Multidimensional symptom management in palliative care: exploring ways to support generalist clinicians across care settings

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CHAPTER 7

General discussion

This thesis presents the results of five studies that aimed to evaluate ways to support generalist clinicians in providing palliative care, and specifically in optimizing multidimensional symptom management. This chapter highlights the main findings, discusses important methodological considerations of our studies, and reviews the implications of study outcomes for clinical practice, research, and policy.

7.1 MAIN FINDINGS

Research question 1 and 2: What do generalist clinicians perceive as barriers to palliative care and as educational needs? And what is their awareness and use of available palliative care support options?

In chapter 2, generalist clinicians working at Leiden University Medical Center mainly reported the late initiation of palliative care and insufficient general palliative care knowledge among themselves or colleagues as barriers to palliative care. Their self-perceived educational needs concerned the management of physical symptoms and basic palliative care principles. Their top two barriers and educational needs were the same in the 2012 and 2016 surveys. When comparing both years, a significant increase of self-reported familiarity with and consultation of the palliative care consultation team (PCCT) and the use of national symptom management guidelines was identified. Referral characteristics showed relatively late initiation of PCCT consultation, shortly before death. The PCCT was infrequently consulted for non-cancer patients (14% of all cases).

Research question 3: What are barriers and facilitators to multidimensional symptom management in generalist palliative care?

Barriers and facilitators to multidimensional symptom management and potential solutions to improve clinical practice were identified in chapter 3 within three main themes: multidimensional symptom assessment, initiating management of non-physical problems and multidisciplinary collaboration. Barriers included limited awareness and insufficient skills among generalist clinicians to adequately assess and manage non-physical problems. A barrier to multidisciplinary collaboration was the hierarchical difficulties reported by generalist nurses and palliative care specialists between them and generalist physicians. Potential solutions included supporting multidimensionality by using structured symptom assessment scales and standardized questions to address non-physical problems.

Research question 4: Which symptoms frequently occur simultaneously in patients with palliative care needs?

To support generalist clinicians in the management of simultaneously occurring symptoms, symptom clusters were evaluated in chapter 4 in patients who may benefit from palliative care, irrespective of their underlying illness. Three clusters were identified using cross-sectional patient-reported data on symptom presence and severity: 1) nausea, dysphagia, and dyspnea; 2) anxiety, depressed mood, pain and sleeping problems; 3) abnormal stool, anorexia, dry mouth, and fatigue.

In chapter 5, the same data were used as in chapter 4, but only including the patients with cancer. Using data from this subgroup, a Bayesian network (BN) was developed. It was evaluated if a BN was able to predict the presence and absence of simultaneously occurring symptoms, based on the presence of the other 10 USD-listed symptoms. The BN showed sufficient predictive performance for 8/11 symptoms and was generally accurate in predicting conditional probabilities.

Research question 5: Is using a clinical decision support system for multidimensional symptom management in generalist palliative care acceptable and feasible?

In the focus groups in chapter 6, participants considered a clinical decision support system (CDSS) that structures symptom assessment and recommends treatment options useful for improving symptom management. Participants thought that the CDSS would, for example, remind clinicians of blind spots and prompt patient participation. Implementation barriers that must be addressed according to the participants included interference with the professional autonomy of physicians, concerns about using a patient-reported symptom assessment system as CDSS input, lack of time, lack of continuity of care and unclear indications for use.

7.2 REFLECTIONS ON THE METHODOLOGY AND CRITICAL DISCUSSION AND INTERPRETATION OF FINDINGS

Below, the methodology of the studies in this thesis is discussed. Moreover, the potential impact of the methodology on the outcomes of each study is discussed, along with an interpretation of the outcomes.

Survey study (chapter 2)

The questionnaire used in chapter 2 was self-developed and not validated. The lack of internal and external validation causes uncertainty about our survey results regarding validity, consistency, and completeness of our findings. This especially applies to the interpretation of the results based on the open-ended questions (1). Participating generalist clinicians may have interpreted these questions about their experienced barriers and educational needs differently than the researchers intended. In addition, because there was no content validation, we do not know whether the results reflect the full range of palliative care support needs of generalist clinicians (1).

When interpreting the differences between 2012 and 2016 results, it should be noted that the survey was not a longitudinal study because respondents were not necessarily the same individual clinicians. The conclusion can be drawn that the needs among a group of generalist clinicians working at LUMC at both time points are the same with five years in between on a cross-sectional basis. Both surveys were considered a representative sample of generalist clinicians in terms of response rate of hospital departments (in 2012 92% of hospital departments (24/26) and in 2016 96% (25/26)). However, it is questionable if survey results are equally generalizable to all hospital departments. In 2012, the percentage of overall responders ranged from 1% respondents from multiple departments to 14% of responders working in hematology and 14% working in the intensive care unit. In 2016, it ranged from 1% of overall respondents from multiple departments, to 13% working in general surgery and 12% in the intensive care unit.

When comparing results between the two time points, it should also be noted that in 2012 18% of respondents were physicians, and in 2016 31%. Overall, both surveys mainly reflect nurses' views and experiences, and to a greater extent in 2012 than in 2016. This is important to note when, for example, developing palliative care education about timely identification of palliative care needs because nurses and physicians differ in basic education, and their role in the primary palliative care team is different.

