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General Discussion

The overall purpose of this thesis was to contribute to the body of literature regarding the role of patients' expectations in treatment outcomes. In the general introduction (Chapter 1) we identified four themes deserving of more attention in the field, namely: 1) the definition, typology and measurement of patients' expectations, 2) the determinants of patients' expectations, 3) the relationship between different types of expectations and treatment outcomes, 4) the mechanisms that relate patients' expectations to treatment outcomes. Several knowledge gaps related to these themes hamper the use of the construct to improve the effectiveness of medical treatments. In the subsequent chapters we used data from several patient populations mostly with musculoskeletal disorders undergoing different treatments to investigate a number of research questions related to the abovementioned themes. In this final chapter we summarize and discuss the results from the studies reported in Chapters 2 to 9 per theme. Based on these results and previous literature we present a refinement and extension of Crow et al's¹ preliminary conceptual model and propose recommendations and suggestions for future clinical research on patients' expectations. We would have liked to represent all possible relationships between the determinants, types of expectations, mechanisms and outcomes in one figure. However, this would yield an unreadable figure. Therefore, the refinements of Crow's model are presented schematically per theme. In appendix 1 the full model is shown, however without the lines connecting the determinants, types of expectations, mechanisms and outcomes. In all of the figures the black squares with bold font represent the concepts that were measured or used in the studies in this thesis, while the squares with non-bold font were based on suggestions from other theoretical frameworks and empirical literature. The solid lines represent (statistically significant) relationships between concepts in the model derived from the studies in this thesis, the dotted lines represent relationships that were studied in this thesis but found to be non-significant.

Theme 1 Definition, typology and measurement

In the qualitative study described in Chapter 2² we studied how low back pain patients themselves conceptualize the expectation construct. We found that patients have expectations related to many different aspects of their care and their outcome. Expectations could be categorized as either outcome (e.g. the patient expects relief of pain) or process related (e.g. the patient expects the practitioner to use certain treatment techniques) and were either value oriented (expectations expressed as 'hope', 'wish', 'want', 'like') or probability oriented (expectations expressed as 'probability', 'prediction', or 'likelihood'). The main categories of outcome expectations, and process expectations encompassed multiple subdomains that more specifically describe different facets of these expectations. Outcome expectations consisted of the subdomains; pain relief, activities of daily living, biomechanical functioning, motivation, self-management/prevention and general recovery. Process expectations consisted of the subdomains; information/education, self-management/prevention, treatment content, provider interaction and treatment setting. The preliminary model by Crow et al¹ also distinguishes expectations about the process from those related to the outcome of care, but adds self-efficacy

expectations to the typology of expectations. Self-efficacy expectations were however rarely reported in our interviews. We categorized self-efficacy and motivation-related expectations as one subdomain of outcome expectations. We did this as the patients articulated that an improved confidence in maintaining the behavior necessary to prevent future complaints was something they would expect to have gained as a result of treatment. It however may be that self-efficacy expectations are not expectations that patients themselves articulate easily without being specifically queried to do so.

Our results are in line with the findings of Hsu et al³ who found that patients talked about both hopes and expectations when being queried about what they would expect from low back pain treatment. Both Hsu et al's and our study partly confirm Kravitz⁴ framework, which distinguishes value expectations and probability expectations. For most of the subdomains, patients expressed value expectations more often than probability expectations, that is, they more readily spoke about what they hope will happen as opposed to what they predict will actually happen. Furthermore we noticed that some patients had difficulties expressing probability expectations. One reason for this could be that the interviews took place before the treatment had started, just after randomization. At this point in time, patients had had no interaction with their practitioner and thus could not develop expectations based on the information and education by the practitioner. Another possible explanation is that patients are sometimes reluctant and afraid to express their (positive) expectations because of concern about jeopardizing future positive outcomes³. We also observed that many patients expressed both value and probability expectations within one subdomain. For example one patient stated: *"I hope that it [back pain] goes away totally, indefinitely. But over time I'll kinda degenerate and go back into the same... same cycle....which is, you know, it'll go back to having, the low back pain will"*. While for some patients the nature and strength of these two different expressions was similar, for others there was a clear difference between they would hope or wish to happen and what they thought most probably would happen (e.g. I hope for a complete recovery, but most probably I will only experience a small benefit from treatment). Our findings were in line with the theoretical model of Leung et al⁵ which suggests that the higher the perceived probability of the hoped for or preferred outcome, the greater the similarities between value and probability expectations.

We observed that expectations were often articulated as hopes, needs or wishes, which mirrors debate in the literature about whether value expectations (or hopes) and probability expectations belong to the same or separate constructs^{4,8}. This finding inspired us to look more closely at constructs that stem from different theoretical and empirical backgrounds but seem to have some definitional overlap with, or are closely related to expectations, namely; credibility, optimism, pessimism and hope in Chapter 3. We specifically aimed to investigate with confirmatory factor analyses whether measurement instruments that are currently used to measure these constructs, the credibility expectancy questionnaire (CEQ) for outcome expectations and treatment credibility^{9,10}; the life orientation test-revised (LOT-R)^{11,12} for optimism and pessimism and the Hope scale

(HS)¹³ for hope are able to distinguish between these constructs. Model 1 hypothesised a full differentiation between the five constructs treatment credibility, treatment expectancy, hope, optimism and pessimism. Thus items of each construct was forced to load on a separate factor. Model 2 hypothesised a differentiation between four constructs. Treatment credibility, treatment expectancy and hope items were forced to load on separate factors, but in this model the optimism and reverse-scored pessimism items were forced to load on one factor as it is controversial whether LOT-R has a uni- or bidimensional structure^{12,14}. Model 3 hypothesised a two factor structure in which the optimism, pessimism and hope (LOT-R and HS) items were forced to load on one factor representing 'generalized positive beliefs about the future' and the treatment credibility and treatment expectancy (CEQ) items were forced to load on one factor representing 'treatment specific beliefs about the future'. This model was tested because of the theoretical plausibility that patients may have general and situational, in this case treatment specific, beliefs about the future. Model 4 hypothesised that treatment credibility, treatment expectancy, hope, optimism and pessimism items load on a single underlying latent factor. This model tested the proposition that optimism, pessimism, hope, treatment credibility and treatment expectancy are not distinguishable at all, in which case the data should fit this one factor model. These analyses showed that the five factor model (model 1) fit the data best. However, strong correlations were found between the expectancy and credibility factor, and between the optimism and hope factors. Therefore a post hoc a bi-factor model was tested in which besides the five separate factors there is a general factor that accounts for the commonality between the items of the separate constructs showed the best fit to the data. This bi-factor model showed a significantly better fit than the five factor model indicating that the measurement instruments used are able to distinguish between the 5 constructs, but that there is some shared variance that should be accounted for when assessing the constructs simultaneously. Similar studies have been performed in the psychological literature^{7, 8, 15, 16} and also found that the constructs were related but distinguishable, however these studies mostly only included the constructs optimism, pessimism and hope or hope and expectations. Credibility was not included so far and the five constructs were never studied together.

