. Inclusion criteria for patients were a diagnosis of an incurable advanced cancer (assessed by their treating physician using the 12-month surprise question[22]) and cognitive ability to participate in a structured interview in Czech language (as perceived by treating oncologists, no formal evaluation used). No further exclusion criteria were applied. All eligible patients at the three sites were invited during the study period. Patients were asked to identify their primary family caregiver to be contacted as part of the study in the consent form. Written informed consent was obtained from all patients during the baseline data collection, which was a face-to-face interview in the hospital, either in the outpatient clinic or during patient's hospitalization. Baseline interviews with family caregivers were in 83% by phone and in 17% in-person. Follow up measurements with patients as well as their caregivers and physicians were conducted either in person or by phone. After each interview with the patients, their family caregivers and treating oncologist were contacted to complete their measurements. All interviews were conducted by experienced researchers (Loučka Martin, Houska Adam, Poláková Kristýna, Houska Adam, Vlčková Karolína) following a structured protocol focussing on the variables described below.

2.1 | Prognostic awareness

Prognostic awareness was measured by three most widely used tools, involving multiple choice questions:

1. How would you define your current health status? (based on Prigerson[23])?
   a. relatively healthy
   b. ill, but it is not serious
   c. seriously ill but not terminal
   d. seriously ill and terminal
2. What is the probability of your illness to be cured? (based on IGEO[24])?

Participants were asked to indicate the likely chance of curability of the disease on visual scale 0%–100%.

3. What is the primary goal of your current cancer treatment? (based on Shin[25])?
   a. to completely cure my disease
   b. to prolong my life (although the disease itself can no longer be cured)
   c. to relieve my symptoms

Patients were perceived as prognostically aware if they answered the first question with the option (d) seriously ill and terminal, the second question by indicating the probability of being cured as less than 10%, and the third question by choosing either the option (b) to prolong their life or (c) to relieve symptoms. Family caregivers were asked the same three questions as patients, referring to their relatives' health status (see Table 1).

Expecting different outcomes of each particular method to assess prognostic awareness, we developed a new composite measure, compiling the scores of all three questions with potential outcome 0 for no correct answers in any of the three questions (patient not aware), one point for at least one accurate answer (patient partially aware), and two points for all questions answered accurately (patients considered to be aware of their prognosis).

2.2 | Health information needs

Patients and their family caregivers were asked three questions regarding their information needs:

1. "How important it is for you to have the information about future development of your disease/disease of your relative (to know the prognosis)?" answering on a Likert-scale (very important–important–not important–not important at all).
2. "Did you speak about the seriousness of your health status with your loved ones?", answering yes/no.
3. "Do you feel you are getting enough information about your illness from your physicians?", answering (a) I would like to have more information, (b) I have as much information as I want, (c) I would prefer to have less information.

TABLE 1 Changes in caregivers' prognostic awareness over time

	T1 (*N* = 88)	T2 (*N* = 28)[a]	T3 (*N* = 18)
Composite measure			
Aware	24(27%)	5 (18.5%)	4 (22%)
Partially aware	51 (59%)	15 (55.5%)	9 (50%)
Not aware	13 (14%)	7 (26%)	5 (28%)
Specific measures			
How would you describe your relative's current health status?			
Aware	52 (59%)	13 (46%)	10 (56%)
Not aware	36 (41%)	15 (54%)	8 (44%)
What is the probability of his/her illness to be cured?			
Aware	31 (34%)	9 (33%)	5 (28%)
Not aware	57 (66%)	18 (67%)	13 (82%)
What is the primary goal of your relative's current cancer treatment?			
Aware	64 (73%)	20 (71%)	13 (72%)
Not aware	24 (27%)	8 (29%)	5 (28%)

[a] One family caregiver did not answer the second question, composite measure is therefore reported only for 27 family caregivers in the second phase.

Family caregivers were asked the same questions as patients with focus on "your relative's disease/illness/health status". Patients and family caregivers were also asked if they recall any conversations with their clinicians about hospice, advanced directives or code status. Demographics were also collected (gender, age, education, spirituality). Ethnicity was not enquired as the Czech population is very homogenous with only about 5% of population representing other races or ethnicities. Due to the poor availability of hospice care, patients were not screened for receipt of hospice care and no patients in the study received hospice care.

At each data collection time, data from physicians were also collected. Physicians were asked the same question about the primary goal of current treatment as patients and if they had a conversation about patients' wishes for end-of-life care. Physicians' age, specialization, spirituality and self-assessed level of palliative care knowledge were recorded.

3 | ANALYSIS

Prognostic awareness was analysed separately using each of the three methods described above and also by using a composite measure described above. In order to test the consistency of the composite measure across the three data collection phases, McNemar-Bowker test of symmetry was used.[26] This method allows to test pairs of related data, so every measure was compared to each other; therefore Bonferroni corrections for multiple testing were used ($p = 0.05/3 = 0.02$). Chi-square and Fisher tests or Fisher-Freeman-Halton (extension of Fisher exact test for contingency table 2 × 3) were used to analyse the associations between composite measure of prognostic awareness and confounder variables. Kappa weighted coefficient was used for assessing agreement between patient, family caregiver and physicians on a question regarding patients' condition. All analyses were conducted in IBM SPSS 27.

4 | RESULTS

The study sample at baseline included 137 patients and 91 relatives. Only complete participant datasets were used in the analysis, excluding three patients and three relatives with some missing data. At baseline, 21 physicians provided their reports for 120 patients. The second data collection after 3 months was completed by 77 patients, and 44 patients completed the third data collection 6 months after baseline. Changes in prognostic awareness have been calculated for the whole sample and specific longitudinal analysis was conducted with the cohort of patients who completed all three measurements. There were slightly more women in the longitudinal cohort (52% vs. 44%) and gastrointestinal cancer was the most common diagnosis in the longitudinal cohort (39% vs. 20% in the

TABLE 2 Description of the sample

	Patients (*N* = 134)	Relatives (*N* = 88)	Patients in the longitudinal analysis (*N* = 44)
Gender			
Male	75 (56%)	22 (25%)	21 (48%)
Female	59 (44%)	66 (75%)	23 (52%)
Age			
Mean	64.8 (SD = 9.2)	53 (SD = 12.5)	64.5 (SD = 9.4)
Diagnosis			
Lung cancer	27 (20%)		6 (13.6%)
Gastrointestinal cancer	27 (20%)		17 (39%)
Breast cancer	14 (11%)		6 (13.6%)
Urinary tract cancer	16 (12%)		3 (6.8%)
Ovarian/prostate cancer	19 (14%)		5 (11%)
Other cancer	31 (23%)		7 (16%)
Relationship to the patient			
Partner		44 (50%)	
Son/daughter		38 (43%)	
Other		6 (7%)	
Education			
Elementary	14 (10%)	3 (3,5%)	4 (9%)
Secondary	93 (70%)	62 (70,4%)	32 (73%)
University	27 (20%)	23 (26,1%)	8 (18%)
Do you consider yourself to be a religious or spiritual person?			
Yes	49 (36.5%)	35 (40%)	16 (36%)
No	85 (63.5%)	53 (60%)	28 (64%)

whole sample). Overall, the demographic differences between the sample and the longitudinal cohort were not statistically significant (for details see Table 2). The reasons for dropout were patients' death (38.6%), did not want to continue (30.7%), could not be reached (16%), transport to hospice (9%), patient unable to communicate (5.7%). Complete baseline data were available for 88 family caregivers, but only for 28 and 18 caregivers in the second and the third data collection.

4.1 | Prognostic awareness

We found significant differences in the level of prognostic awareness based on which tool was used. At the baseline, 34% of patients reported accurate prognostic awareness being asked the first question ("How would you describe your current health status?"), 22% when asked the second question ("What is the probability of your illness to be cured?") and 67% of patients reported accurate prognostic awareness when measured by the third question ("What is the primary goal of your current cancer treatment?").

Using the composite measure, 16% of patients were aware, 58% were partially aware and 26% were not aware of their prognosis at the baseline. The level of prognostic awareness remained stable in the whole sample over the repeated measurements (Table 3), with only small non-significant changes (p = 0.285). No statistically significant differences (Bonferroni correction reflected) were equally found in the longitudinal cohort of the 44 patients who completed all three data collections (McNemar-Bowker test T1 vs. T2: p = 0.706, T1 vs. T3: p = 0.172T2 vs. T3: p = 0.037). Gender, education, spirituality and type of diagnosis were found not to be statistically significant in any of the analyses. If not stated otherwise, composite measure was used in all analyses described below.