Non-response bias will have affected the survey results. It is likely that the responding generalist clinicians had more affinity with palliative care than their non-responding colleagues. Their higher palliative care affinity may have caused more favorable outcomes on familiarity with and rating of the PCCT itself and on national palliative care guideline usage. This implies that the survey results are probably too optimistic and underlines the need for basic palliative care knowledge and awareness of palliative care support options, like consulting the PCCT, even more. Non-response bias might have biased the results drawn from the open-ended questions even more because answering them was not mandatory in both years. As a result, we cannot be sure what type of clinician's views are represented regarding palliative care barriers and educational needs in terms of affinity with and knowledge of palliative care.

Retrospective cohort study (chapter 2)

In retrospective cohort studies, selection bias is usually an important methodological concern. However, the risk of selection bias regarding PCCT referral characteristics was neglectable because in chapter 2 we included all consecutive patients referred to the PCCT in those years, without any missing. In addition, we did not compare two groups but only presented the characteristics of patients referred to the PCCT that were observed. The outcomes on how well generalist clinicians were able to estimate survival of their patients will likely have been affected by selection bias, because there was a considerate amount of missing data on estimated survival based on the surprise question (SQ; *Would I be surprised if my patient dies within this year?*) (2, 3). The absence of these data can be attributed to two plausible factors. Firstly, such data may be absent due to consultations involving patients in the terminal phase of their illness, where their anticipated lifespan was conspicuously brief. Secondly, the omission of these data may stem from generalist clinicians who encountered challenges in responding to the surprise question, prompting them to abstain from responding.

Misclassification bias might have affected our findings on treatment and disease characteristics of the patients referred to the PCCT. First, whether a patient received symptom-directed or disease-directed treatment was categorized at the time of consultation by the PCCT member without detailed definitions for this categorization. Second, the underlying illness was categorized by the researchers retrospectively from the patient records according to the SPICT categorization (4). We tried to minimize this risk of misclassification by having two researchers categorize all diseases independently and discuss differences to reach consensus if categories did not match.

Single center study (chapter 2)

Both the survey study and retrospective cohort study data in chapter 2 were collected in a single center, which limits the generalizability of our results (5). Survey results on the increase in PCCT familiarity, appraisal of the PCCT, and national palliative care guideline usage are likely not generalizable to other insituations, because these findings will be greatly influenced by the clinical and non-clinical activities of the local PCCT. Examples are the marketing of the team itself, and of palliative care in general.

The survey results on self-reported palliative care barriers and educational needs of generalist clinicians are likely comparable to those working in other Dutch hospitals, as basic training levels on palliative care of generalist clinicians are comparable throughout the country. However, since LUMC is an academic teaching hospital with a relatively high turnover of staff, non-academic hospitals' staff might show more 'growth' regarding palliative care awareness and knowledge over time, which may impact the barriers they experience and their educational needs.

It should be noted that the survey data were collected in 2012 and 2016. Since then, there have been many initiatives in the palliative care field to raise awareness and improve knowledge of palliative care among generalist clinicians, such as starting to embed palliative care in basic medical education (6). Therefore, when repeated today, a potential new survey could show different results. It may show more awareness of palliative care support options among generalist clinicians and their current eduational needs may be less about basic palliative care principles and more about specific palliative care topics.

The retrospective cohort data on PCCT referral characteristics (referring department, timing of referall, patient and disease characteristics) may be generalizable to countries where they have the same collaboration system between generalist clinicians and palliative care specialists. A key aspect of the Dutch system is that palliative care specialists are consulted and never take on the role of primary treating clinician, in contast to for example the United States and Canada (7). However, despite having the same collaboration system nationwide, referral charcateristics could very well differ between hospitals in the Netherlands. This will be largely due to the variation in team composition regarding the main medical specialty of the nurse and physician palliative care team members. Most Dutch teams currently consist of at least a medical oncologist and an anesthesiologist. Presence of additional medical specialites, like clinicial geriatrics, neurology, psychiatry and pulmonology, varies greatly (8). These resulting differences in local connections between PCCT members and specific hospital departments will influence knowledge and awareness in these departments of the PCCT and palliative care in general.

Cross-sectional data collection and analysis of simultaneously occurring symptoms (chapters 4 and 5)

