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## **Anxiety in older adults: prevalence and low-threshold psychological interventions**

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## SUMMARY AND GENERAL DISCUSSION

This doctoral thesis aimed to contribute to the understanding of anxiety in later life by examining questions related to its prevalence and psychological treatment. This chapter summarizes and discusses the main findings. We will also address the strengths and limitations of the studies and discuss their implications for future research and clinical practice.

## **1. Prevalence of anxiety in later life**

### **1.1. Summary**

**Chapter 2** contained a systematic review and meta-analysis of studies into the prevalence of anxiety in older adults. The study had a two-fold aim: 1) to compare prevalence rates for subthreshold anxiety and anxiety disorders in adults aged 55 years and over and 2) to examine if prevalence rates varied between different age groups of older adults. Statistical comparisons of the prevalence rates for subthreshold anxiety and anxiety disorders indicated that subthreshold panic, generalized anxiety and specific phobia were significantly more prevalent than the corresponding full-blown disorders. For the other types of anxiety, no statistically significant difference was found between the rates for subthreshold symptoms and the full-blown disorders. To examine if and how prevalence rates for anxiety disorders change throughout the later life span, pooled prevalence rates for four age groups of older adults (55– 64, 65–74, 75– 84, 85+) were compared. For specific phobia, the 75-84 and 85+ groups had significantly lower prevalence rates than the 55-64 and 65-74 groups. We also found that posttraumatic stress disorder was significantly more prevalent in the 55-64 group than in the other age groups, and significantly lower in the 85+ group. No other significant differences between age groups were found. Importantly, only a small number of studies could be included in the statistical analyses and heterogeneity between the reported prevalence rates was large.

### **1.2. Discussion**

Based on the currently available scientific literature on the topic, it can be concluded that subthreshold anxiety in older adults is a subject worthy of scientific and clinical attention. First, as indicated by the meta-analysis in chapter 2, subthreshold forms of anxiety appear to be at least similarly prevalent to full-blown anxiety disorders in older adults. Second, subthreshold anxiety can be clinically relevant, because it is comparable to full-blown anxiety disorders in terms of its associations with multiple

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negative health outcomes [22]. It is clear that considering anxiety in later life only in terms of DSM anxiety disorders hinders a comprehensive understanding of the phenomenon and may result in the underdetection and undertreatment of a large group of older adults with clinically significant anxiety symptoms.

The high heterogeneity of the studies that reported prevalence rates for subthreshold anxiety is probably largely due to the fact that none of the studies operationalized subthreshold anxiety in the same way. However, establishing an empirically based consensus on the operationalization of subthreshold anxiety might be challenging. When attempting to define subthreshold anxiety, one runs into the so called ‘double threshold problem’ [318]. As stated before, the problem with the current diagnostic threshold for full-blown clinical disorders is that it excludes a large group of older adults with subthreshold but clinically relevant conditions. However, an undifferentiated lowering of the threshold could result in a medicalization of everyday life, an enormous increase in health care costs and less resources for seriously ill individuals. Thus, a second empirically defined threshold is required: one that defines normal mental health in older adults. Subthreshold anxiety would then refer to anxiety that is more severe than ‘normal everyday anxiety’, while not meeting the criteria for an anxiety disorder.

A seemingly straightforward way of separating subthreshold anxiety from normal anxiety states in older adults might be a clinical relevance criterion. Most anxiety disorders described in the DSM contain a ‘clinical significance criterion’, which implies that symptoms must cause distress or impairment in social, occupational, or other important areas of functioning. It has repeatedly been argued -especially in relation to subthreshold depression- that the clinical significance criterion does not have much added value in discriminating full-blown disorders from normality, because the severity and number of symptoms required for a diagnosis often already imply a considerable level of impairment and/or distress. However, subthreshold anxiety can consist of less severe symptomatology and/or a less strictly defined number of symptoms. Therefore, to separate individuals with clinically relevant subthreshold anxiety from people with normal anxiety states, the distress and/or impairment criterion could be used [318]. Subthreshold anxiety would then refer to functionally impairing anxiety symptoms that do not meet all symptom criteria for a full-blown disorder. Interestingly, some of the studies included in the meta-analysis in chapter 2 defined subthreshold anxiety as the presence of one or more of the symptom criteria of an anxiety disorder, without it meeting the distress or impairment criterion. Such definitions might result in an overestimation of the number of older adults with clinically relevant anxiety symptoms.

Of course, determining whether somebody is functionally impaired as a result of anxiety symptoms is also not perfectly clear-cut. Clinicians should be aware of older adults being less likely to describe themselves as disabled by psychological problems than younger adults [90]. Furthermore, 'functional impairment' may mean something different for people in different age categories [90]. Determining whether anxiety symptoms in later life are clinically relevant and in need of treatment requires a careful assessment. In any case, clinicians and researchers should not consider anxiety in later life as an all-or nothing phenomenon, but instead as consisting on a continuum regarding the number of symptoms, duration of symptoms, severity of symptoms, and impairment.