Prognostic awareness in our sample was not significantly related to whether patients completed all the three measurements or withdrew from the study (chi square p = 0.14). Prognostic awareness at baseline was also not related to the fact whether patient died during the study or not (Fisher-Freeman-Halton p = 0.054), nor with any other reason for dropout. The agreement rate between patients and physicians on answers to the question about the primary goal of

TABLE 3 Changes in patients' prognostic awareness over time

	Total sample			Longitudinal cohort (N = 44)[a]		
	T1 (N = 134)	T2 (N = 77)	T3 (N = 45)	T1	T2	T3
Composite measure						
Aware	21 (16%)	12 (16%)	11 (24%)	7 (16%)	8 (18%)	11 (25%)
Partially aware	78 (58%)	38 (49%)	21(47%)	21 (48%)	19 (43%)	21 (48%)
Not aware	35 (26%)	27 (35%)	13 (29%)	16 (36%)	17 (39%)	12 (27%)
Specific measures						
How would you describe your current health status?[b]						
Aware	46 (34%)	28 (36%)	17 (37%)	13 (30%)	17 (39%)	17 (39%)
Not aware	88 (66%)	49 (64%)	28 (63%)	31 (70%)	27 (61%)	27 (61%)
What is the probability of your illness to be cured?[c]						
Aware	30 (22%)	19 (25%)	13 (29%)	11 (25%)	10 (23%)	13 (30%)
Not aware	104 (78%)	58 (75%)	32 (71%)	33 (75%)	34 (77%)	31 (70%)
What is the primary goal of your current cancer treatment?[d]						
Aware	90 (67%)	48 (62%)	31 (69%)	25 (57%)	25 (57%)	31 (70%)
Not aware	44 (33%)	29 (38%)	14 (31%)	19 (43%)	19 (43%)	13 (30%)

[a] Patients who completed data collection at all three times.

[b] McNemar-Bowker T1 versus T2: $p = 0.346$; T1 versus T3: $p = 0.344$; T2 versus T3: $p = 1.0$.

[c] McNemar-Bowker T1 versus T2: $p = 1.0$; T1 versus T3: $p = 0.625$; T2 versus T3: $p = 0.375$.

[d] McNemar-Bowker T1 versus T2: $p = 1.0$; T1 versus T3: $p = 0.146$; T2 versus T3: $p = 0.031$.

treatment was 47%, weighted kappa 0.117, at the second phase it was 73% (data available for 48 dyads), weighted kappa 0.192, at the third phase it was 73% (data available fo 36 dyads), weighted kappa 0.182. The estimation of prognosis was not associated with the accuracy of patients' prognostic awareness.

4.2 | Health information needs

There was no association found between participants' answer to “How important it is for you to have the information about future development of your disease/disease of your relative (to know the prognosis)?” and their prognostic awareness (Fisher test $p = 0.264$). Five percent of patients reported prognostic information not to be important for them, 31% to be important, 64% to be very important.

Eighty-one percent of family caregivers reported speaking about the seriousness of their health status with their loved ones, but there was no association found with patient's prognostic awareness (Fisher-Freeman-Halton $p = 0.876$). However, it was significantly associated with prognostic awareness of family caregivers (Fisher-Freeman-Halton $p = 0.014$). Less family caregivers with accurate prognostic awareness reported having this conversation (62.5%) compared to partially aware (91%) and unaware caregivers (85%). Seventy-seven percent of patients reported speaking with their relatives about their health condition but this was not associated with their prognostic awareness ($p = 0.579$) or prognostic awareness of family caregivers ($p = 0.186$).

Having enough information was not associated with the accuracy of patients' prognostic awareness (Fischer-Freeman-Halton p = 0.677). Sixteen percent of patients in the sample would like to have more information, while 84% had enough information. Patients' prognostic awareness was not associated with recollection of discussion about hospice ($p = 0.118$), advance directives ($p = 0.357$) or DNR ($p = 0.158$), although less than 8% of patients in the sample recalled such discussions. Physicians reported that they have talked with patients about their wishes regarding end-of-life care in 25% of all cases, which was not significantly associated with the level of patients' prognostic awareness (Fisher-Freeman-Halton exact test $p = 0.531$). The reasons for not having these conversations with the rest of the patients were: no appropriate opportunity so far (34%), fear of losing hope and cooperation of patients (32%), patients did not want to talk (12%), family did not want us to talk with patients (2%) or other reasons (20%).

4.3 | Caregivers' perspective

Slightly more family caregivers than patients reported accurate prognostic awareness (27% fully aware, 59% partially aware, 14% unaware) when measured by the composite measure (Fisher-Freeman-Halton $p < 0.001$). The agreement rate between patients and their relatives was 59%, weighted kappa 0.348 (CI = 0.185–0.510), in 41% of the sample there was not agreement on prognostic awareness and there was no case when caregiver would be unaware and patient aware. Gender, education, religiosity, age or relationship to the patient were not associated with relatives' prognostic awareness. Being informed about prognosis was very important for 89% of relatives, important for 7% and not important for 4% of relatives. Relatives with accurate prognostic awareness reported higher importance of being informed about prognosis than relatives who were partially or not aware (Fisher-Freeman-Halton $p = 0.034$). There was no significant association between relatives' prognostic awareness and their satisfaction with how much information they had (Fisher-Freeman-Halton $p = 0.92$).

The longitudinal analysis did not reveal any significant changes in the prognostic awareness of family caregivers; however, the sample was very small in the second and third measurement (there were only 9 caregivers providing the data in all three phases).

5 | DISCUSSION

The results of this study suggest that prognostic awareness in advanced cancer patients is a rather stable and firm concept, which is not influenced by prognostic awareness of family caregivers and clinical or demographical factors. In our sample, most patients were not aware, or only partially aware of their prognosis. In similar longitudinal Taiwanese study,[27] prognostic awareness remained also stable, although almost 60% of their sample were accurately aware of their prognosis already at baseline. Our study suggests that patients tend to keep their prognostic awareness regardless its accuracy.

The stability of prognostic awareness might be explained by the fact that oncologists in our sample discussed end of life care issues with only 25% of patients and less than 10% of patients recalled any conversation about hospice, advanced directives or code status. This number could be considered low and communication about these issues could help patients develop more accurate prognostic awareness[28] but other studies showed that patients very often do not recall these discussions (38%[28]–82%[12] of advanced cancer patients reported having no discussion about prognosis with their physician). Without more. information from patients' medical records and their caregivers it can be difficult to find out whether these conversations actually happened, to validate patients' recollections.

The stability of prognostic awareness might be also related to the personality of patients. Achieving the accurate prognostic awareness requires accepting poor prognosis, limited life expectancy or incurable nature of the disease. This is a challenging task for patients who often use various coping strategies to adapt to the life-changing experience of cancer disease.[29] Some patients might choose to keep inaccurate prognostic awareness as part of their coping, although our results showed that most patients wish to receive correct information about their prognosis while not understanding its meaning. A potential explanation of this conflict, also identified in other studies,[10] can be related to psychological factors and personality traits, such as optimism[30] or specific coping style of patients.[29]

Similarly, agreement between patients and family caregivers regarding the patients' prognosis was not very high (59%), with family caregivers being more accurate (27% vs. 16% fully aware). In a recent South Korean study,[15] family discussion about advance care planning was positively associated with patients' better illness understanding. In our sample, 81% of family caregivers reported discussions with their patients about the seriousness of their disease but it was not associated with prognostic awareness of patients, only caregivers themselves. Surprisingly, the aware caregivers less often reported having the conversation with their patients. This suggests that being aware of patient's prognosis can be a challenging barrier for relatives to start this conversation with their loved ones.

Our results highlight the importance of choosing an adequate tool to assess prognostic awareness. Due to the significant differences in responses when asking patients about the seriousness of their health status versus them correctly indicating the goal of their treatment, it is apparent that both researchers and clinicians must carefully consider and operationalize what is the aim of their conversation. In their recent work, Tzuh et al.[19] highlighted the difference between emotional and cognitive prognostic awareness. Grey et al.[18] also discuss behavioural aspect of being aware of prognosis. It is possible that patients and their caregivers would cope with different aspects of prognostic reality differently and measurements should take this into account. Using a composite measure, including several indications of prognostic awareness and assessing patients' understanding in more than just binary variable proved to be helpful in the analysis and was also used in other recent studies.[15,25,28] However, a validated “gold standard” tool to assess prognostic awareness still remains to be developed through future research.[6]

5.1 | Study limitations

This study has several limitations. The sub-sample of participants who completed all three data collections was rather small (in patients as well as family caregivers), so it is possible that with a larger sample more significant differences would be identified. However, the results of the longitudinal analysis were supported by the fact that the level of prognostic awareness was not related to whether the patient died or not during the study and also by cross-sectional analysis of cases at each data collection. Another limitation is that we used a convenience sampling method without recording the number and reasons for not participating in the study, that might have left the patients with different levels of prognostic awareness out of the study scope. Another limitation is that our study focused on patients who were already in the advanced stage of the disease. Stability of the prognostic awareness might be influenced by factors related to earlier experience with the disease and its treatment, which were not covered by our study. We also did not record some variables which might potentially explain the stability of prognostic awareness such as optimism or coping styles. More research is needed to explore the role of psychological factors on the development of prognostic awareness. Longitudinal studies should include the early stages of disease trajectory as they might be crucial for the initial development of prognostic awareness.