Inclusion of patients using the one-year Surprise Question

For the cross-sectional data collection on patient-reported presence and severity of symptoms in chapter 4 and 5, the one-year SQ was used to identify and include patients with palliative care needs. The SQ is considered the gold standard for identifying patients with palliative care needs in the Netherlands and is widely used in research and practice (9). A concern with the SQ is that its' performance to identify those with palliative care needs is unclear, as all evaluations only assessed its' screening test performance in predicting death (2, 3). In those studies, approaching death is used as a surrogate marker, as there is no consensus on how to measure palliative care needs. In one meta-analysis, the overall performance in correctly predicting the outcome of a patient (whether or not the patient died within a year) of the SQ was 74.5% (3). In another meta-analysis, sensitivity in predicting one-year survival of the SQ was 67% (2). Some therefore suggest that the SQ should only be used alongside other prognostic variables (2, 3). The second concern with the SQ was also brought up by our focus group participants. Both specialist and generalist clinicians in these focus groups said generalist clinicians would likely be confused about which patient population is targeted if the SQ was used to identify patients with palliative care needs. Other studies reported that generalist clinicians were confused and felt uncomfortable when using the SQ, because they had concerns about the accuracy of their own answer and believed it to be too subjective to base important decisions on (10-12). A specific concern with the SQ is that it has proven less sensitive to identify patients close to death with non-cancer diagnoses compared to patients with cancer (2). This could especially be a problem when using it in research, such as ours, that aims to include a mixed patient population regarding type of underlying illness. In conclusion, when using the SQ as the sole criterion for including patients who might benefit from a palliative care approach, as we did in chapters 4 and 5, it is likely that not all patients who may have palliative care needs are included. Specifically, using the SQ as the sole inclusion criterion will probably lead to overrepresentation of patients with a cancer diagnosis compared to patients with a non-cancer diagnosis, which limits the generalizability of the identified symptom clusters in chapter 4 to patients with a non-cancer diagnosis.

Data collection and analysis in symptom cluster research (chapter 4)

In chapter 4 we identified three symptom clusters in a general palliative care patient population, irrespective of their underlying life-threatening illness. There are several important considerations when interpretating the identified symptom clusters. The first is the included population in terms of patient, disease and treatment characteristics and setting. Published symptom cluster studies have been performed in patients with advanced cancer (13-15), advanced stage renal failure (16, 17), advanced COPD (18) and severe heart failure patients (NYHA III /IV) (18), which hampers comparisons with our results. Only three studies investigated symptom clusters in populations with more than one underlying illness (19-21), and only one of these studies included both patients with cancer and non-cancer diagnoses (21). Hence, to our knowledge, we were the first to perform a cluster analysis on a heterogenous population of 532 patients with cancer (80.7%) and 127 patients with other diseases than cancer, such as heart failure or COPD, as their primary diagnosis (19.3%). In our study, the only difference in symptom burden in the multivariate analysis between patients with a cancer versus non-cancer condition was dyspnea (more common in non-cancer patients, OR 3.7, $p<0.001$). Although this implies that symptom burden does not greatly differ between cancer and non-cancer conditions, it remains questionable if the identified symptom clusters are applicable to all patients with palliative care needs irrespective of their primary diagnosis. We did not perform a hierarchical cluster analysis (HCA) in subgroups regarding type of underlying illness because the population of non-cancer patients was too small. The hypothesis that symptom clusters may not greatly be affected by the type of underlying illness is strengthened by the study of Stiel et al. that compared patients with both cancer and non-cancer illnesses and identified similar symptom clusters in both groups (21).

A second issue with comparing our results with those of other studies is that various symptom assessment systems have been used as input for symptom cluster analysis. This results in the use of different symptoms and different numbers of symptoms as input for the statistical analysis, which influences key outcomes such as symptom composition (22).

A third issue with symptom cluster research is that there is lack of consensus on the best statistical method to identify symptom clusters (22, 23). Moreover, there are no standards for analytic choices in the diverse types of cluster analysis. As a result, the final clusters are subjective for every type of cluster analysis (22, 23). The most commonly used analysis methods are three multivariate exploratory statistical techniques: principal component analysis (PCA), exploratory factor analysis (EFA) and hierarchical cluster analysis (HCA). Studies that compared these three commonly used methods found little correlation in clusters despite using an identical data set, except for anxiety and depression which were generally clustering together (24-26). We used HCA in chapter 4. We favored HCA because it bases clusters on similarity within the data and assigns every variable (symptom) to a cluster, this way supporting our purpose of alerting clinicians to the simultaneity of symptoms in patients with palliative care needs. EFA was not possible because it requires continuous data and the symptom scores were categorical data. PCA was less suitable because it identifies components (factors) that explain the variance in the dataset, rather than identifying the relation between components (symptoms). As a result, this method may not assign one or multiple symptoms to a cluster.

There are two analytic considerations when interpreting the identified clusters in chapter 4. First, the choice of the similarity measure influences the analysis and there is no consensus on the best measure. We used Euclidean distance, but our clusters could have been different if we chose one of the two other commonly used distance measures (Manhattan distance or Maximum distance). Second, the statistical choice for the distance between clusters, also known as linkage, may affect cluster composition. Most common choices are average-linkage, single-linkage, or complete linkage, and we used the latter.

When comparing the symptom clusters identified in chapter 4 to other studies that used the ESAS as input and HCA as the statistical methodology, (24-26) we also found that anxiety and depressed mood cluster together. However, we did not find that loss of appetite or anorexia cluster together with nausea as in these other studies. This may be because we used the USD, (24) an adapted version of the ESAS that includes additional symptoms (dry mouth, dysphagia, stool difficulties and sleeping problems), which may alter cluster composition. It may also play a role that in our study, nausea was the least prevalent symptom (n= 429, 65.2% with an NRS of 0), compared to anorexia being present in the majority of patients (n=188, 28.6% with an NRS of 0).