Refinement of the preliminary model by Crow et al.

Figure 1 represents the refinements of Crow's model related to theme 1. As different types of expectations may have differential effects on outcomes we suggest that the refinement of Crow's preliminary model should at least distinguish three types of expectations namely expectations about the process of treatment, expectations about the outcome of treatment and self-efficacy expectations. We suggest that in the measurement of expectations a clear distinction should be made between probability expectations and value expectations for outcome expectations and process expectations. Specifically the distinction between value and probability expectations is not captured by current measurement instruments of expectations. For example if patients are asked to rate the following item: 'how much do you expect your back pain to have changed after treatment?' one patient may refer to probabilities while another refers to its hoped for or

preferred outcome. We strongly encourage use of multi-item measurement instruments as single-item measures are unlikely to capture the complexity of the construct.



Figure 1. Extension of Crow's model: types of expectations.

Theme 2 Determinants of expectations

If we want to maximize utility of the expectations construct in clinical practice it is important to know which factors contribute to the construction of expectations regarding medical treatment. Crow et al's¹ preliminary model distinguishes four types of determinants of expectations: factors related to the patient, to the professional, to the patient-practitioner interaction and to the treatment and setting. In the qualitative study in Chapter 2 we explored which factors low back pain patients themselves thought had influenced their expectations. We found that previous experience of patients was the most important determinant of expectations. These findings correspond to social cognitive theories^{17, 18} and previous empirical literature¹⁹⁻²¹. In Crow et al's¹ preliminary framework this factor would fit into 'factors related to the patient'. In our study it was apparent that these prior experiences predominantly influenced the expectations expressed as probabilities, but not those expressed as values. Further, this influence of previous experience was the largest if the patients had had the exact same treatment before. When the previous experience was even slightly different (e.g. previous experience was exercise in a gym for low back pain and current treatment is exercise supervised by a physiotherapist) the influence of the previous experience on expectations was much

less. In contrast, Iles et al²⁰ found that the whole lived experience of a patient influenced expectations for low back pain treatment. Other determinants that could be categorized as ‘factors related to the patient’ were preconceived beliefs and assumptions of patients. In our study we categorized statements of patients as ‘beliefs and assumptions’ if patients did not mention a specific source for these statements. For example one patient did not expect long term pain relieve because his belief was that once you have back problems you never will live without them, without referring to the specific source of those beliefs. However, this category may very well be an intermediate variable that lies between determinants like previous experiences or influences from external sources and the types of expectations. For example if a patients hears an expert on television say that once you have back pain you will most probably never get rid of it, this patient may adopt this belief, which in turn influences his expectation for the outcome of a specific treatment. Other studies have considered patient characteristics (gender, age, and socio economic status)^{22, 23}, current disease status^{22, 24-26} and psychosocial factors (e.g. mental health, generalized optimism and fear)^{27, 28} as patient related determinants of expectations. However, so far except for previous experiences, none of the determinants have been consistently associated with expectations. For example, within total knee and total hip arthroplasty some studies report that a better pre-operative clinical status (function, pain, general health) is associated with more positive expectations while other studies report that worse clinical status preoperatively is associated with more positive expectations²⁹.

In line with Crow et al’s model¹ we found that the type of treatment proposed and setting of the treatment (e.g. the fact that the consultations were in a university clinic was a reason to have positive expectations for the treatment process as well as outcome) also influenced expectations of a small proportion of patients. We also found that experiences of family and friends, and information from various sources like media influenced patients’ expectations. The influence of such external sources have been shown in other studies as well²¹, although they do not fit the categories defined by Crow et al very well as they entail influences not related to the patient nor the practitioner. While the determinants in Crow at al’s categories ‘factors related to the practitioner’ and ‘factors related to the interaction between patient and practitioner’ such as medical rituals, alliance, suggestions and education have been confirmed by other studies³⁰⁻³³, patients in our study did not consider the information, education and interaction with the practitioner as a source of their expectations. The reason for this is that the interviews and expectation assessments were done prior to the start of treatment and therefore practitioner related factors could not have had an influence yet. However, one could also argue whether information from and interaction with the practitioner is a determinant of expectations or a mediator of change in the baseline or pretreatment expectations. Hence, the determinants of expectations identified by a particular study may also depend on the timing of the assessment of expectations in that study.

Refinement of the preliminary model by Crow et al.

Figure 2 represents the refinements of Crow’s model with respect to theme 2. We suggest that Crow’s model should be expanded to include a number of patient-related determinants; previous experiences, preconceived beliefs and assumptions, patient characteristics, mental health and current disease status. Further, we suggest adding an additional category of determinants to encompass external influences consisting of experiences of family and friends, and information from media and other external sources. In Figure 2 lines were drawn between the determinants and the types of expectations found to be related in the qualitative study described in chapter 2. Future research should investigate whether the determinants of expectations are dependent on the type of expectations measured, the type of treatment proposed and the timing of the expectation measurement. Furthermore, much of the research on determinants of expectations is qualitative in nature, quantitative research is necessary to determine which variables are the strongest determinants of expectations.