Regarding the second aim of the review and meta-analysis, we found that for specific phobia and PTSD prevalence rates decreased with age and that for most anxiety disorders the lowest rates were observed in the oldest-old groups (85+). Age thus seems to be related to anxiety disorder prevalence, but we can not draw firm conclusions about this association because we could not distinguish the effect of chronological age from the influence of other important factors (cohort effects, methodological differences between studies, sample differences). As expected, heterogeneity of reported prevalence rates was not adequately explained by age-category only. That is why we aimed to explore interactions between age and other relevant study- and participant factors, which was unfortunately precluded by the limited amount of reported information in the included articles. We therefore encourage future epidemiological studies in older adults to more elaborately describe their study sample, as this will foster the identification of factors associated with anxiety in later life. Such knowledge enriches the clinical portrait of older adults with anxiety and might improve diagnostic procedures. Variables that have so far been consistently linked to higher rates of anxiety disorders are female sex, non-married status, and having a medical condition [167]. To better understand the role of age, studies should more consistently report separate prevalence rates for different age groups. Moreover, longitudinal studies following different cohorts of older adults are necessary to disentangle age effects from cohort effects.

### **1.3. Limitations and strengths**

An important limitation of the systematic review and meta-analysis is the limited generalizability and power of the findings as a result of the small number of studies that could be included in our analyses. Furthermore, we could not examine the association between prevalence rates of subthreshold anxiety and age, and the interaction effects

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between age and other relevant characteristics, because very little to no studies were suited to answer these questions. This underscores that most studies into the prevalence of anxiety in later life have not focused on the more nuanced questions related to this topic and that much work remains to be done in this field of study.

The findings of the meta-analysis should be interpreted with caution, and do not allow for firm conclusions due to the high heterogeneity between included studies. While it could be argued that no meta-analysis should be conducted in the presence of large heterogeneity, we think that an integration of available information on a topic should still be preferred over leaving clinicians and scientists to make their own estimation of pooled effect sizes. Our elaborate search procedure resulted in the description and integration of a large number of studies into the prevalence of anxiety in older adults conducted over the last decades. Chapter 2 therefore provides a good overview of this field of study, the shortcomings and gaps in the currently available literature, and topics requiring further scientific attention.

## 2. Psychological treatment of anxiety in later life

### 2.1. Effectiveness of the interventions

#### *2.1.1. Summary*

**Chapter 3** contained the study protocol for the Randomized Controlled Trial (RCT) that compared the effectiveness of a brief blended Acceptance and Commitment Therapy (ACT) intervention to a brief Cognitive Behavioral Therapy (CBT) intervention. The two interventions were provided by mental health counselors working at the general practice. The study was a cluster-randomized trial, which means that randomization took place on the level of the mental health counselor: each participating mental health counselor was randomized to either only provide the Blended ACT intervention or the CBT intervention to participants from their practice. Both interventions consisted of 4 face-to-face sessions that were provided over a timespan of 9 to 12 weeks. In between the sessions, participants in the ACT-condition worked with the online module 'Living to the Full', while participants in the CBT-intervention were given their homework assignments on paper. Adults aged 55-75 years with mild to moderately severe anxiety symptomatology could participate in the study. The RCT included 4 main assessments, consisting of online self-report questionnaires and telephone interviews conducted by trained research assistants: a baseline assessment (before treatment), a posttreatment assessment (3 months after baseline) and two follow-ups

(6 and 12 months after baseline). Furthermore, participants were asked to complete a short online questionnaire multiple times during the intervention. Chapters 4 to 7 reported on the results of this RCT.

**Chapter 4** reported on the comparative clinical effectiveness of the blended ACT and CBT intervention. A total of 314 older adults with mild to moderately severe anxiety symptoms participated in the study, of which 150 were allocated to the ACT intervention and 164 to the CBT intervention. Participants were recruited from 38 general practices across the Netherlands, which employed a total of 40 mental health counselors that were randomized to the ACT (n=20) or CBT (n=20) condition. We did not find a statistically significant difference between the conditions in terms of the primary outcome, anxiety symptom severity as measured with the Generalized Anxiety Disorder-7 (GAD-7). Participants in both conditions showed large reductions in anxiety symptom severity from baseline to posttreatment. At the 6-month and 12-month follow-up, the conditions did also not differ: the reduction in anxiety symptom severity was sustained in both interventions. The trajectories of the secondary outcomes of depression symptom severity and the presence/absence of an anxiety disorder did not differ between the two groups: both groups showed medium to large improvements from baseline to posttreatment, that had sustained at the 12-month follow-up. Two statistically significant differences were found, both in favor of the blended ACT intervention. First, from posttreatment to 1-year follow-up, positive mental health decreased in the CBT group, but increased in the ACT group. Second, posttreatment treatment satisfaction ratings were higher in the ACT group than in the CBT group, a result that likely resulted from selective attrition.