5.2 | Clinical implications

The results of this study highlight the need for honest and effective communication about prognosis early in the disease trajectory. Clinicians should use the ask-tell-ask principle and other techniques to ensure that patients understand their situation correctly, if they wish to be informed.[4,31] Our results also highlight the need to ask specifically about prognostic awareness as the correct understanding of the goal of treatment does not necessarily mean that patients would understand the seriousness of their illness or their prognosis. Family meetings could be a good opportunity to level the prognostic understanding of patients and their family caregivers, who can support further advance care planning.

6 | Conclusions

Prognostic awareness is a complex phenomenon, influenced by a number of factors. It seems to be a stable concept, influenced by individual psychological factors rather than clinical or demographical context. As it can significantly influence patients' ability to engage in advance care planning, more research about determinants and the ways how to improve prognostic awareness is needed. Due to the difficult recruitment and the likely drop-out rates, larger longitudinal studies are required to further improve our knowledge in this area.

ACKNOWLEDGEMENTS

This study was supported by the Czech Science Foundation grant 17-26722Y “Integrative model of prognostic awareness in patients with advanced cancer”.

CONFLICT OF INTEREST

Authors have no conflicts of interests to declare.

AUTHOR CONTRIBUTIONS

Martin Loucka conceived the study. Martin Loucka, Anna Tuckova, Kristyna Polakova, Adam Houska, Karolina Vlckova, Martin Mateju and Zuzana Donatova collected the data. Anna Tuckova, Karolina Vlckova and Martin Loucka analysed and interpreted the data. Martin Loucka drafted the manuscript. All authors contributed and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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How to cite this article: Loučka M, Vlčková K, Tučková A, et al. Prognostic awareness in advanced cancer patients and their caregivers: A longitudinal cohort study. *Psycho-Oncology*. 2021;1–8. https://doi.org/10.1002/pon.5704

Vlckova *et al. BMC Palliat Care* (2021) 20:80
https://doi.org/10.1186/s12904-021-00779-2

BMC Palliative Care

RESEARCH ARTICLE

Open Access

Views of patients with advanced disease and their relatives on participation in palliative care research

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Abstract

Background: Patients with advanced disease may not be invited to participate in research based on the assumption that participation would be too burdensome for them. The aim of this study was to explore how patients with advanced disease and their relatives evaluate their experience with research participation.

Method: This study used data from two parts of a larger project. The first dataset was a cross-sectional questionnaire study focused on priorities at the end of life. The second dataset used a longitudinal design with structured interviews on prognostic awareness. In both studies, participants evaluated their experience on a 5-point Likert scale and specified their motivation in an open-ended question.

Data were collected in 6 hospitals in the Czech Republic with patients with advanced disease and life expectancy less than 1 year and their relatives. Data were analysed using non-parametric tests and thematic analysis.

Results: First dataset consisted of 167 patients and 102 relatives, and second dataset consisted of 135 patients and 92 relatives (in total, 496 respondents). Results were similar in both datasets, with half of the sample (53%, 48%) scoring neutral, and over 30% of the sample identified their experience as interesting. The most significant factors associated with the evaluation were religiosity ($p = 0.001$) and the type of diagnosis ($p = 0.04$). Motivation for participation was to improve care, support research, express own opinion, opportunity to talk and trusting relationship.

Conclusions: Patients with advanced disease and relatives do not mind participating in palliative care research, and it can be even a positive experience for them.

Keywords: Research ethics, Family, Patients, Palliative care, Research subjects, Research participation

Background

Patients in need of palliative care are often seen as too vulnerable to participate in end-of-life research, but this should not lead to the assumption that they should not be included in palliative care research [1]. With respect to their autonomy, patients should be given a choice to decide about their research participation by themselves [2, 3]. Denying patients and their family carers of this choice is deemed as unethical [1] and paternalistic [4] and can jeopardise the further development of evidence-based palliative care. Current evidence suggests that patients and their relatives have a positive attitude toward end-of-life research and describe their experience of participation in research as positive or even therapeutic [2–4]. By participating in research, patients have the opportunity to express their altruism, which was identified as one of the main reasons for their engagement with research in several studies [2, 3, 5–7]. Nevertheless, their willingness is strongly connected to the invasiveness

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of the study [8], which indicates a possible difference in patient's attitudes based on the study design.

The likelihood of patients and their relatives being invited to participate in end-of-life research is greatly influenced by health care professionals who act as gatekeepers [9]. In a recent systematic review, the "fear of burdening the patient" was identified as the main reason for not approaching patients in end-of-life research [9]. The urgency to protect potentially vulnerable participant means healthcare professionals may be reluctant to recruit eligible patients into a palliative care study [1, 9, 10].

To challenge this perception of patients' participation in end-of-life research, studies focused on exploring how patients and their relatives themselves experienced their participation in research are necessary. Available studies focused on this topic originate dominantly from the USA, United Kingdom or Australia and are predominantly set in a cancer patient population [4].

The aim of this study was to explore how patients with advanced disease (both cancer and other) and their relatives feel about their participation in palliative care research. The study was a part of a three-year-long research project focused on prognostic awareness in patients with advanced cancer (Integrative model of prognostic awareness in patients with advanced cancer—IMPAC), and the results are based on two datasets from different parts of this project.

Dataset 1

Methods

This dataset was collected during a multicentre cross-sectional study aimed to identify the priorities of patients with advanced disease and their informal caregivers. Participants were recruited from May till September 2018 at various departments in 2 regional and 3 university hospitals in the Czech Republic. Inclusion criteria for patients were age 18+, cognitive ability to participate, and patients' life expectancy less than 1 year estimated by their physicians using the surprise question [11]. Eligible patients were invited to participate during hospital admission by their physicians, who informed them about the purpose of the study. Recruitment of relatives happened during their hospital visit, and they were eligible to participate if they were related to a person fulfilling the patient inclusion criteria. All participants provided written consent, and the study was approved by research ethics committee at each data collection site.

Data were collected by a questionnaire which was designed specifically for this study and was based on findings from a non-published qualitative pre-study conducted during the IMPAC project, focused on exploring the priorities of patients with advanced cancer. The results of this pre-study informed the development of the final questionnaire consisting of 40 different factors. Participants of this questionnaire study were asked to rank the factors by their importance on 5-point Likert scale. Demographic factors and the relationship of relatives to the patients were also collected. Additionally, in open-ended question, participants were asked to state their main motivation for agreeing to participate in the study and to evaluate how they felt about their experience on 5-point Likert scale (Very interesting, Interesting, I did not mind, Unpleasant, Very unpleasant). Patients had the questionnaire administrated by trained medical staff while relatives completed the questionnaire by themselves.

Analysis

Distribution of data was analysed using Kolmogorov–Smirnov test, which found that the distribution was not normal, therefore for further analysis, non-parametric methods were used (Mann–Whitney test, Spearman's correlation). Statistical analysis was conducted in IBM SPSS 26.

Written answers to the open-ended question were analysed by two researchers independently (KP, KV) using thematic analysis approach [12]. Verbatim responses were extracted and analysed separately for patients and relatives.

Results

The sample consisted of 170 patients and 108 relatives, but 9 respondents (3 patients, 6 relatives) were excluded from the analysis because they did not complete the question evaluating their research experience. Demographics of the final sample ($N = 269$) are reported in Table 1.

Half of the sample (53%) did not mind participating in this study and for almost 40% it was an interesting or very interesting experience. Detailed information is provided in Table 2.

The difference in answers of patients and relatives was not significant ($p = 0.52$). In the group of patients, the answers did not correlate with age ($R = 0.1$; $p = 0.23$) and did not differ based on gender ($p = 0.17$), being religious ($p = 0.5$), education ($p = 0.19$) or the level of prognostic awareness ($p = 0.5$). Similarly, in the group of relatives, the answers did not correlate with age ($R = 0.1$; $p = 0.3$) and did not differ based on gender ($p = 0.25$), education ($p = 0.5$) or being religious ($p = 0.14$). The answers differed based on the type of diagnosis ($p = 0.04$) because patients with noncancer diagnosis evaluated their participation positively (Median = 4) versus cancer patients (Median = 3).