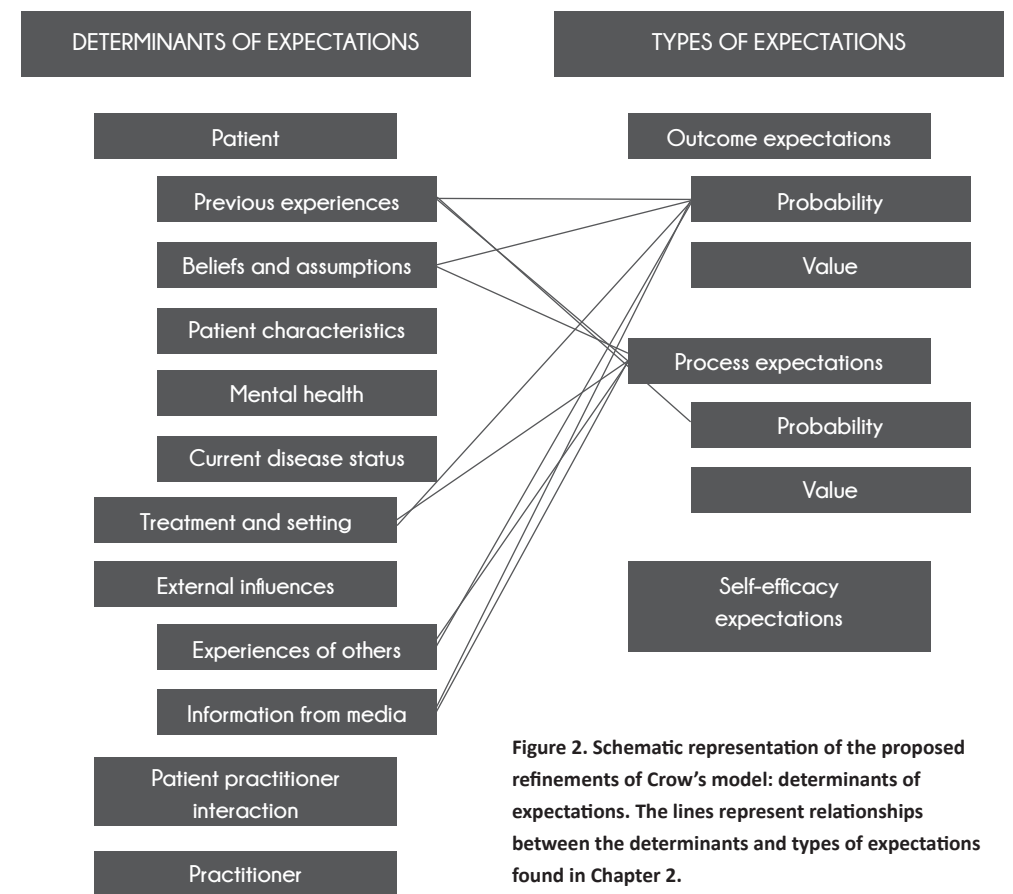


Figure 2. Schematic representation of the proposed refinements of Crow’s model: determinants of expectations. The lines represent relationships between the determinants and types of expectations found in Chapter 2.

Theme 3 the relationship between patients' expectations and treatment outcomes
 Many clinical studies suggest that patients' expectations about their outcome play an important role in clinical outcome in a range of conditions^{1,34}, including musculoskeletal disorders^{19,35,36}. Understanding the nature of the relation between patients' expectations and treatment outcomes may be helpful clinically in a number of ways. In particular, clarifying the role of expectations as a prognostic factor for treatment outcomes and/or as a treatment effect modifier offers potentially very useful information. Below we discuss the findings of the studies in this thesis with respect to these two roles. We also sought to explore some possible sources that may explain the large variations found in the clinical literature regarding the association between patients' expectations and treatment outcomes.

Patients' expectations as a prognostic factor for treatment outcomes

If baseline expectations are associated with later outcome, patients' expectations are potentially relevant in giving individualized prognostic advice to patients. In this thesis we attempted to gain more insight about the possible prognostic role of expectations in Chapter 6 (TKA/THA patients), Chapter 7 (neck pain patients) and Chapter 8 (diabetes patients). Prognostic (or predictive) variables are most useful in clinical practice if they add predictive value to already known predictive factors that are already part of routine consultation. Therefore we examined the predictive value of (baseline) expectations above and beyond other commonly-collected clinical, psychological and demographic predictive variables for the outcomes of global perceived effect, pain and disability (Chapter 7) and for quality of life and HbA1c (Chapter 8). In Chapter 6 we took a slightly different approach by assessing whether patients' expectations about treatment outcomes of TKA and THA had predictive value for the outcomes pain and function when regarded as one of the candidate predictive variables alongside other clinical, psychological and demographic variables. We showed that patients' expectations were part of the final prediction models for all outcomes in both TKA and THA. However, it is worth noting that the total amount of variance in outcome explained by the prediction models was relatively low (ranging between 17.0% and 30.3%) of which between 1.3% and 6.5% was explained by expectations alone. In Chapter 7 we found that outcome expectations measured with the expectancy subscale of the credibility expectancy questionnaire (CEQ) consistently added a significant amount of predictive value to a range of clinical and demographic variables in predicting all outcomes at short term (7 weeks after baseline) and medium term (26 weeks after baseline) for patients undergoing physiotherapy or manual therapy for neck pain. In this study the amount of variance in outcomes explained by expectations alone ranged between 5.6% and 17.7% for the total group of patients (manual therapy and physiotherapy). Interestingly, other psychological variables that also have been hypothesized to be related to outcomes in musculoskeletal disorders like locus of control³⁷, fear avoidance beliefs^{38,39} and treatment credibility⁴⁰ did not predict outcomes in our study. It seems that, at least for this population, expectations of treatment outcome are the most important psychological predictive variable. In Chapter 8 we assessed whether baseline

illness perceptions were associated with changes in health related quality of life and HbA1c (a marker of blood glucose levels over the past three months) in recently diagnosed type 2 diabetes mellitus patients. More specifically we studied the types of illness perceptions about how long the illness will last, perceptions about the health consequences of type 2 diabetes mellitus, perceptions about how well one would be able to perform the behavior necessary to control the disease (self-efficacy expectations), perceptions about how effective the proposed treatment would be (outcome expectations) and perceptions about the course of symptoms. We found that these variables were not predictive of the abovementioned outcomes, when assessed above and beyond other important variables like comorbidities, BMI, gender, age and education level. Thus, in this thesis baseline expectations were predictive of outcomes for treatment of neck pain and TKA and THA but not for outcomes of diabetes treatment. In all of our studies that examined baseline outcome expectations as a predictor of later outcome the direction of the effect was similar. The more positive (or 'higher') the expectation, the more positive the outcome (for example less pain or increased function).

Patients' expectations as a treatment effect modifier

Most of the theoretical models described in chapter one of this thesis, suggest that expectations are be causally related to outcomes, offering the possibility for clinicians to attempt to change expectations of their patients in order to enhance clinical outcomes. In multiple experimental placebo studies in which expectations were induced with verbal suggestions, medical rituals or conditioning procedures it indeed was shown that the groups with heightened expectations of pain relief actually experienced more pain relief when a placebo was administered as compared to the groups without heightened expectations. Most of these studies however were done in laboratory settings with primarily healthy students as research subjects and with acute pain stimuli like cold or hot pressor tasks^{40,41}. Clinical research shows other results; a series of systematic reviews assessed the strength of the placebo effect in clinical trials with three arms by comparing the no treatment or usual care groups with the placebo group and found very modest placebo effects for subjective outcomes and no effects for objective outcomes^{42,43}. Moreover, in 2001 DiBlasi et al⁴⁴ systematically reviewed all randomized controlled trials that aimed to study the effect of contextual factors on treatment outcome. One of the 25 studies in the review specifically targeted enhancing outcome expectations and 18 other studies examined the effect of interventions that potentially influenced the expectation of patients, the other six studies examined context effects that were not related to patients' expectations. Examples include randomizing patients to different levels of positivity of the consultation, different levels of diagnostic certainty and treatment (clear diagnosis and treatment versus uncertain diagnosis and treatment) or presenting information on side effects in various ways. Ten of the 19 studies found a significant difference between outcomes in the treatment groups, with low quality studies more often reporting a positive intervention effect. Most of the studies included in DiBlasi's review were performed between 1950's and the 1990's and did not measure whether their intervention actually changed the patients' expectations. Hence, no firm conclusions can

be drawn about whether modification of expectations leads to improved outcomes in clinical settings. In orthopedic surgery Mancuso et al conducted a randomized controlled trial to test whether expectations could be modified by delivering a specific education module designed to address patient expectations for long-term recovery. They found that patients' preoperative expectations about postoperative recovery could indeed be successfully modified, however they did not test whether those altered expectations in the intervention group led to better outcomes as compared to the control group that only got usual care⁴⁵. In recent years a small number of new trial protocols of studies that aim to enhance treatment expectations have been published^{46,47}, but the results are not yet available.