Considering the aforementioned limitations of cluster research, it is perhaps unsurprising that systematic reviews on patients with advanced cancer found limited consistency in symptom clusters. Therefore, cluster research in palliative care remains inconclusive (13, 15).

Bayesian network development to identify simultaneously occurring symptoms (chapter 5)

In chapter 5, a Bayesian Network (BN) was developed to assess whether a clinically relevant USD-listed symptom could be predicted based on the presence or absence of the other 10 USD-listed symptoms. The dichotomized symptom scores of the 11 USD-listed symptoms were used as input for the network analysis the network’s variables. BN development consists of two stages. During the first stage, structure learning, a graphical structure is constructed, representing direct associations between symptoms. An AUC-ROC was calculated per simultaneous symptom, which indicates how well the BN model can determine the outcome for an individual patient (simultaneous symptom present or absent), based on the presence or absence of the other USD-listed symptoms. During the second stage, parameter learning, conditional probabilities for presence/absence for each symptom are calculated. To determine how accurate the BN was in predicting the conditional probabilities a calibration plot was constructed.

Our ultimate aim of using BN development for symptom prediction would be to present generalist clinicians with the probability that their patient experiences specific simultaneous symptoms, based on the symptom(s) that the patient reports during regular history taking. However, we had no data available on which symptom(s) patients would have spontaneously mentioned during history taking, that way preventing this aim.

To develop the BN, USD scores were dichotomized into clinically relevant (≥4) and not relevant (<4) since an ESAS score of ≥4 is generally considered as the cut off point for symptoms that require additional assessment (27, 28). This choice was made because BN development is easier to illustrate using dichotomized variables, as it minimizes the number of combinations and opportunities. However, there is debate on whether the same cut-off point should be used for all ESAS/USD symptoms (28, 29). In future research, instead of dichotomizing the symptoms, the USD scores could also be categorized into severity categories (mild, moderate, severe) to better represent the clinical revelance of symptoms.

The developed BN model had an AUC-ROC of ≥0.65 for 8 out of 11 USD-listed symptoms. An AUC-ROC of <0.5 implies a lack of predictive performance and an AUC-ROC of >0.9 implies outstanding predictive performance (30). The identified AUC-ROCs seem low in comparison todiagnostic tests in which is generally strived for AUC scores >0.95. We considered an AUC-ROC of ≥0.65 a satisfactory predictive performance for the purpose of developing a symptom prediction system, because it is considerably better than chance and the consequences of a symptom prediction system being wrong are much less severe than in diagnostic tests that evaluate absence or presence of a disease.

Lastly, when interpreting the developed BN, it needs to be emphasized that the network does not show causal relations. For this study, the developed BN did not need to represent causality to predict simultaneously occurring symptoms. We used automated structure learning to develop the network and as a result the direction of the edges is not necessarily based on causality. The direction of edges may also be a result of the automated simplification of the constructed network. We were unable to develop the network based on hybrid causal learning, which is a combination of input of previous knowledge and automated structure learning (31). This is because there is no previous knowledge available on the causal relations between symptoms because the interaction of symptoms in patients in a palliative care trajectory is complex and symptoms often mutually reinforce each other. For example, it is not well established whether, or in which cases, dyspnea causes anxiety or whether anxiety causes dyspnea, or whether both symptoms are caused by a common pathway (32-34).

Focus group study (chapters 3 and 6)

The participating generalist clinicians of the focus group studies in chapters 3 and 6 may have had more affinity with palliative care than non-participants because of the combined purposive and convenience sampling (non-response bias). In addition, participating patient representatives may have had more affinity with palliative care and more proactive attitudes towards care in general than average patients. This means that the identified barriers and facilitators to multidimensional symptom management and to the use of a symptom management clinical decision support system (CDSS) may not reflect those of a general clinician and patient population, which limits the generalizability of our results. The identified themes may reflect more awareness of and more positive attitudes towards multidimensional symptom management. For example, all participants expressed positive attitudes towards using a symptom assessment system, whereas it has been proven difficult to implement such systems in generalist palliative care settings (30). Also, they expressed positive attitudes to the benefits of using a CDSS for symptom management. These positive attitudes may be because generalist clinicians with more palliative care affinity have more positive attitudes towards putting time and effort in using a CDSS for symptom management, which have proven a significant concern in CDSS implementation and actual use in clinical practice. On the other hand, clinicians with more palliative care affinity could have had more negative attitudes towards a support system because they believe they do not need support because they are already good at providing palliative care, a known barrier to CDSS use known as 'interference with professional autonomy' (35, 36).

When aiming to support hospital clinicians who care for patients with non-cancer conditions, the barriers and facilitators identified in this study to multidimensional symptom management and to CDSS use should be interpreted with caution. Our outcome may not be generalizable because the focus groups consisted of relatively few clinicians working solely at a non-oncology department (three out of nine participating hospital physicians and two out of eight hospital nurses).

A particular strength of the focus group study is that the experiences of a broad group of stakeholders from different disciplines and settings were evaluated, including nurses, physicians, palliative care specialists and patient representatives, doing justice to the multidisciplinary nature of palliative care. This way, barriers, and facilitators to the complete process of multidimensional symptom management could be identified.