The cost-effectiveness and cost-utility analyses described in **chapter 5** mainly confirmed the absence of major differences between the blended ACT and the CBT intervention. In these analyses, health benefits were expressed in terms of reliable change on the GAD-7 between baseline and the twelve-month follow-up (cost-effectiveness) and in Quality Adjusted Life Years (QALYs) calculated over the study period (cost-utility). The differences between the conditions on these outcomes were minimal and not statistically significant. The economic evaluation was conducted from a societal perspective, which means that it included both healthcare costs and non-health care costs (e.g., losses in work (voluntary) work and informal care productivity). Regarding societal costs, the analyses pointed to a possible benefit of blended ACT: compared to the CBT intervention, the ACT intervention was associated with reduced costs, as participants in the ACT group reported less health-problem related



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absenteeism and presenteeism at (voluntary) work. Overall, the results did not indicate a clear preference for either blended ACT or CBT from a health-economic perspective.

### *2.1.2. Discussion*

First, for the sake of completeness, it is important to note that chapter 4 does not report on all the assessed clinical outcome variables. As can be seen in the study protocol in chapter 3, we also assessed several cognitive coping strategies (e.g., blaming yourself, rumination, reappraisal and catastrophizing), mindfulness and experiential avoidance. Appendix 1 contains the results from the statistical analyses of these variables (which were conducted following the same procedure as described in Chapter 4), which also indicate no differences between the conditions.

The current findings on the non-significant differences between blended ACT and CBT add to earlier studies in general adult samples with anxiety, which also did not indicate major differences between the two approaches [242,243]. These accumulating findings thus suggest that adult anxiety symptoms can be effectively treated with both ACT and CBT. For clinicians, this offers greater flexibility in the delivery of psychological interventions to patients with anxiety. Still, since the RCT described in this doctoral thesis was the first large-scale trial into an ACT intervention for older adults with anxiety, establishing the clinical value of ACT for this population will require more research that replicates and elaborates upon this first trial.

Strictly speaking, the null findings in our study do not allow for the conclusion that ACT and CBT are equally effective. First, the study did not have a waitlist condition, which precludes conclusions about the absolute effectiveness of the studied interventions. However, when we compare the effect sizes in our study ( $d=0.96$  (ACT);  $d=1.09$  (CBT)) to those found in waitlist groups of older adults with anxiety symptoms (Cohen  $d$  values of 0.38 and 0.31 [81,82]), it seems safe to conclude that the improvements in both conditions can mainly be ascribed to the participants receiving an intervention. Second, it may be that our study was underpowered to detect small but relevant differences in effectiveness. Furthermore, the interventions might have different effects on clinical outcomes that were not assessed in the current RCT. Another possible reason for the lack of a significant difference between the groups is that the mental health counselors in the study were on average more experienced in providing CBT than ACT, as CBT is the most commonly used treatment approach for anxiety and the gold-standard treatment in psychotherapy in general. This prior experience may have inflated the effect size for the CBT intervention, although findings on the effect of prior therapist

experience with a specific treatment approach and clinical outcomes are mixed [319]. On the other hand, many of the mental health counselors that participated in the study did so out of an interest or affinity with the ACT-approach. Since treatment allegiance has been shown to increase effect sizes, one could also argue that effect sizes for ACT were inflated in the current RCT [319]. We unfortunately did not properly assess mental health counselors' prior experience with the treatment approaches and their treatment allegiance. For future studies that compare two active treatments, it is important to assess therapist experience and therapist allegiance and examine how these factors are associated with treatment outcomes.

Although the general picture that arises from our findings is one of no important differences between the ACT and CBT intervention regarding their clinical effectiveness, it is worth elaborating upon the differences that did emerge. First, the significant (but small) difference between the ACT and CBT intervention regarding the long-term effects on positive mental health is an interesting finding, because it concurs with the fact that ACT explicitly aims to increase positive mental health while this is not the case for traditional CBT. In ACT, symptom reduction is not the main goal of treatment but considered a byproduct of engaging with life in personally meaningful ways and an increased acceptance of (negative) internal experiences [51]. This conceptualization of mental health as a positive state of well-being and not the absence of illness or symptoms, aligns with the WHO definition of health: "a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community" [320]. Empirical research has also confirmed that mental health can best be conceptualized as consisting of two related but distinct dimensions: positive mental health and psychopathology [321]. Furthermore, interventions that are effective in promoting positive mental health are not always effective in reducing psychopathology, and vice versa, although a moderate correlation exists between these effects [322]. So, although the idea that psychological treatment should not only be evaluated in terms of symptomatic change can hardly be called controversial, a large majority of clinical trials still exclusively focus on symptom change as treatment outcome, even when the theoretical underpinnings of the evaluated treatment do not align with this view [323]. For example, we are not aware of other studies comparing ACT to other active treatments in terms of positive mental health. To fully understand the functions and benefits of psychological interventions, clinical trials should more systematically evaluate treatments in terms of positive mental health and related outcomes.