Although not definitive, observational studies may also give an impression of whether changes in patient's expectations are associated with changes in outcome. Results of such studies can inform researchers whether it can be valuable to do a clinical trial on modifying expectations. In Chapter 8 of this thesis we performed a longitudinal observational study investigating whether 5 different dimensions of cognitive illness perceptions (that are conceptual similar to outcome and self-efficacy expectations) changed over time in patients that were recently diagnosed with type 2 diabetes. Between the two measurements of illness perceptions (baseline and one month thereafter) a consultation took place with a diabetes nurse who was trained in motivational interviewing. Results showed that there were very small non-significant mean changes towards more positive illness perceptions in some of the domains. However, the change scores showed some variation, suggesting that the perceptions of some patients changed towards more positive, but for others towards more negative perceptions. Only the change in perceptions about the consequences of the diabetes was associated with a change in physical health related quality of life. Patients that believed that their disease had less serious consequences experienced a positive change in physical health related quality of life between baseline and four months thereafter. I participated in another longitudinal study⁴⁸ (not included in this thesis) in low back pain patients receiving care from the general practitioner or chiropractor in Denmark. We showed using latent profile analysis that the majority of patients (80%) maintained a fairly stable level of expectations but differed in how positive their expectations were, a high stable, moderate stable, low stable group was defined. About 15% had decreasing expectations and 5% had increasing expectations. For the groups with the stable expectations the levels of expectations (either low, moderate or high) were relatively well aligned with their outcomes. Those with high expectations throughout experienced the largest improvements and ended up with relatively low symptom levels while those with stable low expectations experienced the smallest improvements and ended up with relatively high symptom levels. For the group (15%) with the decreasing expectations the expectations remained high/stable in the first two weeks while symptoms were improving, but the level of expectations dropped substantially when the rate of improvement decreased. This suggests that expectations may follow the course of symptoms instead of the other way around. Unfortunately, the study did not have sufficient power to investigate this hypothesis in the small subsample

with decreasing expectations. In the total sample no relationship could be established between either an early change in expectations and a later change in outcomes/symptoms, or an early change in outcomes/symptoms and a later change in expectations. This may be due to the fact that for the vast majority of patients their expectations did not change over time. It would be interesting and relevant to investigate this 'chicken or egg question' in another sample. These two studies suggest that expectations do not change very easily following the sort of interventions delivered as part of usual care for the majority of patients. It also may be that the measurement instruments used were not sufficiently responsive to measure changes in expectations. If the first is true then specific interventions targeted at creating appropriate expectations may be needed.

To develop interventions that influence expectations, it is necessary to know which expectations are (in)appropriate. In Chapter 5 we attempted to determine which expectations are inappropriate for outcomes of TKA and THA. More specifically, we studied the expectations for a wide range of very specific function and pain outcomes (e.g. expectation for improvement in walking upstairs) in a sample of patients undergoing TKA or THA and whether each of these expectations were fulfilled one year after surgery. Expectations that are not fulfilled after treatment may be regarded as inappropriate expectations. One possible intervention strategy may be to preoperatively address the expectations that have a high probability of remaining unfulfilled after treatment in preoperative education. For TKA and THA we showed that expectations for the outcomes of surgery were in general very high, most patients expected to have large improvements or even return to their 'normal' level of ability. Most of these high expectations were fulfilled for the majority of patients, thereby indicating these high expectations are appropriate. We were able to identify a number of expectations that were commonly (>30% of patients) unfulfilled after surgery. For TKA the expectations about being able to kneel down and being able to squat were unfulfilled most frequently (In respectively 44% and 47% of patients) and for THA the expectations about walking long distances, walking stairs and ability to cut toenails (in respectively 31%, 33% and 38% of patients). These results align with several other studies that measured expectations prior to TKA and THA^{49,50}. This may have implications for orthopedic surgeons who could decide to pay extra attention to those expectations that were not fulfilled in their preoperative consultation.

Sources of variation in the association between patients' expectations and treatment outcomes

Although the positive association between expectations and treatment outcomes has been widely suggested^{24,35}, findings in clinical studies have not consistently supported this assumption. Some studies conclude that there is no statistically significant relationship or predictive value of patients' expectations or even report a negative relationship²⁵. Investigating what the possible sources of this variability in associations are may provide more insight as to which expectations relate to which types of outcomes, under which circumstances. For example, it may be that self-efficacy expectations are specifically linked to behavior, but not directly to pain and that expectations about the treatment

process are related to post-treatment satisfaction, but not to behavior. In Chapter 4, in a systematic review we aimed to investigate and summarize the relationship between three types of expectations (treatment outcome expectations, expectations about the treatment process, and self-efficacy expectations) and five outcomes (pain, function, stiffness, general perceived effect, and satisfaction) relevant to patients undergoing a TKA or THA. None of the included studies measured expectations about the care process and thus only studies assessing outcome expectations and self-efficacy expectations were included in the systematic review. We did not find consistent relationships between any of the types of pre-operative expectations and any of the five types of outcomes. The most promising associations were found between self-efficacy expectations and postoperative pain and function, and between outcome expectations and postoperative pain and function. Even within these comparisons however, studies showing positive and studies showing no association were found. Therefore we cannot draw firm conclusions about which specific type of expectations is related to which type of outcome. Corresponding with our results Waljee⁵¹ et al. found no consistent relationship between outcome expectations and 5 different types of patient reported outcomes (satisfaction, quality of life, disability, mood disorders and pain) in a systematic review including a range of surgical treatments. For all outcomes combined they found that 28 out of the 60 studies (45%) found a positive association, 20 studies found no association and 14 studies found a negative association between preoperative expectations and postoperative outcomes. A systematic review by Dyck et al²⁹ found that probability expectations were consistently positively associated with disease specific outcomes like the WOMAC score in all 5 included studies. However, probability expectations were positively associated with general health (SF-36) outcomes in only one study and no association was found in the other four studies. The review concluded that value expectations were not consistently associated with outcomes, although only one study measured value expectations. Hence, the suggestion that probability expectations are associated with outcomes while value expectations are not needs further confirmation within as well as outside of orthopedic surgery. In our own systematic review we also sought to explain the variability in associations found by considering the timing of the outcome measurement (<6 weeks; 6 weeks - 6 months and > 6 months), the methodological quality of the studies included in the review and whether the studies adjusted for confounding factors in their analyses. None of these possible sources of variation however seemed to explain the variability found in the results between the individual studies in the review. Besides the different types of expectations and different types of outcomes there may be other factors that could explain the variation in the associations between patients' expectations and treatment outcomes. Iles et al³⁶ for instance suggested that the specificity of the measurement used to measure expectations is a possible source of variation in the relationship between expectations and outcomes. They found in their systematic review on the association between expectations about their recovery and outcomes in low back pain patients that the more specific measurements of expectations showed a larger associations with the outcomes. For example one study found a strong association between the expectations and return to work and used the following item: Will you be able to do your regular job without any restrictions 4