7.3 IMPLICATIONS OF FINDINGS FOR PRACTICE, POLICY, AND FUTURE RESEARCH

Here we address eight themes derived from the results of this thesis that have implications for improving daily practice, necessary changes in policy and we provide suggestions for future research.

7.3.1 Supporting generalist clinicians in improving basic palliative care knowledge and skills

The fact that generalist clinicians often do not seem aware of the importance of considering non-physical problems when trying to relieve symptom burden, and their need for support with basic palliative care knowledge have implications for practice. The basic palliative care knowledge and skills of generalist clinicians should first be secured before they can improve the way they manage the total symptom burden of patients in a multidimensional manner. After all, generalist clinicians will have difficulties to fully grasp the importance of multidimensional symptom management if they are unaware of the core principles of palliative care. The core principles include maintaining the patient's optimal quality of life through adequate management of potential physical and non-physical problems, and timely integration with disease-directed care through advance care planning and anticipating to potential future symptoms (9). This is confirmed by the fact that, despite continuous efforts of specialists in palliative care, generalist clinicians working in our academic medical center continuously express the need for support with basic palliative knowledge and skills. One of the likely causes is that there is still a lack of sufficient palliative care education in the basic medical curricula (6). A key article by Grol & Wensing (2004) states that there are largely two levels to target when trying to establish change in clinical practice: individual professionals and interpersonal factors or system characteristics (37). The authors proposed the following steps to change individual professional behavior: orientation, insight, acceptance, implementing the actual change, and lastly, maintaining that change. Within the first step, orientation, they note that it is important to promote awareness of the innovation and stimulate interest and involvement. Our surveys show that respondents were, at least in part, aware of their own need for support with the basic principles of palliative care, which is an important first step for improving clinical practice. In the future, it is key to continue to raise palliative care awareness and educate about palliative care knowledge and skills, and to focus on the next steps: improving insight in and acceptance of the integration of a palliative care approach by generalist clinicians for every patient who will likely benefit from it.

Future research should focus on how to target the barriers to the acceptance among generalist clinicians of integrating a palliative care approach in a timely manner.

7.3.2 Supporting generalist clinicians with timely initiating a palliative care approach

Our survey results showed that generalist clinicians felt that palliative care was often initiated too late, which is in line with our finding that PCCT referrals were initiated late (median less than 1 month before death), and the outcome of other studies (40-43). The underlying problem is that generalist clinicians have difficulties identifying patients who might benefit from a palliative care approach (44). First, it is key to start educating palliative care generalists about the advantages of integration of a palliative care approach alongside life-prolonging treatment, and the importance of a multidimensional approach to the patient and their quality of life. To support generalist clinicians with timely recognizing patients who might need a palliative care approach, tools such as the SQ, could be further implemented. However, due to the difficulties that generalist clinicians have with using the SQ in practice, they may need identification tools that use additional items on for example performance scores, unplanned hospital visits, and the phase of the disease. Such tools are available, including the Supportive and Palliative care indicators tool (SPict), Gold Standards Framework Prognostic indicator Guidance (GSF-PiG), rADboud indicators for PAlliative care needs (rADPAc), Nececidades paliativas (NECPAL) and the (Ingegrated) Palliative Care Outcome Scale ((I)POS) (45, 46). It is problematic for integrating identification tools of palliative care needs in clinical practice that most research has focused on the theoretical development of such tools or on their predictive performance, but there is little research on the opinions of generalist clinicians of using the different available tools.

In our ongoing KWF project, research focusses on composing patient profiles to identify patients that would benefit most from a palliative care approach. Predictors (patient data and patient reported outcome measures (PROMS)) are evaluated using two existing databases on symptom burden and quality of life of patients with advanced cancer (Experienced quality of life of patients with advanced cancer (eQuiPe) (47), n>1100 and SYMptom monitoring with Patient-Reported Outcomes (SYMPRO) (48), n>150).

Future research should focus at identifying those patients who are at considerable risk of having a high symptom burden in terms of multiple simultaneous symptoms and high symptom severity. Moreover, research should focus on the perception of generalist clinicians of using the available palliative care needs identification tools, to try and overcome barriers to the actual widespread use of these tools in generalist palliative care settings.

7.3.3 Supporting generalist clinicians to provide palliative care for patients with non-cancer illnesses

The WHO states that 66% of patients with palliative care needs suffer from a non-cancer illness (49). Our findings are in line with those of others that patients with non-cancer conditions are referred less to specialist palliative care services (50), and, moreover, are referred later in the disease trajectory with a worse performance status compared to patients with cancer (51). It shows that it is important to support generalist clinicians caring for patients with non-cancer illnesses to identify when they themselves should integrate a palliative care approach and in case of complex problems, when their patients should be referred for specialist palliative care.

Patients with non-cancer conditions largely have the same symptoms, problems and needs as patients with cancer (21, 52). Some research has shown they even have a heavier burden of symptoms and problems than patients with cancer (53). In patients with non-cancer illness trajectories, organ failure usually increases gradually, combined with acute exacerbations that may or may not lead to death. In these patients, death is often seemingly unexpected because between exacerbations, palliative care needs may be less apparent (54-56). Unfortunately, identification tools such as the SQ, have worse performance in predicting death in non-cancer patients (2).