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In the economic evaluation in Chapter 5 we found that although the ACT and CBT interventions did not differ regarding reported anxiety symptoms and overall health, participants in the ACT-group did report less interference of their (mental) health problems with their work productivity. Although not a statistically significant difference (cost data have a high variance and it would therefore require a very large sample size to detect a statistically significant difference), it is an interesting result, which could possibly also be understood as stemming from the specific therapy aims of ACT. ACT aims to increase acceptance-based emotion regulation and value-oriented behavior. People are stimulated to live a vital and active life, also in the presence of physical problems or psychological pain. The finding in chapter 5 may reflect this: maybe the participants in the ACT condition were able to live a more active and vital life (including (voluntary) work), even when faced with comparable physical or mental health problems as participants in the CBT group. Of course, this finding is only preliminary and the interpretation is speculative. Our study was the first economic evaluation of an ACT intervention vs. a CBT intervention in any patient population. In anticipation of more studies into the cost-effectiveness of ACT interventions vs. CBT interventions, the choice between ACT and CBT for anxious older adults should for now be guided by ethical, personal and practical considerations of both clinicians and patients.

The last statistically significant difference between the two conditions concerned treatment satisfaction: at posttreatment average treatment satisfaction was higher in the ACT group than the CBT group. This finding does however not justify the conclusion that ACT leads to higher patient treatment satisfaction. Data on treatment satisfaction were predominantly derived from participants who attended all the face-to-face sessions, and more participants in the ACT than the CBT group dropped out of treatment before having attended all sessions. As treatment dissatisfaction can be a reason for treatment drop-out, it is possible that the difference in treatment satisfaction is the result of selective attrition. Therefore, this result for now mostly invites us to take a closer look at the drop-out rates in our study.

Drop-out is commonly thought of as an adverse treatment outcome, being perceived as a sign that the treatment is too demanding, ineffective or not tailored to the wishes of the client [324]. However, people can also drop out for reasons not directly related to treatment. People regularly drop-out before the first therapy session, due to low motivation or the timing for treatment not being optimal in their view. Furthermore, external difficulties such as transport problems, moving house/job and family circumstances are commonly reported as a reason to discontinue treatment

[324]. Lastly, patients can also prematurely quit treatment if they feel that they have already sufficiently improved [18]. In those cases, drop-out could even be thought of as a favorable outcome.

If we define drop-out in our study as participants not attending all four face-to-face sessions after being included in the study, 45% (n=68) of the participants in the ACT group and 34% (n=55) of participants in the CBT group would be considered drop-outs. However, these rates include 13 participants in the ACT group and 17 participants in the CBT group that did not show up for the first session. As these participants never started treatment, this type of drop-out does not reflect dissatisfaction with the intervention. Of the included participants who started treatment (e.g., attended the first session), 40% (55/137) in the ACT group and 26% (38/147) in the CBT group dropped-out before attending all four sessions. These participants were asked for their reason for dropping out, but data are unfortunately incomplete. For five participants in the ACT group the reason for not completing the intervention was that their mental health counselor became severely ill and stopped working. This reflects another instance in which drop-out should not be interpreted as reflecting poorly on the intervention. Among the other participants that reported their reason for dropping out, 16 participants terminated treatment due to private circumstances, 6 reported that they felt their anxiety symptoms had sufficiently improved and 7 reported treatment/therapist dissatisfaction as their reason for drop-out. Although we can not draw any firm conclusions, from these data it appears that in our study drop-out was not an adverse outcome per se. The above furthermore illustrates that drop-out is a somewhat elusive outcome, which can be defined in multiple different ways, with the definitions varying in terms of their relevance for evaluating an intervention.