Table 1 Demographics of participants dataset 1

	Patients ($n = 167$)	Relatives ($n = 102$)
Sex	49% female	72% female
Mean age (SD)	69.6 (12.7)	57.8 (14.5)
Education		
Elementary school	14.5%	8.8%
High school	66.2%	57.8%
Graduate degree	19.3%	33.3%
Being religious	40%	45.5%
Relationship to patient		
Spouse/ Husband	NA	25.5%
Daughter / Son	NA	48%
Granddaughter / grandson	NA	9.8%
Sibling	NA	3%
Other	NA	13.7%

Open-ended question

The open-ended question about participants' motivation was answered by 78 patients and 42 relatives.

In the group of patients following five themes were identified: Improving care, Supporting research, Expressing own opinion, Trust, Opportunity to talk. In the relative's group, there were four analytical themes, which were identical to the themes in the patient's group (Improving care, Supporting research, Express own opinion, Trusting relationship). These findings indicate that patient and relatives are motivated by similar aspects. Therefore, the results of the analysis are presented together.

Theme 1: Improving care

Improving health care for others was a major motivation for participation in both groups of respondents. Patients and relatives had a desire to help to improve not only medical care but also the relationship and communication between patients and physicians and to help others in a similar situation:

> *(I have) a great interest to improve care for other patients. (Patient)*

Table 2 Evaluation of participation in dataset 1

	Patients	Relatives
Very unpleasant	1%	0%
Unpleasant	6%	2%
I do not mind	53%	57%
Interesting	33%	33%
Very interesting	7%	8%
N	167	103

Theme 2: Supporting research

Patients and relatives expressed a strong wish to support research focused on a topic they sought as important and interesting. The respondents believed that research is necessary for developing knowledge in this field, and their participation in research is thus meaningful and important.

> *I like to help, and I think that the research is meaningful. (Patient)*

Theme 3: Expressing own opinion

The participation in research was also motivated by the wish to express their opinion. Being able to express own feelings and experiences was acknowledged as an important aspect of medical care, and respondents felt that it is important for doctors to know what they think.

> *It is important to know the opinions of the closest people of the patients. (Relative)*

Theme 4: Trusting relationship

Patients and relatives were motivated to participate in research because they were approached by a health care staff whom they trusted and have already developed a relationship with. It was also an opportunity to express their gratitude for the care they received.

> *I was approached by the doctor who is taking excellent care of my mother. (Relative)*

> *Because I trust you. (Patient).*

Theme 5: Opportunity to talk

This theme was identified only in the patients' group. Participation in research gave patients an opportunity to talk with somebody and think about topics they otherwise would not. The desire to speak with someone was driven by the sense of loneliness and by the stereotype of their days while staying at the hospital. Answering the questionnaire helped them to explore their feelings and opinions and gave them an opportunity to get new experience.

> *I am alone in the hospital room; therefore, I am glad I can speak with somebody. Maybe I will learn something new. (Patient)*

Dataset 2

Methods

The second dataset was collected during a multicentre longitudinal cohort study which was another part of the IMPAC project from September 2018 till September 2019 at oncology departments in three university hospitals in Prague.

The study included patients with advanced cancer and their relatives. Inclusion criteria for patients were a diagnosis of advanced cancer with limited prognosis (assessed by treating physician using the 12-month surprise question) and cognitive ability to participate in a structured interview. Relatives were invited to participate if identified by patients as their primary caregivers. Written or verbal consent was obtained from all participants. A research ethics committee approved the study at each data collection site.

Data were collected by experienced researchers who followed a structured interview protocol focused on participant's prognostic awareness and their quality of life (Integrated Palliative Outcome Scale [13]). The protocol included a question evaluating participants' research experience (for complete questionnaire, see Additional file 1). The data collection was repeated twice over 9 months after the baseline contact. The baseline data collection with patients was conducted face-to-face at the hospital. The second and third measurements and data collection with the relatives were conducted mainly by phone.

Analysis

Distribution of data was analysed using Kolmogorov–Smirnov test, which found that the distribution was not normal, therefore for further analysis, non-parametric methods were used (Spearman's correlation test, Mann–Whitney test, Kruskal–Wallis test, and Friedman test). Statistical analysis was conducted in IBM SPSS 26.

Results

The study sample included 137 patients and 94 relatives. For further analysis, 4 participants (2 patients and 2 relatives) were excluded because they did not complete the question evaluating their participation in the study. Detailed demographics of the final samples are reported in Table 3.

Half of the sample of patients (48%) did not mind participating in this research, 34% found it as interesting and 17% as very interesting experience (see Table 4). The answers were not associated with sex ($p=0.75$), education ($p=0.56$), level of prognostic awareness ($p=0.89$), quality of life as measured with IPOS ($R=-0.1$; $p=0.2$) or pain ($R=0.05$; $p=0.6$) but were positively associated with being religious (Z = -3.4; $p=0.001$) and slightly with older age ($R=0.2$; $p=0.03$).

Table 3 Demographics of participants dataset 2

	Patients ($n=135$)	**Relatives ($n=92$)**
Sex	44,5% female	74.5% female
Mean age (SD)	64.6 (9.2)	52.9 (12.5)
Education		
Elementary school	10%	5%
High school	70%	71.5%
Graduate degree	20%	24.5%
Being religious	50%	38%
Relationship to patient		
Spouse/ Husband	NA	33.6%
Daughter / Son	NA	29.2%
Granddaughter / grandson	NA	0.7%
Sibling	NA	2.9%
Other	NA	2.2%
Not available	NA	31.4%

The data collection was repeated every 2–3 months, with all three measurements being completed by 33,8% of the patients' sample. In total, 92 patients dropped out of the study for various reasons. The main reason was death (41 patients), patient's will to quit the study (31 patients), hospice referral (7 patients), non-functional contact (17 patients) and deterioration of health (8 patients). The reason for withdrawal from the study was not possible to identify in 10 respondents. The evaluation of participation did not differ in patients who withdraw from the study ($N=92$) from patients who completed all three measurements ($N=43$ Z = -0.29; $p=0.8$). In the group of patients who completed all three waves was no significant difference in the evaluation of their experience when measured over time ($N=43$; $\chi2=2.9$; $p=0.2$).

In the sample of relatives, 53% of the respondents did not mind participating in this research, 32% found it as interesting and 11% as a very interesting experience. The answers were not associated with age ($R=0.01$; $p=0.9$), sex ($p=0.7$), education ($p=0.85$), or being religious ($p=0.8$). Relatives evaluated their participation in the study similarly to patients, and the difference was not significant (Z = -1,4; $p=0.16$). The dropout of relatives was bigger than in the patient group (81% in relative vs 69% in patient's group).

Discussion

The results of the presented study indicate that patients and relatives do not mind participating in palliative care research. Moreover, many of them describe their participation as an interesting experience. Positive attitudes towards participation in research identified in our study are consistent with previous research [8, 14–17]. This

Table 4 Evaluation of participation dataset 2

	W1 patients	W1 relatives	W2 patients	W2 relatives	W3 patients	W3 relatives
Very unpleasant	**0%**	**0%**	**0%**	**0%**	**0%**	**0%**
Unpleasant	**1%**	**3%**	**1%**	**5%**	**4.5%**	**6%**
I do not mind	**48%**	**54%**	**64%**	**57%**	**54.5%**	**71%**
Interesting	**34%**	**32%**	**22%**	**19%**	**27%**	**12%**
Very interesting	**17%**	**11%**	**13%**	**19%**	**14%**	**12%**
N	**135**	**92**	**69**	**21**	**43**	**17**

study adds new evidence that patients and relatives evaluate their participation positively even when measured over time in a longitudinal study.

The positive evaluation of participation in research might be influenced by several factors such as gender, level of education, pain, prognostic awareness, or quality of life [5, 8, 15]. In the presented study, three factors were positively associated with the experience of patients but not the relatives.

The first identified factor was the type of diagnosis. Patients with non-cancer diagnosis evaluate their experience positively versus patients with cancer. This is a very important finding because in previous studies, attitudes of cancer patients were mainly studied [7, 15]. On the other hand, this result is consistent with a previous study that showed that patients with cancer more often declined participation in research against patients with neuron disease [6]. This might be explained by the various explanations that cancer patients with a more predictable prognosis might be more distressed, or they might have other priorities. This needs to be further studied.

The second significant factor was religiosity. Participants which identified themselves as being religious evaluated their participation as more positive. On the other hand, the percentage of religious respondents was higher in our sample than is in the general Czech population. This may indicate that considering yourself as a religious person might be a moderate factor for the evaluation of research participation. Thus, this finding supports previous research identifying religious people as less stressed while participating in palliative care research [15, 18].

The third identified factor with a positive correlation with a positive evaluation of participation was higher age. This finding must be interpreted with caution as the correlation was weak, and it was identified only in the dataset from the longitudinal study. Association between research participation and age has been reported elsewhere with mixed results [5, 8, 15], with younger patients being more willing to participate in research than older patients [5, 8]. The role of age thus remains unclear and more research focused on this factor is needed.