weeks from now?⁵² While another study that asked 'do you believe your complaints will improve?' showed a much weaker relationship with outcome⁵³. We attempted to replicate the findings of Iles et al in Chapter 6 of this thesis in a sample of patients undergoing TKA or THA who completed two validated expectation measurement instruments, the credibility expectancy questionnaire^{9, 10} and the hospital for special surgery total hip and total knee arthroplasty expectation surveys⁵⁴. The credibility expectancy questionnaire (CEQ) expectancy subscale is more general in nature and contains items like 'how much improvement in your symptoms do you feel will occur after having your total hip or total knee replacement' whereas the hospital for special surgery knee or hip replacement expectations surveys contain items related to more specific functional abilities and activities for example 'How much relief or improvement do you expect in walking upstairs as a result of hip or knee replacement surgery'. In contrast to Iles' findings we found that the more general measure of expectations (CEQ expectancy subscale) explained a slightly larger amount of variance for both the outcomes pain and function. However these differences were too small to prefer the use of either of the two measurements for predicting function and pain in TKA and THA.

Refinements of the preliminary model by Crow et al.

Figure 3 represents the refinements of Crow et al's model based on the results of the studies in this thesis related to theme 3. The solid lines represent the relationships found between outcome expectations (expressed as probability) and the outcomes pain (Chapters 4,6 and 7), function (Chapters 4,6 and 7) and general perceived effect (Chapter 7). Represented by dotted lines in figure 3, in Chapter 8 no associations were found between several types of (baseline) illness perceptions (that show conceptual similarities to outcome expectations and self-efficacy expectations) and quality of life and HbA1c. Based on the studies in this thesis related to theme 3 we suggest that outcome expectations are of value in predicting who will or will not benefit from manual therapy and physiotherapy for neck pain, TKA and THA. We consistently found that patients with more positive expectations are more likely to report better health outcomes. However as the variance in outcomes explained by outcome expectations is limited practitioners should not attempt to predict outcomes based on a patients outcome expectations solely, but rather a range of factors of which outcome expectations are part.

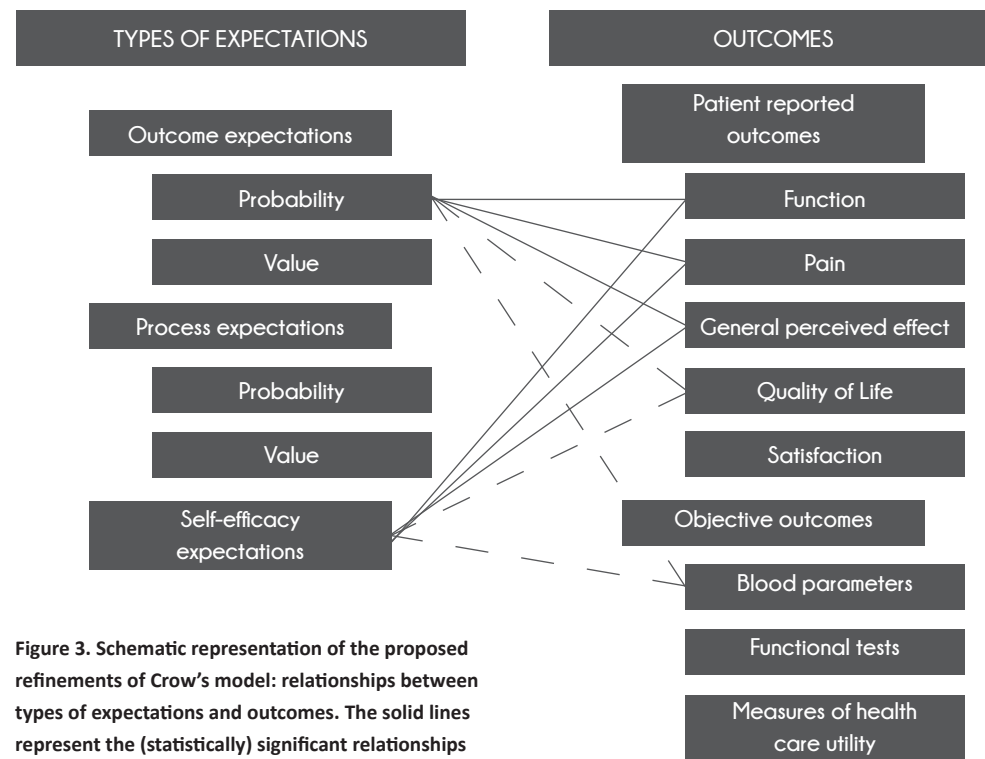


Figure 3. Schematic representation of the proposed refinements of Crow's model: relationships between types of expectations and outcomes. The solid lines represent the (statistically) significant relationships between the types of expectations and the outcomes found in Chapter 4, 6 and 7. The dotted lines represent the non-significant associations found in chapter 8.

Theme 4: the mechanisms through which patients' expectations influence treatment outcomes.

The mechanisms through which expectations translate to health outcomes have been primarily studied in experimental placebo research. For example laboratory research has shown that expectations of pain relief have an influence on the actual pain through the release of endogenous opioids⁵⁵. Besides this physiological pathway Barry Flood et al⁵⁶ hypothesized 4 other mechanisms that may mediate the relationship between expectations and treatment outcomes; 1) conditioning the patient to observe certain types of outcomes and ignore others 2) changing the understanding of the disease 3) acting in concert with anxiety to heighten or reduce symptoms 4) motivation of patients to achieve better outcomes.