A last important finding from the RCT is that none of the participants reported any adverse events or side-effects related to the interventions during the study period. This mainly indicates that psychological interventions may be preferable over treatment with benzodiazepines or antidepressants, which are often prescribed to older adults with anxiety [325,326]. Long-term use of these types of psychotropic drugs by older adults has been linked to increased risks for falling, fractures, cognitive impairment and abuse of or dependence on the drug. Especially benzodiazepines are known to be highly addictive [327]. Over the last decade benzodiazepine prescriptions have been decreasing in the Netherlands at a rate of approximately 2% per year. However, benzodiazepines are still one of the most prescribed classes of psychotropic drugs in primary care, and among the group of long-term benzodiazepine users older adults are

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still overrepresented [328]. Looking at the sample of our RCT, 17.8% of the participants used a stable dose of either benzodiazepines or SSRI's for at least 3 months. We decided to not exclude people with stabilized benzodiazepine or SSRI use, because general practitioners in our advisory committee warned us that this would lead to the exclusion of a large group of older adults with anxiety and drastically limit the generalizability of the study. The statistics on psychotropic drug use among older adults with anxiety underline the importance of general practitioners becoming more aware of the availability of effective short-term psychological interventions. To help older adults with anxiety in a constructive way, such interventions are more valuable than psychotropic drugs.

### *2.1.3. Clinical implications*

Concluding, the studies described in chapter 4 and chapter 5 did not find major differences between the blended ACT intervention and the CBT intervention. Blended ACT appears to be a valuable treatment alternative to face-to-face CBT. The differences between the conditions that did emerge were small and/or might have resulted from bias. They should therefore be interpreted with caution and should mainly be considered as indicators of viable areas for further research. The findings from chapter 4 and 5 stem hopeful as they indicate that the currently underserved patient population of older adults with anxiety symptoms can be successfully treated in a primary care setting with low-threshold, brief psychological interventions. The fact that a partly web-based intervention does not differ from a face-to-face intervention in terms of effectiveness is important: easily scalable web-based interventions might be invaluable in providing this growing patient population with adequate psychological treatment.

To fully realize the potential of these interventions and to do justice to the time and resources spend on their evaluation, we want to follow-up our study with proper dissemination and implementation. In terms of implementation of the treatments, blended ACT interventions are already available to many mental health counselors working in general practices in the Netherlands, because most general practices use e-health portals that contain an ACT-module. Furthermore, CBT is the most widely taught and used psychological intervention in the Netherlands, so we can assume that most mental health counselors working for general practitioners are trained in working with this approach. We therefore feel that our efforts at dissemination should not be primarily focused on increasing the availability of the specific interventions that were evaluated in our RCT. Rather, we want to bring across the message that the specific

population of older adults with anxiety symptomatology (which is a large group) can benefit from brief, low-intensity ACT and CBT. We want to inform both older adults and mental health professionals about the fact that anxiety symptoms are highly prevalent in later life and that they can be successfully treated in the general practice, using either low-intensity blended ACT or CBT. Our experiences during the recruitment phase of our RCT underscore the importance of this message. Multiple general practitioners and mental health counselors that collaborated in the RCT reported that they were surprised by the number of patients that registered for participation. For a subgroup of participants, it was not known at the practice that they struggled with anxiety (even in cases where the anxiety was quite severe and/or long lasting) before they registered for study participation. Multiple participants, on the other hand, reported that before receiving the study invitation they were unaware of the possibility to receive psychological treatment for their anxiety symptoms at their general practice. This underscores the importance of actively disseminating information about mental health problems and available treatment options. Evidence-based interventions are of limited value as long as a large part of the patient population and many health care providers are unaware of their availability and effectivity.

In terms of dissemination we have so far created information videos in both Dutch and English about the prevalence and nature of anxiety in later life and the effective blended ACT and CBT intervention. We created one video targeted at older adults and one at clinicians. These videos have been published on several online media outlets. See Appendix 2 for the hyperlinks to the videos. Furthermore, with financial support from a ZonMw implementation fund we will collaborate on a project with which we aim to increase the awareness of the low-threshold psychological help that is available at the general practice among groups that currently make relatively little use of this service, such as people with low social economic status, people with limited mastery of the Dutch language and older people.

Lastly, it is important to note that findings like those presented in chapter 4 and 5, that indicate no major differences in effectiveness between two different psychological interventions, are common. So far, RCTs and meta-analyses have not demonstrated consistent differences in the average effect sizes of psychological treatments [302,329]. Moreover, despite the accumulation of evidence-based psychological treatments, overall effectiveness of psychotherapy has not increased over recent decades and there is still substantial room for improvement [302]. It is clear that increasing the effectiveness of mental health care will require more than developing new treatments

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and performing clinical trials to evaluate their effectiveness. The studies in chapter 6 and 7 reflect two approaches towards improving the effectiveness of psychological care.