The relatives' evaluation of research participation was also predominantly positive which supports findings from Aoun et al. study focused on relative's perception on participating in research with majority of them identifying their experience as beneficial [19].

Patients and relatives were motivated to participate in the presented study by several reasons, including a desire to improve medical care for others and to support research. Similar reasons which motivated patients to participate in research were identified in previous studies, with altruism being the main motive for participation [5, 6, 15]. Those findings suggest that patients have a desire to help others, and participation in research serves as an opportunity how to do this. Research participation was also perceived by patients as an opportunity for social interaction during a hospital admission which helped them to pass their time in the hospital. This is consistent with previous research in this field [2, 4, 6, 15] and suggests that timing of data collection might be crucial for successful recruitment of patients in the study, such as interviewing patient while waiting for chemotherapy. Also, being approached by a familiar person with whom the patients have already established a relationship can enhance the patient's motivation to get involved in research [2, 14, 17].

The dropout analysis in the longitudinal study indicates the ability of participants to decide about their research participation. The dropout rate was not driven by a negative experience, on the contrary, those respondents identified research participating as an interesting endeavour. This finding supports the idea that patients with advanced disease are able to choose if they want to participate in research or not [15], and rather than protecting them on the assumption of research participation being harmful to them, they should be given a choice to make this decision for themselves.

The main strength of this study is including participants who have real experience with participation in palliative care research, also involving patients with another advanced disease than cancer and using a longitudinal design. This study also has several limitations. Patients could underreport their discomfort due to social desirability factors and because the evaluation question was administered by the same person as the whole questionnaire. The qualitative question was not answered by all participants; thus the motivation of those who did not answer could be different. The thematic analysis was done on written responses, which could lead to misinterpretation of its meaning. Additionally, the results may differ in research focused on other aspects than prognostic awareness, quality of life or patients' preferences.

Conclusion

This study highlights some important aspect in research with patients with advanced illness and their relatives. Most of the study participants identified their participation as an interesting experience giving them an opportunity to express their opinion and to do some good such as support research or improve care. Participation in a longitudinal study with repetitive measurements was not experienced as unpleasant, and respondents were able to withdraw from the study if it became too burdensome. The need to respect patient's autonomy should be acknowledged in research. This paper supports evidence that patients with advanced illness should be given the option to participate in research as they are able to decide for themselves.

Abbreviations

IPOS: Integrated Palliative Outcome Scale; IMPAC: Integrated model of prognostic awareness in patients with advanced cancer study.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12904-021-00779-2.

Additional file 1

Acknowledgements

We would like to thank all patients and relatives who took part in this study. We are grateful to the medical staff who helped us with patients recruitment and data collection from following hospitals: University Hospital of Královské Vinohrady, Regional Hospital in Liberec, University Hospital of Motol, Thomayer Hospital, General University Hospital, Prague, Hospital at Bulovka.

Authors' contributions

KV contributed to the data collection, investigation, data analysis and overall writing of the manuscript. KP contributed to the data collection, investigation, data analysis and overall writing of the manuscript. AT and AH contributed to data collection and editing of the manuscript. ML contributed to conceptualisation, funding acquisition, data collection and editing of the manuscript. All authors have read and approved the manuscript.

Funding

This study was supported by grant no. 17-26722Y Czech Science Foundation. The funder had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of data; the preparation, review, and approval of the manuscript; or the decision to submit the manuscript for publication.

Availability of data and materials

The datasets used during the study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was submitted as part of a larger study and was approved by the Ethical Committee of Center for Palliative Care on 23rd March 2015.Following local ethical committees at hospitals involved in the data collection provided ethical approval of the study.• Ethics committee of University Hospital of Královské Vinohrady ref. EK-VP/50/0/2017.• Ethics Committee of the Regional Hospital in Liberec, ref. EK/175/2017.• Ethics Committee of the University Hospital of Motol, ref. EK-992/18.• Ethics Committee of the Institute for Clinical and Experimental Medicine and Thomayer Hospital, ref. G-18–57 13782/2018.• Ethics Committee of the General University Hospital, Prague, ref. 1033/18 S.• Ethics Committee of the Hospital at Bulovka, ref. 4.2.2019/9034/EK-Z.All participants were given written information about the purpose of the study and they provided written or verbal consent. Verbal consent was obtained from participants who were contacted by phone only if they were not inpatients and this was approved by the ethical committees. An ongoing verbal consent was obtained each time during data collection in the longitudinal study design. All participants were informed about the possibility of withdrawing from the study at any time they would feel like it and that this withdrawal will not affect their treatment in any way.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 28 October 2020 Accepted: 24 May 2021

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Publisher's Note

7 Discussion

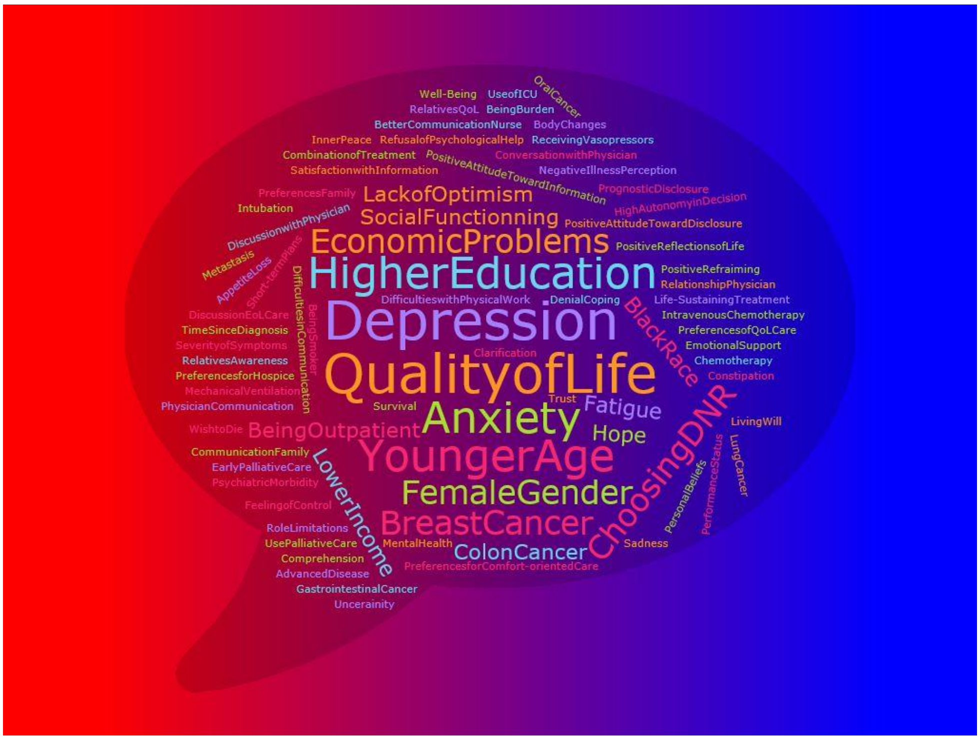
This thesis focused on prognostic awareness in patients with advanced cancer. This thesis aimed to describe this phenomenon in more detail and bring some new theoretical knowledge about this phenomenon. The main aim was to look at possible factors that influence prognostic awareness and to assess its longitudinal stability throughout the disease. The second goal of this thesis was to assess how patients and their caregivers evaluate participation in palliative care research.

7.1 Contribution to new theoretical knowledge

7.1.1 Factors associated with prognostic awareness

Prognostic awareness was found to be associated with several factors which confirmed the expected complexity of this phenomenon. Our analysis in Chapter 2 revealed that accurate prognostic awareness was associated with some factors positively, with some factors negatively and with mixed results in many others which makes the interpretation of the role of these factors very difficult. We have identified 102 different factors which have some significant relations to prognostic awareness (see Figure 1). The bigger font on the picture means more studies were conducted on this factor.

Figure 1 – Factors associated with prognostic awareness



Our results showed that prognostic awareness is associated with demographic factors, coping strategies, mental health, different amount of communication with the physician and different levels of end-of-life care (Chapter 2). A recent review on this topic identified similar factors and suggested an important distinction between precondition, correlates and possible consequences of prognostic awareness (Kühne et al. 2021). Readiness was identified as a precondition to prognostic awareness (Chen et al. 2019). In prospective cohort studies, there were 3 factors identified as consequences of accurate prognostic awareness – patients having more conversations about their health care, receiving less aggressive treatment (Chen et al. 2019; Tang et al. 2018) and reporting more depressive symptoms (El-Jawahri et al. 2014). As most of the research in this area has a cross-sectional design, most factors are considered correlates of prognostic awareness, and we are mostly not able to understand the causality of the associations between these factors. However, it is still useful to know about factors that may be important and may hinder or facilitate difficult conversations about prognosis.