A first step towards specifically supporting generalist clinicians in providing palliative care for patients with non-cancer illnesses may be to develop and implement identification tools that are specifically designed for non-cancer conditions. These include, for example, tools for heart failure patients, such as the Needs assessment tools progressive disease - heart failure (NAT: PD-HF), Heart failure needs assessment questionnaire (HFNAQ), Care related quality of life for chronic heart failure questionnaire (CareQol CHF), and the Heart failure palliative approach to care (HeFPAC) (45). In the Netherlands, the I-HARP tool was recently developed. (57) Specific tools also exist for COPD, such as the Dutch ProPal-COPD tool (58), which adds six disease-specific predictors to the surprise question. An obvious downside of the implementation of more elaborate tools for identifying patients who might benefit from a palliative care approach is that they take more time to use.

Future research should focus on evaluating the effect of using non-cancer identification tools on quality of life or symptom burden of patients with an advanced life-limiting illness, compared to using general identification tools for palliative care needs.

7.3.4 Supporting generalist clinicians with identifying simultaneously occurring symptoms and problems

One of the barriers to using a symptom assessment system in generalist palliative care settings is a lack of time (59). This indicates the need for other methods to evaluate simultaneously occurring symptoms more efficiently. A time-efficient way might be to alert patients and clinicians to symptoms that tend to cluster, as for example identified in this thesis and other previous symptom cluster studies. However, consensus on the value and method of identification of symptom clusters is needed before wide implementation can be achieved. A more innovative approach could be to use a symptom prediction system based on a Bayesian network (BN) that alerts the clinician to the specific probability that a patient is also experiencing other symptoms.

In future research:

- additional characteristics could be used as input for the BN to refine symptom prediction (60), for example by using the patient's age, gender, the primary advanced life-threatening illness, functional status, and disease-modifying treatment during the previous three months.
- in addition, problems in other than the physical and psychological dimension of palliative care could be used as variables in the BN, to gain insight in co-occurrence.
- studies should incorporate the opinions of the targeted end-users about the user experience of the symptom prediction system, to be able to target the implementation barriers of such a technological system in clinical practice.

7.3.5 Supporting generalist clinicians with four-dimensional, systematic assessment of symptoms and problems

Our focus group participants mentioned the use of systematic assessment systems as a solution to improve assessment of multidimensional symptoms and problems. They also believed that providing generalist clinicians with standardized questions to address non-physical problems would help. Both suggestions are known to increase the number of symptom and problems identified (61). Many multidimensional assessment tools for palliative care have been described (62) but those that are widely used in clinical practice, such as the Edmonton Symptom Assessment System (ESAS) (63), only address physical symptoms and psychological problems and are in fact two-dimensional. To fully establish multidimensional symptom management, tools that assess all four dimensions of palliative care should be further implemented, such as the Palliative Care Outcome Scale (POS) (64), the Functional Assessment of Chronic Illness Therapy - Palliative Care (FACIT-Pal) (65), the McGill Quality of Life Questionnaire (MQOL) – Revised (66) or the Utrecht Symptom Diary-4 dimensional (USD-4D) (67). In addition to offering a systematic approach and standardized questions for addressing non-physical dimensions, the use of four-dimensional assessment tools may increase awareness among generalists of the importance of addressing non-physical problems and may prompt patients to discuss the non-physical problems.

Our results and those of others indicate that it is paramount to address potential barriers to using symptom assessment systems in daily practice. A multidimensional symptom assessment system will take time, which clinicians often lack, clinicians have beliefs that an assessment scale does not represent true symptom burden, and that it will be a burden to patients (59, 68).

Future research should focus on how to overcome barriers to the routine implementation of four-dimensional assessment systems in generalist palliative care settings, because until now the implementation of a two-dimensional assessment system has already proven difficult. If such routine implementation would be achieved, it is equally important to evaluate how the assessment system scores actually lead to adequate clinical actions to relieve symptom burden and suffering, as this is still often lacking in settings where symptom severity screening is routinely implemented (63).

7.3.6 Supporting generalist clinicians with assessing the social and spiritual dimensions

The question whether an assessment system does truly represent the patient's burden of symptoms and problems is likely even more applicable when it comes to psychosocial and spiritual problems. Especially social and spiritual problems need to be explored in depth to fully understand them, and to decide which intervention or referral may be needed (69). This is challenging because generalist clinicians have limited training in in-depth exploring socio-spiritual needs and have limited time (70-74). One solution may be referring every patient to a specialist palliative care service if their non-physical needs need to be further explored. However, the number of patients in need of palliative care already grossly exceeds specialist care team capacity (75, 76). A second solution may be standardized referrals to psychologists and spiritual caregivers at least once in each palliative care trajectory but this will also grossly exceed the capacity of psychosocial and spiritual caregivers. A third option is to support generalist clinician with tools that screen socio-spiritual needs and problems in a standardized manner. More than thirty-five spiritual assessment tools have been described, of which most have only been used in research (77). The Ars Moriendi model has been implemented in practice and was found feasible and useful by clinicians working in palliative home care (77). The questions of this model are formulated in spoken language and five tension fields are presented (i.e., autonomy, pain control, attachment and relations, guilt and evil, and the meaning of life) (78). These five themes play a crucial role in the dying process, discussing them assists the patient with making his or her own choices and facilitates communication (78). It should be noted again that more elaborate instruments like the Ars Moriendi model will have barriers for implementation, most obviously because they are too time consuming. It will be key to implement a time-efficient socio-spiritual assessment system in generalist palliative care settings to identify those patients who need support, for example by referral to a palliative care consultation team or a spiritual caregiver. A solution may be found in the USD-4D, a recent content validated adaptation of the Dutch version of the ESAS, in which the tension fields of the Ars Moriendi model were added as standardized statements (67).