The first mechanism posits that positive expectations help the patients focus on what is improved and minimize or ignore unfavorable outcomes⁵⁷. Thereby it is suggested that expectations do not affect actual outcomes, but rather the perception of the outcome. The second mechanism proposes that information and education, whether accurate or not, is important mediator in the relationship between expectations and outcomes. Those with positive/good expectations are more receptive to information that allows them to reconceptualize their disorder, symptoms and perceptions. This mechanism may be influenced by the communication and alliance between the patient and practitioner. Those who have a good alliance may have their expectations altered by the information and education of the practitioner while when there is not a good alliance the patient may be reluctant to accept the explanations and information offered by the practitioner. While seen as a mechanism between expectations and outcomes by Barry Flood, this mechanism can also be seen as a determinant of (informed) expectations. The third mechanism postulates that having positive expectations may reduce anxiety, and a reduction in anxiety and fear can lead to better health outcomes⁵⁸. The fourth mechanism suggests that higher or more positive expectations motivate a patient to cooperate with treatment and to cope with the disease. Patients with positive expectations are more likely to have beneficial coping mechanisms that make them confront their problems and establish control over their situation. Additionally they are more likely to try harder to achieve successful outcomes via their own behavior and therefore more likely to reach them. This suggestion aligns with some of the behavioral models^{17,59,60} that propose that expectations influence health behavior like adherence to treatment recommendations. In Chapter 9 we aimed to test whether higher outcome expectations lead to better adherence to treatment which then subsequently leads to better outcomes. This study made use of data from a large double blind placebo controlled clinical trial on the use of paracetamol for acute low back pain⁶¹⁻⁶³. Before treatment commenced expectations of patients regarding the effectiveness of the proposed treatment (which could either be paracetamol or placebo paracetamol) were measured with the expectancy subscale of the credibility expectancy questionnaire, adherence to the treatment regimen was measured with a daily medication diary, and outcomes were recovery and pain intensity. There was a statistically significant, but small relationship between pretreatment outcome expectations and both outcomes (recovery and pain intensity). However, adherence to treatment only partially mediated the relationship between patients' outcome expectations and the outcomes; 3.3% of the relationship between outcome expectations and recovery, and 14.2% of the relationship between outcome expectations and pain intensity⁶⁴. Based on our results and two other studies that concluded that expectations still had an influence on health outcomes when adherence was controlled for^{65,66} we conclude that adherence to treatment is not likely to be one of the most important mechanisms mediating the relationship between patients' expectations and treatment outcomes for acute low back pain patients. As the participants were taking analgesics (or placebo analgesics) for their back pain, it may be that in this specific population the expression of endogenous opioids have played a major role. Another explanation for the limited mediation by adherence to treatment is that adherence to treatment is a complex behavioral process which can be influenced by

many factors including environmental and organizational factors⁶⁷, and apparently the other factors have had a stronger influence on adherence than expectations for treatment outcome. This explanation corresponds with our finding that the relationship between expectancy and adherence was quite weak, weaker than the associations between expectations and outcome, and adherence and outcome. However as other studies have found stronger relationships between expectations and adherence, specifically in treatment where a large effort is required from the patient himself, such as exercise therapy⁶⁸⁻⁷⁰ it may be that the mediated effect by adherence is stronger for other types of treatment. A mechanism not mentioned by Barry Flood, but suggested by literature related to patient satisfaction is that expectations may be related to health outcomes through having them fulfilled. For instance patients undergoing total knee arthroplasty who reported that their expectations were fulfilled had a significantly higher health related quality of life, and greater improvements in function and symptoms after surgery^{29, 71-73}.

Refinement of the preliminary model by Crow et al

In figure 4 the possible mechanisms through which expectations may influence treatment outcomes are depicted. In the preliminary model by Crow, the possible mechanisms or pathways by which patients' expectations can influence health outcomes are not described. We consider research into these mechanisms as very important as they can provide a better understanding of how expectations may affect treatment outcomes. In this thesis only one of these mechanisms was assessed (Chapter 9). The lines in figure 4 represent the relationships found in this study. In our study adherence was not one of the primary pathway linking patients expectations to health outcomes⁶⁴. However this may be different for other types of treatments or conditions. It is likely that multiple mechanisms interact or simultaneously play a role in translating patients' expectations to health outcomes. It may be that these mechanisms are complex processes encompassing multiple variables that may be modified by other variables, like the type of treatment and patients' characteristics and disease history. Furthermore, these mechanisms may be dependent on the type of treatment and type of outcome measured. Therefore we propose to add candidate mechanisms to Crow et al's model namely: physiological responses, emphasizing beneficial health changes and ignoring others, information and education, anxiety reduction, motivation/adherence and fulfillment of expectations.

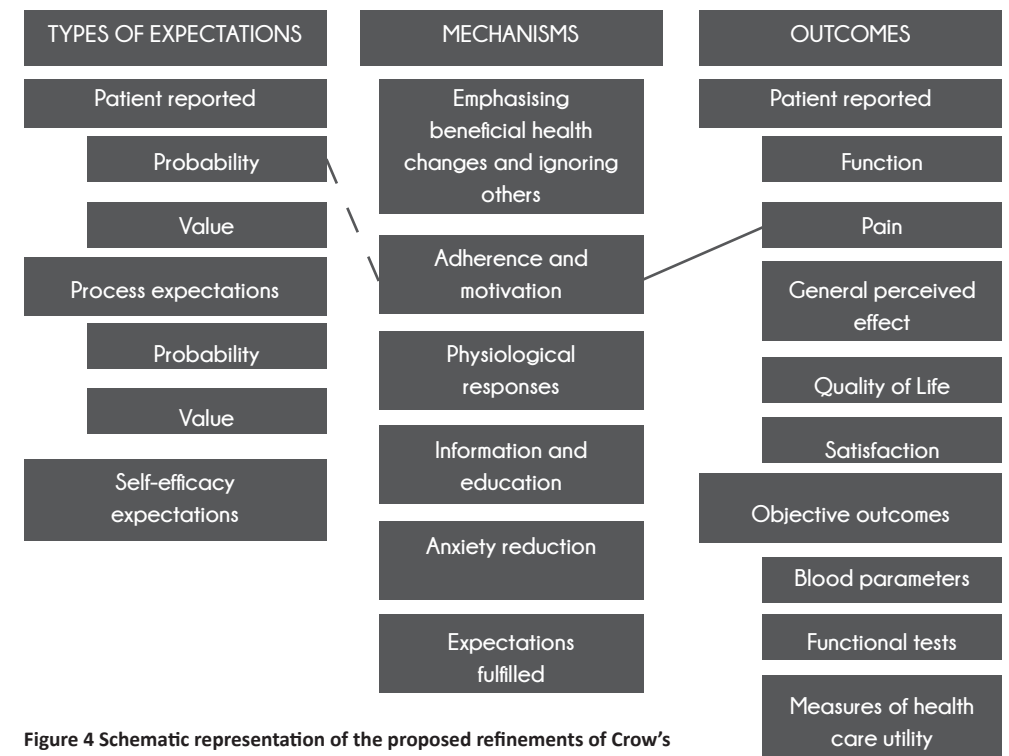


Figure 4 Schematic representation of the proposed refinements of Crow's model: mechanisms between types of expectations and outcomes. The dotted line represents the non-significant relationship between outcome expectations (probability) and adherence found in Chapter 9. The solid line represents the significant association found between adherence and pain/recovery from back pain in chapter 9.