For example, it is important to note that for some groups of patients it might be more difficult to understand prognosis when they are older, male, or less educated (Chapter 2). Black race was also found to be associated with inaccurate prognostic awareness (Duberstein et al. 2018; Trevino et al. 2017).

As this topic has been extensively studied in the last 20 years, we already know that there is a difference in the prevalence of prognostic awareness based on countries, which suggests the impact of culture, specifically higher prevalence of accurate prognostic awareness was identified in Australia and East Asia and lower prevalence in Europe (Chen, S.-C. Kuo, et al. 2017; Yennurajalingam et al. 2018).

Another group of factors is related to the health condition. More severe symptoms and lung or breast cancer were identified to have a negative association with accurate prognostic awareness (Chapter 2). For some of the identified factors mixed findings were found, e.g. cognitive functioning, but another recent study confirmed that memory impairment is negatively associated with accurate prognostic awareness (Diamond et al. 2017). Therefore, in this group, it is necessary to discuss the prognosis with the relatives or proxies of patients.

In our review, we also found that there is some association between accurate prognostic awareness and heath care which is provided to patients. Achieving accurate prognostic awareness is related to the care that is in line with patients' priorities (Wen et al. 2019). Not surprisingly, the accuracy of prognostic awareness is usually related to less aggressive treatment which means that patients less often do not receive mechanical ventilation (Tang, Wen, et al. 2016), chemotherapy (Craft et al. 2005; Temel et al. 2011) or use of intensive care unit at the end of life (Yennurajalingam et al. 2018; Yun et al. 2010). Many studies reported an association of accurate prognostic awareness with do-non-resuscitate orders and a recent clinical trial which had a goal to increase do-not-resuscitate orders in a patient with advanced cancer resulted in helping patients with developing prognostic awareness (Wen et al. 2020). This result indicates that in these two factors the causality may work in both directions.

Some of the reported factors were assessed in more studies with mixed results, therefore it will be needed to conduct a meta-analysis to have a reliable conclusion about the correlates of prognostic awareness. This discrepancy might be also explained by the fact that the development of prognostic awareness might be influenced by specific personality traits. However, so far only some specific aspects of personality were assessed and it was found that dispositional optimism was related to less accurate prognostic awareness (Soylu et al. 2016). Personality traits such as lower neuroticism, conscientiousness and openness were found to be associated with better health behaviour (Rochefort et al. 2019), health-related quality of life in advanced disease (Ibrahim et al. 2015), and linked to specific medical decision-making preferences (Butler et al. 2016; Flynn and Smith 2007). However, to our knowledge, there is no study specifically exploring the relationship between the core personality traits and prognostic awareness.

Few studies also assessed the perception of family caregivers. Family caregivers´ prognostic awareness is associated with better quality of life (Papadopoulos et al. 2011), lower anxiety and reduced burden but this works only when there is a concordance between the view of patients and their loved ones (Lai et al. 2021). Younger, white caregivers, and in the position of a child compared to a spouse, have a higher probability of having accurate prognostic awareness than those who had more knowledge or contact with patients (Gray et al. 2021; Tang et al. 2021). Understanding the situation of their loved ones was not associated with anxiety or depressive symptoms (Gray et al. 2021).

Most of the 102 factors were measured only in patients with advanced cancer and thus there is very little evidence of prognostic awareness in other chronic diseases. A recent study assessed prognostic awareness in patients with heart failure and it was found that demographics, documented advance directives or any disease-related factors (such as a number of admission or ICD shocks) did not have a significant association with accurate prognostic awareness (Gelfman et al. 2020). Similarly to our findings from the systematic review (Chapter 2) younger patients were more likely to have accurate prognostic awareness (Gelfman et al. 2020). Prevalence of accurate prognostic awareness was much higher (78 %) than in patients with advanced cancer, however, it does not necessarily mean that the decision making process began because only 26 % of the sample reported having goals of care conversation (Gelfman et al. 2020).

7.1.2 Association between quality of life and prognostic awareness

Most of the factors identified in Chapter 2 had weak evidence, usually, only one study assessed this particular association, but for some factors, we found a lot of evidence, especially for mental health factors (such as depression, quality of life, anxiety). However, for some of these factors mixed evidence was found, especially the association between quality of life and accurate prognostic awareness was unclear. This led us to collect data about the quality of life in our IMPAC study and to the assessment of the association between quality of life and accurate prognostic awareness.

For measuring the quality of life, we used Integrated Palliative Outcome Scale (IPOS) which was found to be a reliable and valid method to use in Czech patients with advanced disease (Chapter 3). Our study showed that worse quality of life was associated with accurate prognostic awareness, however detailed analysis showed that these findings were valid only for the physical domain, not for emotional or information subscales of the IPOS. There were some similar findings to ours (Costantini et al. 2015; Lee et al. 2020). Most available cross-sectional studies speak contradictory though indicating a negative relationship between accurate prognostic awareness and emotional quality of life (El-Jawahri et al. 2014; Fan et al. 2011; Greer et al. 2014; Kim et al. 2013; Yanwei et al. 2017) or indicating no significant association between emotional quality of life and accurate prognostic awareness (Lee et al. 2020)

However, another recent longitudinal study showed that prognostic disclosure had a negative impact on the quality of life of patients (Kang et al. 2020). This study repeatedly measured quality of life in patients with advanced cancer over 6 months but it did not capture the change in prognostic awareness and relation of this change to worse quality of life, it captured only the change in the quality of life (emotional, physical and overall quality of life) which was significantly improved in the unaware group of patients (Kang et al. 2020).

Contradictory results were published in a recent systematic review which found a positive relationship between prognostic disclosure and quality of life and cognitive functions

(Wattanapisit, Wagland, and Hunt 2021). However, these results were not completely supported by studies which assessed prognostic awareness. This might be explained by the fact that in these studies limited information was provided on how prognostic disclosure happened and whether it was revealed by physicians or whether patients guessed themselves (Wattanapisit et al. 2021). Prognostic disclosure and prognostic awareness are not the same concepts which were supported also in our data (Chapter 5) where 16 % of the sample reported accurate prognostic awareness but only 8 % recalled discussion about end-of-life care options (such as hospice care, do-not-resuscitate orders etc.). We did not directly ask whether the patients discussed with their treating physicians about their prognosis, but this might be also an indirect way how to find out what was discussed with patients, and it revealed that prognostic disclosure is not the only way how patients figure out their prognosis.

Therefore, the discrepancies in results might be explained by different trajectories of developing prognostic awareness. This suggests that delivering bad news about prognosis by a physician might be a protective factor against emotional distress in patients. This is supported by the fact that patients who get the information from their physicians have a better quality of life, and less emotional distress compared to those who learnt it by chance or from their worsening condition (Yun et al. 2010).

It is also important to note here that similarly to different methods for measuring prognostic awareness which we discussed in Chapter 1.2., quality of life is measured by various tools with different psychometric properties and also different appropriateness for use in palliative care which complicates the interpretation and the comparability of the results (Albers et al. 2010).

Overall, these inconsistent results suggest that the association between quality of life and prognostic awareness is much more complicated and probably other confounding factors influence the relationship such as coping strategies, personality traits and or prognostic acceptance (Tang et al. 2020). On the other hand, quality of life itself in patients with advanced cancer is influenced by various factors, such as worse performance status (Kuon et al. 2021), gender (Laghousi et al. 2019; Oreel et al. 2020) age, education (Lee et al. 2013) or type of cancer (Kim et al. 2013).

However, these findings should not lead to avoiding prognostic disclosure, more important is to pay attention to how to disclose the prognosis and whether patients are prepared to receive it. The explanation of the association between prognostic awareness and quality of life needs more research with experimental design to understand their mutual causality.

7.1.3 Stability of prognostic awareness

The most important question of this thesis was whether prognostic awareness remains stable throughout the disease or if it depends on the communication with a physician or whether every patient eventually develops it when they are closer to death. Our study in Chapter 5 revealed that prognostic awareness remains stable over the course of the disease which was a different result than expected.