## **2.2. Moderators and mechanisms of change**

### *2.2.1. Summary*

**Chapter 6** described an explorative study into treatment moderation. We used the data collected during the RCT to examine moderator variables, which are baseline patient characteristics that are predictive of differential treatment response to the ACT intervention and the CBT intervention. We included a variety of demographic and clinical variables in our exploratory analyses. As a secondary goal, we set out to identify non-specific predictor variables, which are variables associated with treatment response in both the ACT and the CBT intervention. The following baseline characteristics were examined as potential moderators/non-specific predictors: 1) demographics (sex, age, education, work hours, relationship status, negative life events); 2) (psycho)pathology (anxiety severity, depression severity, presence anxiety disorder, medication use, somatic comorbidity); 3) social support (problem solving support, affective support); 4) psychological processes (self-esteem, mastery, experiential avoidance, mindfulness, emotion regulation). Anxiety symptom severity (measured with the GAD-7) was the outcome variable. Analyses did not identify any moderator variables, which means that based on the examined baseline variables we could not distinguish subgroups of participants that responded better/worse to the ACT and the CBT intervention. Two non-specific predictors were identified: more severe depression symptoms predicted worse short-term and long-term response to ACT and CBT, and higher levels of mastery predicted better short-term treatment response in both conditions.

With the study in **Chapter 7** we aimed to gain more insight into possible mechanisms of change in the ACT and CBT intervention. We categorized the examined candidate mechanisms into those directly related to the theories underlying ACT and CBT (cognitive reappraisal, acceptance, rumination, distraction, suppression, behavioral avoidance) and so called 'common factors'- mechanisms that proposedly drive change in most psychological treatments (therapeutic alliance, treatment expectancy and treatment self-efficacy). We hypothesized that acceptance, rumination, suppression and distraction were ACT-specific mediators, while cognitive reappraisal was expected to mediate treatment outcome in CBT. Furthermore, we hypothesized that behavioral avoidance, client-rated therapeutic alliance and treatment expectancies

would be equally predictive of changes in anxiety symptom severity in both the ACT and CBT group. To test the hypotheses, we used data collected at multiple assessment waves during treatment, and a statistical procedure which allowed us to examine the hypothesized associations on the within-person level. We did not find support for our hypotheses. The candidate mechanisms did not prospectively predict anxiety symptom change and the hypothesized mediational pathways were also not statistically significant. The results do therefore not lend support to the theories of change in ACT and CBT and the common factor theory.

### *2.2.2. Discussion*

The study in chapter 6 fits into a tradition of scientific efforts to increase the effectiveness of psychological treatment through personalized treatment selection. Personalized treatment selection means that instead of providing one treatment to all patients, each individual patient is provided with the intervention that is most likely to be optimal for him or her [264]. This requires the identification of subgroups of patients that seem to respond most favorably to a specific type of treatment. Two earlier studies comparing ACT and CBT for anxiety suggested that anxiety treatment approaches resonate better with patients when they draw upon a patient's strengths rather than remediating their shortcomings. Specifically, people with a greater ability and desire to reduce/control anxiety may be more receptive to CBT and people with a greater willingness to experience anxiety may be more responsive to ACT [30,31]. This was not replicated by the study in chapter 6, as measures related to acceptance (e.g., experiential avoidance, mindfulness) did not predict better outcomes in ACT. The findings in chapter 6 suggest that based on the included predictor variables, no subgroups of older adults with anxiety can be distinguished that respond more or less favorably to either ACT or CBT. This indicates that for now all older adults with anxiety symptoms can be offered either blended ACT or face-to-face CBT: the choice can be guided by client- and therapist preferences and practical considerations.

The lack of statistically significant moderators precluded the development of a personalized treatment assignment tool, which was one aim of our study. The model would combine information from multiple moderator variables to predict which treatment is optimal for each individual patient. Such models have earlier been deemed promising for personalized mental health care [264]. However, it is important to note that despite the often-emphasized promise of personalization tools, research into personalized mental health care is still in its infancy. For example, there have only been



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a handful of studies that tested personalized treatment assignment models outside of the sample in which they were developed, and the results were disappointing [332]. Moreover, considering personalized treatment assignment for people with anxiety specifically, research so far has not yet identified consistent moderators of treatment response to different therapies [333]. Much work is still required before personalization tools can become part of clinical decision making in mental health care. First, findings on moderator variables need to be replicated across multiple studies. Subsequently, findings on consistent moderators can be translated into personalization tools that need to be thoroughly evaluated in terms of their feasibility, acceptability, and effectiveness. These tools should only be implemented in mental health care if they will prove to outperform current clinical decision making.

The study in chapter 7 reflects another approach towards improving treatment effectiveness: the identification of the mechanisms of change of psychotherapies. Understanding how a treatment achieves its effects can translate into treatment augmentation strategies, by optimizing those aspects of the treatment that directly target the processes responsible for change and minimizing or eliminating those that do not [227]. With our study we did not find evidence that cognitive emotion regulation strategies prospectively mediated change in anxiety symptom severity during the ACT and CBT intervention. Furthermore, we did also not find evidence that behavioral avoidance, therapeutic alliance and treatment expectancies predicted anxiety symptom severity over the course of the two interventions.