Future research should focus on further developing and validating a time-efficient system for the assessment of the social and spiritual dimension, that is feasible to use in generalist palliative care settings.

7.3.7 Supporting generalist clinicians to empower patients and caregivers

The findings of this thesis highlight the importance of empowerment of patients and their family in multidimensional symptom management. Results of chapter 3 show that patient factors are a barrier to the assessment of the non-physical dimensions of palliative care. Patients usually think about physical symptoms first when thinking about palliative care. Also, they may be less willing to talk about non-physical problems, which may be especially the case when patients have a closed personality or coping issues. These findings are in line with previous studies on addressing psychosocial and spiritual issues in palliative care (79-81). Empowerment is defined by the WHO as 'a process through which people gain greater control over decisions and actions affecting their health' and is one of the core principles when looking at the definition of palliative care of the Dutch quality framework (9). Specific factors that are associated with being or becoming empowered have been identified in patients with an advanced life-threatening illness (figure 1) (82). Maintaining self-identity facilitates empowerment, which comprises the beliefs of a patient about their self-esteem, self-image, and ideal self. Other factors that help to become empowered are if patients participate in their care, rather than having a passive role with their clinicians assuming a paternalistic role. Moreover, a factor that plays a significant role in empowerment is whether patients acknowledge their terminal illness, including their impending death. Coping with and adapting to continued physical and social losses also facilitates empowerment, which is done by changing priorities, sorting personal affairs, and planning for further deteriorations. Lastly, personalized patient education supports empowerment, for example on basic pathophysiology of symptoms (82).

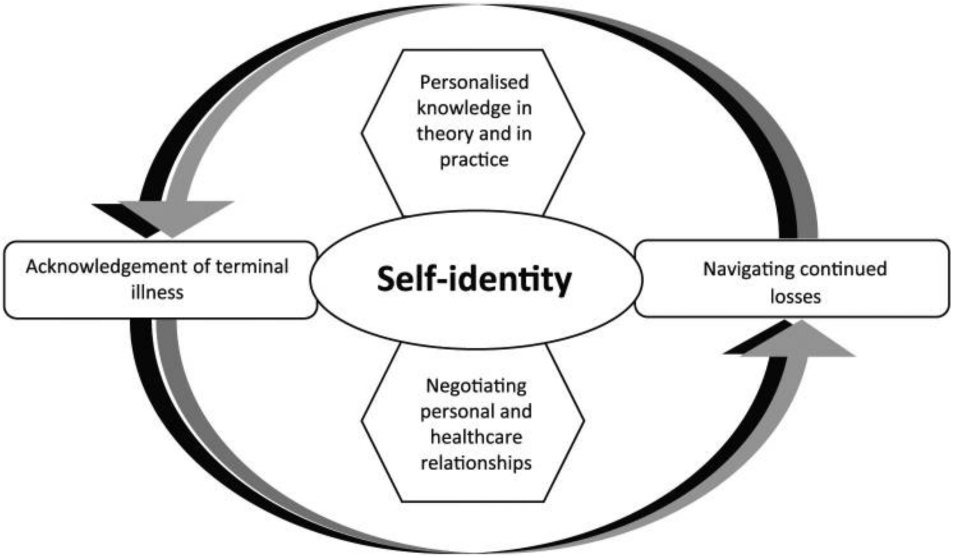

Figure 1. Conceptual model of patient empowerment for adults with advanced life-threatening illness proposed by Wakefield et al. (76)

Future research should focus on how patients can best be empowered in the management of their own symptoms and problems. It would be particularly interesting to investigate if symptom burden is relieved more promptly if a patient or caregiver is co-end-user of a palliative care symptom management CDSS compared to the clinician being the sole end-user. A CDSS where the patient is co-end-user could entail patient education on symptom etiology and self-management advice, as proposed by our focus group participants, including information about the influence of non-physical problems on their symptom burden.

7.3.8 Supporting generalist clinicians with a tool to support multidimensional symptom management

To develop a feasible and usable system, the potential barriers to implementation identified in this thesis and previous CDSS studies should be further explored, including unclear indications for use, interference with professional autonomy of clinicians and a lack of time (35, 36). To explore these barriers, a feasibility study is needed to evaluate how usable and useful clinicians find the first version of a tool to support multidimensional symptom management. This tool incorporates all advice provided in the Dutch national guidelines regarding anxiety, depression, and sleep problems. This tool will be testes in patients with pain, as these symptoms are clustered with each other. To assess the system's feasibility in practice, a modified Technology Acceptance Model (TAM) is proposed as a theoretical framework (figure 2) (83). This widely recognized TAM has shown to predict the use and acceptance of technology in healthcare well. The modified TAM consists of two main domains: perceived usefulness and perceived ease-of-use. Specifically in the healthcare setting, additional factors influence adoption of a technology by its end-users (individual context, the technological context, and the organizational context).