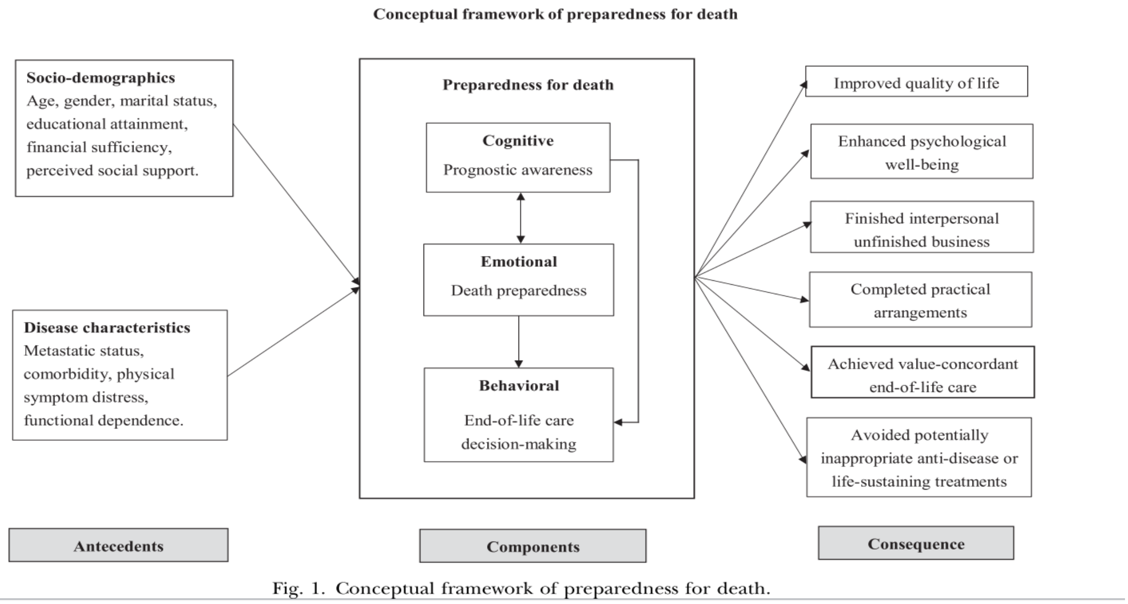
Our longitudinal cohort study showed that prognostic awareness remains stable over the course of the disease (Chapter 5). There is a piece of scarce evidence about the stability of prognostic awareness, however similar studies also confirmed the stability of prognostic awareness throughout disease (Hsiu Chen et al. 2017; Kang et al. 2020). However, some of the studies reported short survival as a factor related to the accuracy of prognostic awareness which implies that prognostic awareness might change toward death (Greer et al. 2014; Hsiu Chen et al. 2017; Kim et al. 2013; Liu et al. 2014). This suggests that toward death more patients may develop prognostic awareness, however, this was based on cross-sectional analysis, and it was not supported by our longitudinal data. When we conducted secondary analysis only at the subgroup of our sample who died during the study (Table 1), we found that there was not a significantly higher number of patients with accurate prognostic awareness compared to patients who did not die during the study (Vlckova et al. 2021).

Table 1 Secondary analysis – prognostic awareness of patients who died during the study

	PA – before death (N= 62)	PA1 (sample without patients who died)	PA2 (sample without patients who died)	PA3 (sample without patients who died)
Aware	24 %	11 %	13 %	25 %
Partially aware	55 %	58 %	50 %	44 %
Unaware	21 %	31 %	37 %	31 %

The difference in our results might be also explained by the problems related to the conceptualization of prognostic awareness which was discussed in Chapter 1. In our study, we used 3 different methods to assess prognostic awareness that have been widely used in previous research and surprisingly we got very different results analysing them separately. When we asked about their health condition (question 1), 34 % of patients in our sample reported accurate prognostic awareness, 22 % when we asked about the probability of being cured (question 2) and 67 % when we asked about the goal of their treatment (question 3, see Chapter 5). Our results suggest that these methods do not measure the same phenomenon, or they measure various aspects of prognostic awareness. Some of them may measure only the awareness of status (e.g. healthy, seriously ill or terminally ill) but some of the might measure also the acknowledgement of patients (e.g. what is the goal of treatment or life expectancy etc.) (Hui, Mo, and Eduardo Paiva 2021) which might be two different things for some of the patients. This is illustrated by another study which found that 33 % of patients with metastatic cancer stated that the primary treatment goal was to cure their cancer, although 45 % of these patients also reported that their oncologist's goal was not to cure (Nipp et al. 2017). This inconsistency might be explained by the conceptual framework of preparedness (see Figure 1) for death which was developed by Tang and her colleagues (2020). Their model presents prognostic awareness as a cognitive component of preparedness for death and does not imply that patients with accurate prognostic awareness are already prepared for the end of life care decision making (Tang et al. 2020) and therefore, they might answer questions used in research such as ours differently. This again highlights the need for validation of the method for assessing prognostic awareness which will help us in understanding this phenomenon by asking patients the right questions. The question of the probability to be cured seems to be tricky which was revealed in our data and the question on the estimation of the life expectancy has a similar problem as patients tend to overestimate their life expectancy (Taber, Stacey, and Sheehan 2021). A study with parents of children with advanced disease showed that prognostic awareness developed once physicians mentioned direct statement of incurability of disease which means that this may work as a clue to the development of prognostic awareness (Kaye et al. 2021).

Figure 2- Conceptual framework of preparedness for death (Tang et al. 2020)



These contradictory findings might be also caused by different levels of communication skills in treating physicians and in general the level of palliative care available to patients and their families (Finkelstein et al. 2021). This was supported by our data when only 8 % of our sample recalled having a conversation with physicians about end-of-life care (Chapter 5). Taking together we have strong evidence that the prognostic awareness is a complex phenomenon and the development of it is complicated and influenced by personality traits and coping mechanisms of patients and it is very much also related to the way of prognostic disclosure by physicians (Epstein et al. 2016; Liu et al. 2014).

The important question that is remaining is what are the turning points which help patients to develop prognostic awareness? Factors that help patients to prepare themselves for understanding prognostic awareness are well described in a qualitative study by (Walczak et al. 2013). Walczak et al. found that there are some factors which are important in developing patients´ readiness for discussion about prognosis. From the patients' perspective, it is the experience with severe symptoms, to have mental capacity and the disease has to be accepted by family carers (Walczak et al. 2013). Relationship with the physician was also important as well as their perceived communication skills (Walczak et al. 2013) (see Figure 3).

Figure 3 – Factors related to the discussion of prognosis and end of life issues (Walczak et al. 2013)