The null findings from chapter 7 can not easily be compared to earlier literature, because of profound methodological differences between our study and earlier research. The study in chapter 7 of this doctoral thesis sets itself apart from much previous research in terms of its potential to infer causality. First, we established a timeline, that allowed to examine if the candidate mechanisms *preceded* treatment outcome. Second, we separated within-person variance from between-person variance in our statistical analyses. This allowed us to report on the associations between the examined candidate mechanisms and anxiety symptom severity on the within-person level. An association on the within-person level is more likely to point to a causal process than an association on the between-person level [313]. Most previous studies into the mechanisms of change of ACT and CBT (and other psychotherapies) have only demonstrated correlations between putative mechanisms and treatment outcome. Such studies do not allow for any causal inferences, while demonstrating that a factor is likely to play a causal role is exactly what research into

treatment mechanisms should aim for [227]. We therefore prompt future studies into mechanisms of psychotherapeutic change to use longitudinal design and statistical analyses that allow for statements about within-person processes.

Here it is also important to note that establishing temporality and disentangling within- and between-person variance are necessary but not sufficient to identify mechanisms of psychotherapeutic change. Establishing that a factor is indeed a mechanism of action in psychotherapy requires multiple research strategies, including direct experimental manipulation of the candidate mechanism, studies demonstrating a dose–response association between proposed mechanisms and treatment outcome, and studies establishing that there is no third variable that is responsible for changes in the mediator and the outcome [227]. In sum, considering the examination of mechanisms of change of psychotherapy, we can draw a similar conclusion to the one we made in relation to personalized treatment selection: there is still a long way to go. It will take many individual studies and a great collaborative effort to elucidate the working mechanisms of psychological treatment.

### **2.3. Limitations and strengths**

The main limitation of the studies in chapter 4-7 concerns the generalizability of the findings. Generalizability is limited because people that were severely impaired by their psychological, cognitive or physical problems were excluded from participation in the trial, as were adults over 75 years of age. Furthermore, to be included people had to register online, which required internet access and some skills in working with computers. This resulted in a sample that is not representative for the study population: all participants were community-dwelling, 98% were of Dutch nationality, and most had middle to high education levels.

Second, an inherent limitation of defining a research sample in terms of chronological age, is that this does not account for cohort effects. This means that the generalizability of the findings is limited because the current 55-75 year olds differ from the 55-75 year olds of the (near) future in multiple potentially clinically important ways. For example, during the writing of the grant proposal for the RCT that chapters 4-7 report on (this was around 2015), it was decided to exclude adults over 75 years from participation, because digital literacy was generally still low in this group and this could introduce bias to the data [334]. However, from 2015 to 2020 the percentage of adults aged 75 years and over that used the internet on a daily basis increased from 30 to 49 percent, so it plausible that currently the majority of this age group is used to

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working with computers and the internet [334]. Of course, digital literacy is only one of many factors on which future 55-75 year-olds may differ from the adults that are currently in this age range.

Another important limitation that was already touched upon is the absence of an inactive control condition, which precludes direct conclusions about the effectiveness of the studies interventions in absolute terms.

Considering strengths, the studies in chapter 4 -7 constitute the first large-scale and comprehensive clinical evaluation of an ACT intervention vs. a CBT intervention for older adults with anxiety symptoms. Besides an evaluation in terms of clinical effectiveness (chapter 4), we also conducted an economic evaluation (chapter 5), an explorative moderator analyses (chapter 6) and an examination of potential mechanisms of change of the two interventions (chapter 7). Together, these studies form a thorough clinical evaluation and comparison of the blended ACT and the face-to-face CBT intervention for older adults with anxiety symptomatology. To our knowledge the sample size of 314 is larger than that of any other study into the psychological treatment for anxiety in older adults. Furthermore, we compared the effectiveness of the interventions over a period of 12-months, thereby also gaining insight into the longer-term effects of the treatments.

### 3. Overall conclusion

With this doctoral thesis we aimed to improve the understanding of the prevalence and treatment of anxiety in later life. Our systematic review and meta-analysis of prevalence studies suggests that subthreshold anxiety might be at least equally prevalent to full-blown anxiety disorders in later life, and that for some types of anxiety prevalence rates seem to decrease throughout the later life span. The review article also highlights that little is still known about the ways in which age is associated with the prevalence and manifestation of anxiety. As earlier studies have indicated that anxiety is among the most common mental health problem in later life, it is important that future research focuses on answering more delicate questions regarding the presentation and prevalence of anxiety in older adults.