Methodological reflections

The data included in this thesis come from a variety of sources which have various limitations. These limitations should be considered in the interpretation and generalization of the results presented in this thesis.

One limitation that is relevant to all studies in this thesis is the fact that participation in a study may have influenced the expectations of the participants. Aspects like providing information and explanation about the study and treatment are, at least in the Netherlands, more extensive and formal in clinical studies than in regular care. We did not formally assess whether study information influenced expectations, however, in our qualitative study some of the participants mentioned that being in a study had influenced their expectations positively². However, evidence has shown that informed

consent procedures can influence expectations negatively and induce nocebo effects⁷⁴. Furthermore, research shows that expectations for treatment outcome are lower for placebo controlled trials as compared to RCT's with another comparator like usual care⁷⁵. In Chapter 9 of this thesis data from a double blinded placebo controlled trial⁶³ were used and although the expectations were balanced between treatment groups, it may be that expectations were lower than if paracetamol had been prescribed as part of a non-study situation. In Chapters 2 and 7 data from randomized controlled trials was also used. But in these trials patients were not blinded, and expectations were assessed after randomization when patients were aware of the type of treatment they would get. For these two studies expectations may have been more similar to those for the same treatment in a non-study situation. However, in contrast to these negative effects, the group of patients willing to participate in a study may as well be people with relatively high expectations and relatively high degree of adherence to treatment.

The studies described in Chapters 2, 3, 4, 7 and 9 are based on secondary data analyses of randomized trials or longitudinal cohort studies. Secondary data analyses involves 'further analysis of an existing data set which presents interpretations, conclusions or knowledge additional to, or different from, those presented in the first report on the enquiry as a whole and its main results'^{76,77}. The advantages of secondary data analyses relate to time and cost saving, however, there are limitations. The sample size and power calculations of secondary data are based on the primary analyses. Thus there is a risk that the study is underpowered for the secondary analyses. In our studies we tried to take power issues into account by limiting the number of predictive factors in the multivariate models by carefully choosing them based on previous literature and discussions with clinicians about which factors they consider in daily practice. Another disadvantage of using secondary data is that the researcher of the secondary analyses has no or only very limited influence on design related aspects of the study⁷⁷ like the choice of variables measured, the timing of measurement and the measurement instruments. In our studies this resulted in different timing of expectation measurement for some of the studies. In the study in Chapter 7 the measurement of expectations was done after the first treatment session, while in the other studies the measurement of expectations was done before the start of the first treatment session. The treatment rationale and expected prognosis is often explained to the patient in the first treatment session, and may influence the expectations that the patient has, while for the other studies the expectations were relatively naïve. For the studies in Chapters 3 and 7, in which data collection was already ongoing when we developed our research questions, we were able to add only a limited number of questionnaires for the remainder of the study inclusion period. A consequence was that the sample size that could be used for answering the research questions was limited.

Some considerations specifically apply to the qualitative study presented in Chapter 2. The main strength of qualitative research lies in the depth of understanding that it allows⁷⁸. Therefore a qualitative study was appropriate to gain insight into how patients conceptualize the expectations construct and to explore the breadth and range of

expectations with which patients present at the start of treatment. The data used for this study stem from a randomized controlled trial comparing three treatment options for patients with chronic low back pain. For our study a consecutive sample of 77 trial participants was invited for two interviews, one before treatment commenced and one after finishing the treatment. The initial purpose of the interviews was to gain a better understanding of the primary results of the RCT by examining patients' expectations and actual experiences, rather than to address conceptual questions regarding patients' expectations. The interview was semi-structured and after a first broad question patients were asked to think about their expectations related to certain domains (e.g. expectations related to their pain and their daily activities). Furthermore, the interviews were guided by previous work of Kravitz⁴; the interviewers queried about both value expectations and probability expectations in the interviews. Focus on these two aspects may have led to underreporting of the range of expectations expressed and underestimation of the importance of the expectations that were not specifically queried. Another well-established limitation of qualitative research in general is that the findings rely unduly on the interpretation and opinion of the researcher⁷⁹. We attempted to limit the influence of this bias by having analysis done independently by two researchers and randomly checked by a third researcher.

Finally, the terminology and definitions used to describe expectations and related constructs varies widely in the literature, which made it challenging to design a comprehensive search strategy for the systematic review and identify relevant studies for the introduction and discussion sections. Furthermore, we noticed that it was hard to find studies that included patients' expectations (or related constructs) as one of many candidate variables in multivariable models based on the assessment of titles and abstracts of the studies. We may therefore have missed studies that provided an estimate of the association between expectations and outcomes.

Future directions in patients' expectation research

In this thesis several research questions related to the role of patients' expectations in medical treatment for predominantly musculoskeletal disorders were addressed. One of the major issues in expectations research identified in the introductory chapter was the lack of theoretical framing of patients' expectations within a medical treatment setting. Results presented in this thesis lead to some refinements and extensions of the preliminary framework by Crow et al. However still many questions are unanswered. Furthermore the studies in this thesis have highlighted new research questions. In each of the separate chapters of this thesis suggestions for future research related to the research questions of that specific chapter are presented. Below we highlight some suggestions for future research of a more overarching nature.

One consistent finding from previous literature and the studies in this thesis is that patients' expectations are a complex construct with a poor current standard of measurement^{2, 29, 80, 81, 82}. Patients' expectations have many dimensions: expectations have

a definitional orientation (value vs probability), have varying content (process, self-efficacy or outcome related), expectations can be positive, negative or neutral and have a certain magnitude and a level of importance. At this point we do not know which dimensions are most important in which context or in relation to which outcome. Current measurement methods of expectations do not take all these dimensions into account. Future research is necessary to determine whether all the dimensions of expectations can be captured within one measurement instrument. Currently, measurement instruments are often treatment and condition specific and therefore it is difficult to compare and synthesize patients' expectations research across treatments and conditions. It would therefore be interesting to develop a measurement method that can easily be adjusted to fit different treatment, conditions and their relevant outcomes or an item bank of expectations items measured on the same scale. For now, we recommend careful consideration of which dimensions of patients' expectations are of interest and what theoretical rationale sits behind their research hypothesis. Based on these considerations and the clinimetric properties of existing instruments an appropriate measurement instrument can be chosen. If no appropriate instrument exists for the treatment or health condition of interest, existing instruments should be modified or a new measurement instrument developed and clinimetrically evaluated⁸³. We further suggest that researchers report their decisions about which dimensions of expectations to measure, and the accompanying theoretical framework in their publications. This makes it easier to interpret and compare the results of studies. Another important question that remains unanswered is "when to measure expectations?" Expectations regarding medical treatment can be measured before the start of treatment or more after one consultation or, depending on whether the treatment consist of one or more consultations, after a few consultations. This decision has implications for the amount of information the patient has, which may in turn influence their expectations.