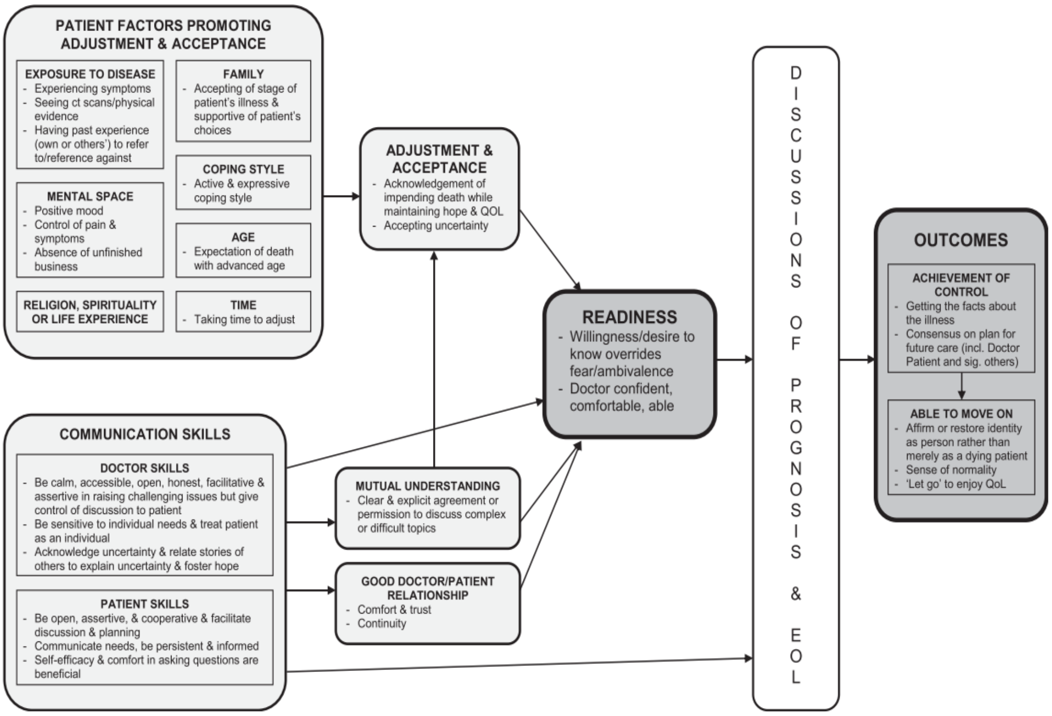


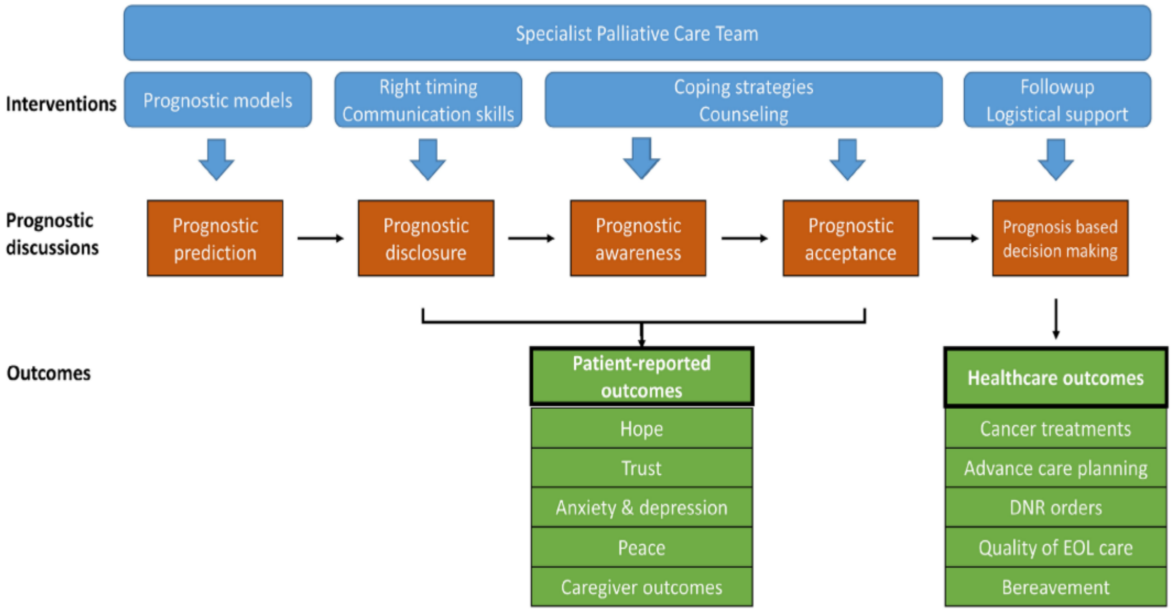
Fig. 1. Relationships between optimising factors, discussions of prognosis and end-of-life issues and outcomes.

Timing of prognostic disclosure and preparedness of patients is crucial for successful and meaningful communication with patients. If the conversation is not done at the right time, it might have a negative effect on patients (Hui et al. 2021). As prognostic awareness seems to be a very complex phenomenon it was suggested to use a prognostic continuum (see Figure 4) when thinking about this with patients (Hui et al. 2021). Hui and his colleagues use this continuum which includes patients´ readiness to engage in prognostic conversation and developing prognostic awareness followed by supporting prognostic acceptance before involving patients in the decision making process (Hui et al. 2021). This continuum is very useful for clinical practice because it also suggests what kind of intervention should be provided to patients to comfort them.

Discussion about correlates of prognostic awareness (Chapters 2 and 4) may imply the question of whether accurate prognostic awareness is something bad or good and whether it has positive or negative consequences. This is also related to the fear of physicians about the loss of hope, emotional distress or disruption in the patient-physician relationship (Hancock et al. 2007). However, this is very much related to the view on prognostic awareness as a pendulum when patients oscillate between being more and less aware over time (Jackson et al. 2013) and also to the assumption that prognostic awareness may negatively influence hope in patients. However, from the available evidence, it seems that hope and prognostic awareness are not mutually exclusive phenomena (Kaye et al. 2020). Moreover, the direction of hope in patients with advanced cancer does not have to always aim to be cured (Beng et al. 2020).

Taking together we see that empathic prognostic disclosure at the right time can help in developing prognostic awareness while sustaining hope and trust (Butow, Clayton, and Epstein 2020). And finally, this process will end up in a shared decision making process (Hui et al. 2021) that will assure that patients will receive the end of life care based on their preferences. Moreover, accurate prognostic awareness in caregivers facilitates their bereavement (Wen et al. 2021). And therefore, using this prognostic continuum in practice might help physicians not to be afraid of prognostic disclosure.

Figure 4– Prognostic continuum (Hui et al. 2021)



7.1.4 Evaluation of participation in palliative care research

The second goal of this thesis was to evaluate how patients and their family carers evaluate participation in palliative care research. This goal was achieved through two steps: in the first participants in the cross-sectional study were asked about their preferences for end of life care and also about their motivation to participate in the research. The second step was asking participants in our longitudinal cohort study to evaluate their experience. The results were described in Chapter 6. We found that most of our participants did not mind taking part in these studies, and half of them even considered it an interesting experience. This result was similar for patients as well as for family carers.

Our findings are consistent with other studies on this topic (Moorcraft et al. 2016; Terry et al. 2006; Todd et al. 2009; White and Luce 2004) which indicates that we do not have to be afraid of inviting patients with advanced disease or their families in research because they are capable of assessing their ability and willingness to participate. Their motivation for participation is consistent through various studies and it is mostly driven by the desire to help (in improving care or supporting research) or the desire to express themselves (opportunity to talk) (Bloomer et al. 2018).

But what was the reason for this study? Conducting palliative care research is seen as a very challenging procedure for several reasons (Beaver, Luker, and Woods 1999; Davies et al. 2010; Harris and Dyson 2001). One of the main reasons is the phenomenon of gatekeeping (Ehrlich and Walker 2018; Gonella et al. 2021; Pleschberger et al. 2011). Gatekeeping is a situation when health care staff, family caregivers or other involved parties prevent eligible patients from participating in a study mainly because they want to protect them from additional burdens (Kars et al. 2015). It is a rather common situation as it is very often required from the hospital or other data collection sites that the potential participants are firstly contacted by their staff (Davies et al. 2010; Hawthorne et al. 2006) that follows the relevant legislation and fits in the organizational culture (Harris and Dyson 2001). Therefore, researchers need to explain their inclusion criteria to staff (Beaver et al. 1999) and they need them to cooperate on that. As prevention of gatekeeping, it might help to further engage staff in the project (Zermansky et al. 2007). This could be done by showing them all relevant materials to the project, asking them about their opinion (Seymour et al. 2005) and also using materials that will provide enough information for potential participants as it might be the only thing that they will see before they decide (Pleschberger et al. 2011). Engaging stakeholders or using public and patient

involvement to the projects from the beginning seems as a very good option how to prevent from gatekeeping (Davies et al. 2010; Pleschberger et al. 2011)
This was also the situation of our IMPAC project where it was very crucial to explain well the purpose of the study to physicians in the hospital and get at least one of them at each site on board for cooperation and help with the recruitment. It was partly supported by money reimbursement, however, we do not think that the amount of money was big enough that it would serve as the only motivation for their participation in research (Largent et al. 2012).

Taking together it is essential to provide data that patients in palliative care are not too burdened by the research and they can decide for themselves. We hope that our data may serve in future as evidence for justifying research in this field for stakeholders, ethical committees, or health care staff in the Czech Republic or elsewhere.

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8 Conclusion

This thesis showed that prognostic awareness is a very complex phenomenon which is related to various factors with inconsistent data about the direction of their association. We also showed that prognostic awareness is a stable phenomenon which does not change throughout the disease. We also found that patients and their relatives do not mind participating in research even when they are facing serious and advanced stages of their diseases. Possible limitations are discussed in the Discussion sections of all articles.

8.1 Future directions

Future directions in this area should explore the association of prognostic awareness with core personality traits which may help to understand inconsistent results related to some correlates of prognostic awareness. Such research may also help in developing interventions focused on the development of prognostic awareness. Another problem in this area is the fact that most of the methods that are used for assessing prognostic awareness do not have their psychometric properties evaluated therefore their reliability and validity are limited. This needs to be done and the involvement of patients in the process of developing the assessment tools would be highly beneficial.

After extensive studying of this topic, it seems that it is part of some more complex process. We have to distinguish between prognostic awareness, which is a cognitive process, and prognostic acceptance, which is an emotional process. The next step is to evaluate the effectiveness of communication interventions that are being developed (Bloom et al. 2022) and to assess how and whether they can influence both these processes. It might be also important to understand better whether this conceptual framework also works for family caregivers. Also, it will be important to assess prognostic awareness in other chronic diseases than cancer, where the trajectory is more complicated and to explore the possible differences in the development of prognostic awareness across patient populations.

8.2 Clinical implications

This thesis has several important implications for clinical practice. Our results showed that there is a need for honest and effective communication about prognosis as most of the patients in our sample did not have an accurate understanding of their condition. It might be helpful to use specific techniques or protocols (such as SICP – Serious Illness Care

Program)(Bernacki et al. 2015) to be successful in delivering this information to patients that have not been previously validated in the Czech Republic. In clinical practice, it might be important to use the concept of the prognostic continuum and adjust communication to the readiness of patients and other related factors. To conclude, it is important to use an individualized approach to patients and also assess their values and preferences as soon as possible, preferably before starting the actual prognostic disclosure.

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