If the tool will prove feasible in practice, an efficacy study should evaluate if the use of the finalized MuSt-PC tool will lead to a more prompt and effective relief of symptom burden compared to usual care. Proposed primary endpoint of a future cluster-randomized efficacy study is the time until a clinically relevant decrease in symptom burden is seen in the intervention group (use of MuSt-PC) versus a control group (usual care), measured by the USD-4D. If the MuSt-PC is effective in more promptly reducing symptom burden, the aim is to implement it nationally in clinical practice. After implementation, it is key to evaluate the level of uptake through further research, for example using the RE-AIM framework (84). RE-AIM consists of the following elements: reach (in this case proportion of clinicians that started to use the tool), effectiveness (outcomes regarding knowledge, skills, and attitudes of the clinicians that used MuSt-PC), adoption (proportion of clinicians who actually use the tool in practice) and implementation (the extent to which the intervention is implemented as intended in daily practice and maintenance).

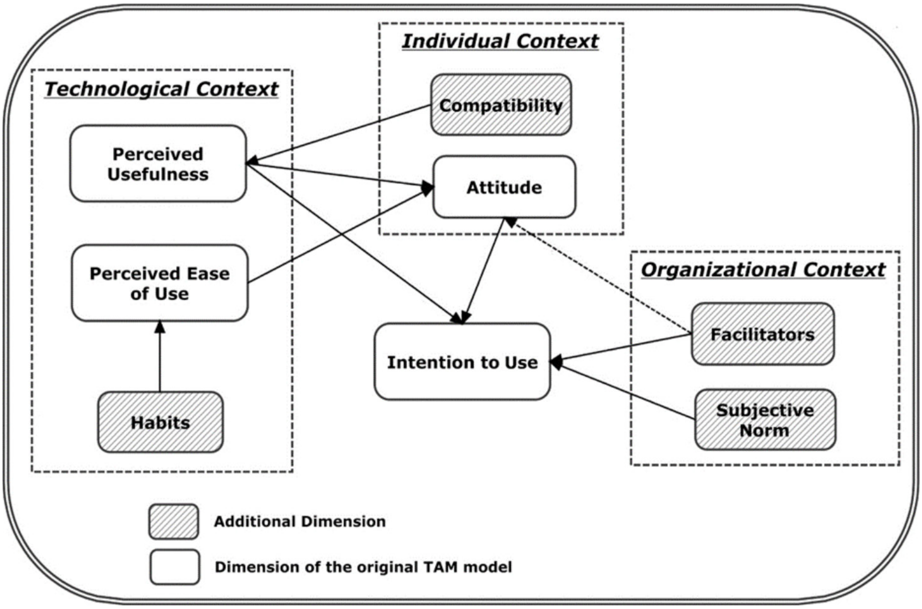

Figure 2. Modified Technology Acceptance Model (TAM).

Ongoing development of the MuSt-PC tool

The preliminary design of the MuSt-PC tool starts with the Utrecht Symptom Diary 4 dimensional (USD-4D) (27). Each symptom or problem is linked to treatment recommendations from the national palliative care symptom management guidelines. For future versions, it is key that treatment recommendations for simultaneously occurring symptoms are developed and implemented. Although many papers in symptom cluster research emphasize the need for integrated treatment strategies for simultaneous symptoms, not many have been described (22, 85). There is some research on treatment for common clusters, but in general, these studies were aimed at patient education and self-management of total symptom burden and did not aim to treat specific symptom clusters (34). Cross-over treatment recommendations for simultaneously occurring symptoms and problems are currently developed for the MuSt-PC tool according to the methods proposed by Kwekkeboom et al (86). For this, our group is extracting overlapping non-pharmacological and pharmacological treatments strategies for two or more USD-4D-listed symptoms and problems from the national palliative care symptom management guidelines for individual symptoms. For example, referral to other health care providers is recommended for patients experiencing anxiety and sleep disorders.

Our goal is that in the future versions of the MuSt-PC tool, symptom assessment and treatment recommendations are tailored to optimize symptom management.

For example, through collection of patients- and disease characteristics in the CDSS, symptom clusters could be adjusted depending on the patient's expected survival or underlying illness. However, legislation on the processing of patient data is an important barrier to achieving this goal. This way of generating evidence with data that are already automatically collected in clinical patient care ('big data'), may optimize symptom assessment and treatment strategies for patients with palliative care needs. These patients are difficult to include in clinical trials due to their vulnerability (89). Also, palliative care research often faces problems due to perceptions such as that patients with palliative care needs are less capable of understanding research, or that participating in research is an inappropriate intrusion at the end of life (90). A prerequisite for using big data to update the MuSt-PC tool would be that it is linked to the electronic patient record, to ensure that input entails actual patient data.

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