One question that has, to the best of our knowledge, not been addressed by previous research is "which expectations are most beneficial?" Without this knowledge it may not be wise to attempt to change expectations, because it is not known what the target is. Although the majority of the studies in this thesis suggest that more positive expectations are associated with more positive outcomes, theoretically there seems to be a contradiction between health services/ patient satisfaction studies and placebo related studies. In the clinical setting it may be that expectations should be realistic and not too high in order to prevent dissatisfaction in the event that expectations are not met, while experimental research suggests that expectations should be high, or very optimistic in order to fully benefit from the 'placebo effect'. Perhaps optimistic realism or realistic optimism may be the appropriate balance between preventing dissatisfaction and optimizing context effects. Finally, large intelligently designed studies are needed to study the complete process from the determinants of expectations to the final outcome assessments. In those studies multiple types of expectations should be measured at multiple time points, and several possible mechanisms should be assessed. These quantitative studies should be complemented with qualitative studies to better understand

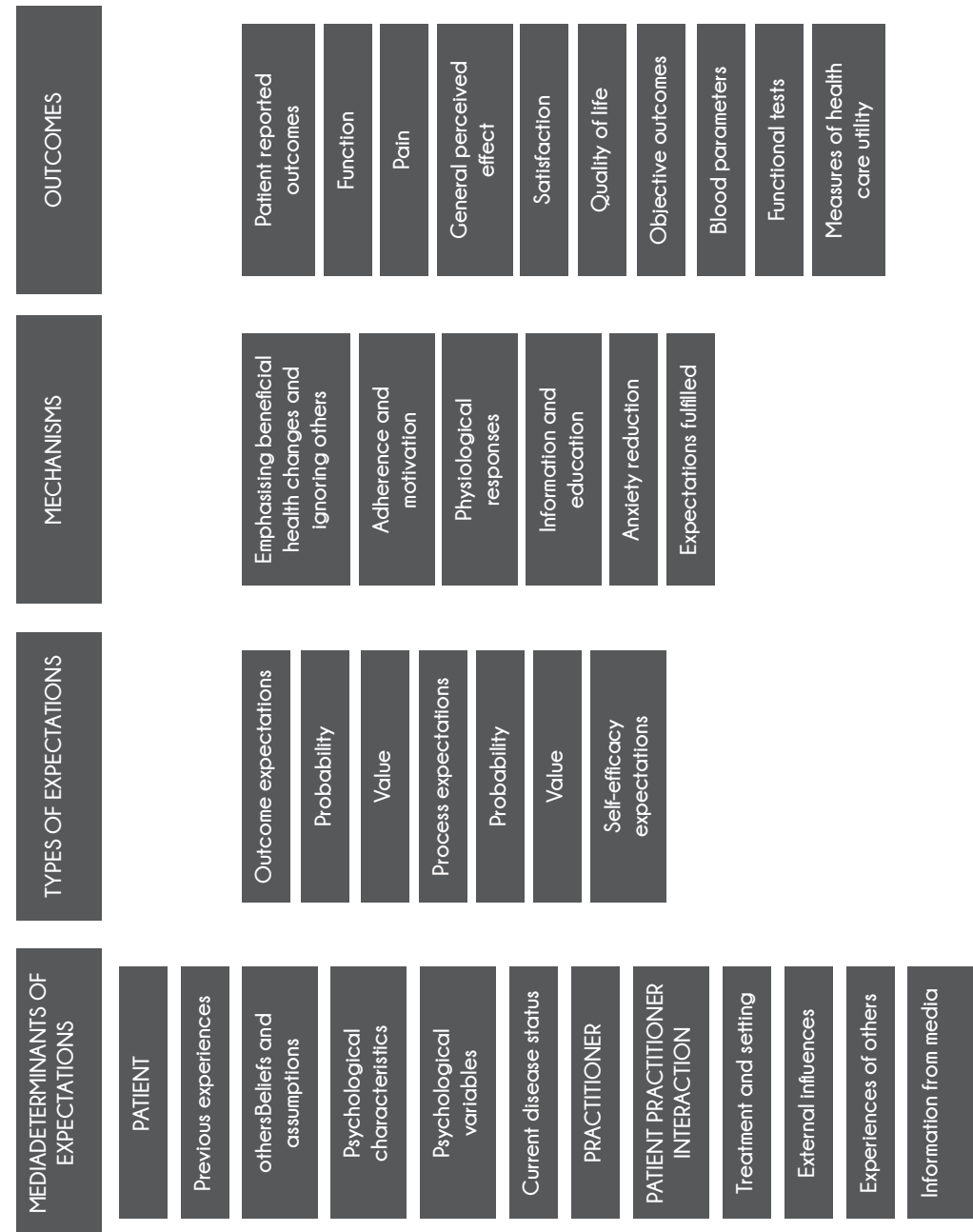
how different types of expectations change over time during the course of treatment. The studies in this thesis may contribute to the design and theoretical frameworks behind such studies.

Concluding remarks and implications for clinical practice

The literature on expectations is very heterogeneous with respect to (amongst others) the terminology used, type of expectations assessed, measurement instruments used to assess expectations, types of outcomes assessed, the type of treatments studied and the theoretical frameworks used. In an attempt to promote uniformity in future research we proposed an refinement and extension of the preliminary model by Crow et al. Although our refinements make the model more complicated, this refined and extended model does provide guidance for future research. Furthermore, attempting to refine this model also led to many new/still unanswered questions.

The studies in this thesis showed that for several conservative and surgical treatments for musculoskeletal disorders (back pain, neck pain and osteoarthritis) patients' (probability) outcome expectations are predictive of treatment outcome. This predictive value exists above and beyond baseline clinical status, demographic variables and other psychosocial factors. Although the direction of the effect was consistent (the more positive the expectations the better the outcome), the contribution of patients' expectations to the variance explained in outcomes was limited in most studies. Still, we think that routinely assessing patients' expectations in clinical practice is advisable because besides this predictive role discussing patients' expectations has more functions in a treatment setting. Assessing and discussing patient's expectations may also valuable for patient-practitioner communication and shared decision making. However, practitioners should not attempt to predict outcomes based on a patients outcome expectations solely, but rather a range of factors of which outcome expectations are part. We believe that at this moment it is too soon to recommend specific interventions to alter expectations during treatment in order to achieve better outcomes. Although experimental research shows that such interventions may be promising, translations of these findings to feasible and effective interventions for clinical practice is not easily done. Future research has to establish which expectations are most beneficial in which situations and for which outcomes.

Appendix 1. The full model of determinants, types of expectations, mechanisms and outcomes.



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