Considering the psychological treatment of anxiety in later life, we found that a brief blended ACT intervention and a brief CBT intervention did not differ regarding their effects on anxiety symptom severity and related clinical outcomes. In both treatment conditions, large reductions of anxiety symptom severity were observed. Also, in terms of cost-effectiveness and cost-utility, there is no clear preference for

one of the two interventions. Furthermore, we explored whether baseline participant characteristics moderated treatment response to the two interventions. We did not identify moderator variables, which indicates that there are no specific subgroups of patients that benefitted more from one of the two treatments. Lastly, we examined potential working mechanisms of the two interventions, but did not find evidence that the examined candidate mechanisms were related to anxiety symptom change during the ACT and CBT intervention.

The results are promising, because they show that older adults with mild to moderately anxiety symptomatology can be effectively treated in a primary care setting with two low-threshold, brief psychological interventions. Mental health counselors and clients can together decide on their preferred treatment approach. These psychological interventions form a more constructive alternative to psychotropic drugs, which are still often prescribed to older adults with anxiety. Low-intensity psychological interventions for anxiety in later life have not previously been studied on such a large scale. This doctoral thesis therefore makes a timely and important contribution to the evidence-based treatment of the highly prevalent problem of anxiety in older adults. Hopefully our research will inspire more scientific and clinical attention for anxiety symptoms in later life. Ultimately, we hope that successful implementation and an increased uptake of evidence-based psychological interventions will improve the mental well-being and quality of life of older adults.

## Appendix 1

**Table A1.** Mixed model analyses comparing the differences between the blended acceptance and commitment therapy and cognitive behavioral therapy group over time

Outcome	b	SE	t	p
<u>Blaming yourself</u>				
T0-T1	-0.93	0.26	-3.54	< 0.001
T1-T2	-0.90	0.29	-3.08	0.002
T1-T3	-0.95	0.30	-3.15	0.002
T0-T1 * condition	-0.05	0.53		0.93
T1-T2 * condition	-0.22	0.59	-0.09	0.71
T1-T3*condition	-0.23	0.60	0.37	0.70
<u>Rumination</u>				
T0-T1	-1.10	0.27	-4.09	< 0.001
T1-T2	-0.97	0.30	-3.22	0.001
T1-T3	-0.93	0.31	-3.01	0.003
T0-T1 * condition	0.40	0.54	0.74	0.46
T1-T2 * condition	-0.64	0.60	-1.07	0.28
T1-T3*condition	-1.18	0.62	-1.91	0.06
<u>Reappraisal</u>				
T0-T1	0.09	0.33	0.27	0.79
T1-T2	-0.93	0.37	-2.50	0.01
T1-T3	-1.04	0.38	-2.74	0.001
T0-T1 * condition	0.73	0.67	2.00	0.27
T1-T2 * condition	-0.31	0.74	-0.42	0.67
T1-T3*condition	-0.24	0.76	-0.31	0.76
<u>Catastrophizing</u>				
T0-T1	-0.68	0.21	-3.31	<0.001
T1-T2	-0.30	0.23	-1.29	0.20
T1-T3	-0.35	0.24	-1.47	0.14
T0-T1 * condition	0.34	0.42	0.83	0.41
T1-T2 * condition	-0.60	0.46	-1.32	0.19
T1-T3*condition	-0.52	0.47	-1.10	0.27
<u>Mindfulness</u>				
T0-T1	3.80	0.93	4.08	< 0.001
T1-T2	0.90	1.04	0.86	0.39
T1-T3	1.86	1.07	1.75	0.08
T0-T1 * condition	1.41	1.86	0.76	0.45
T1-T2 * condition	0.27	2.08	0.13	0.90
T1-T3*condition	2.00	2.13	0.94	0.35
<u>Experiential avoidance</u>				
T0-T1	-2.79	0.67	-4.13	< 0.001
T1-T2	-2.68	0.75	3.57	< 0.001
T1-T3	-3.02	0.77	-3.93	< 0.001
T0-T1 * condition	2.77	1.35	2.06	0.06
T1-T2 * condition	-2.10	1.50	-1.40	0.16
T1-T3*condition	-2.48	1.54	-1.61	0.11

## Appendix 2

**Supplementary material 1.** Links to videos created for older adults

Dutch

**<https://www.youtube.com/watch?v=QCcDCvt9N5E>**

English

**[https://www.youtube.com/watch?v=HIBp\\_5oUeMw](https://www.youtube.com/watch?v=HIBp_5oUeMw)**

**Supplementary material 2.** Links to videos created for clinicians

Dutch

**<https://www.youtube.com/watch?v=4zUTpkXTR1c>**

English

**<https://www.youtube.com/watch?v=d4BMGtrHTi0>**

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