

**UNIVERSIDAD COMPLUTENSE DE MADRID  
FACULTAD DE PSICOLOGÍA**



**TESIS DOCTORAL**

**Sesgos emocionales de interpretación: desarrollo y validación  
de un programa breve de modificación de sesgos cognitivos  
con una aproximación clínica (MSC-IClin)**

**Emotional interpretation biases : Development and validation  
of a brief clinically-based cognitive bias modification program  
(CBM-IClin)**

MEMORIA PARA OPTAR AL GRADO DE DOCTOR

PRESENTADA POR

**Inés Nieto Romero**

Director

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Madrid

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Becoming a doctor is like a journey. It starts with high levels of enthusiasm, openness to learn, and unconsciousness from the unknown. Then, you find struggling moments, doubts, fear, frustrations, but also personal growth, satisfaction and proud. And, at the end, like in many journeys you just can't wait to see what comes next. However, the most important part of this journey is that you don't do it alone and I would like to thank to every person who has walk with me during the last five years.

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## SCIENTIFIC ARTICLES INCLUDED IN THE DISSERTATION

The present doctoral dissertation includes the following published articles:

- Nieto, I., Robles, E., & Vazquez, C. (2020). Self-reported cognitive biases in depression: A meta-analysis. *Clinical Psychology Review*, 82, 101934. <https://doi.org/10.1016/j.cpr.2020.101934>
- Nieto, I., Vazquez, C. (2021). ‘Relearning how to think’: A brief online intervention to modify biased interpretations in emotional disorders-study protocol for a randomized controlled trial. *Trials*. 22, 510. <https://doi.org/10.1186/s13063-021-05459-32.2>.
- Nieto, I., & Vazquez, C. (2021). Disentangling the mediating role of modifying interpretation bias on emotional distress using a novel cognitive bias modification program. *Journal of Anxiety Disorders*, 83, 102459. <https://doi.org/10.1016/j.janxdis.2021.102459>

There is a brief summary of each article to integrate their content into the main text. Moreover, this dissertation includes a General introduction, a non-published study in Chapter 4, and a General discussion about the main findings and their relevance to the field.

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## ABSTRACT

**Background.** When faced with ambiguous information, humans often try to give meaning to the situation. The tendency to provide negative interpretations at any time and context has come to be known as negative interpretation bias. This cognitive process is consistently found in emotional disorders and has been proposed as a precipitating and maintaining factor of symptoms of depression and anxiety. Given the high rates of prevalence and chronicity of these disorders in the population, it is necessary to find new treatment alternatives that can alleviate symptoms and increase functionality and well-being. The present dissertation had three main aims. First, it systematically analyzed the presence of Beck's categories of interpretation bias in depression as measured by self-report questionnaires. Second, it aimed to design a new program to modify negative interpretation biases commonly found in depression and anxiety. Finally, the efficacy of this new program and its mechanisms of action were evaluated.

**Method.** This dissertation is divided in four studies. The first one is a systematic review and meta-analysis comparing, with the standardized mean difference effect size, the levels of interpretation biases in samples of depressed and healthy individuals. The second study presents the rationale and development of a new cognitive bias modification program (CBM-IClin) to modify interpretation biases and other related variables to be used in a randomized controlled trial. The third study evaluates the change in interpretation bias and symptoms of depression, stress, and anxiety in a sample of university students after the application of this new protocol in comparison to a wait-list control group. Finally, the fourth study includes mediation models to analyze how the change in negative interpretation bias, given the intervention, mediates the change in other related variables, such as attention and memory biases, dysfunctional attitudes, rumination, and well-being.

**Results.** The first article revealed, with the analysis of 63 primary studies, large effect sizes when comparing the levels of catastrophizing and general interpretation bias in depression and healthy samples. These effect sizes were characterized by high levels of heterogeneity, which were explained by moderator variables such as gender, geographic location, measurement instruments, and study design. Study 3 showed that the new CBM-IClin (described in Study 2) was able to significantly improve interpretation bias, but not depression, stress, or anxiety levels. However, Study 4 showed that the change in interpretation bias mediated the change in depression symptoms, meaning that the intervention was able to improve depression levels via the improvement in negative interpretations. Moreover, it was also found that the program had a direct effect in the change of memory bias (i.e., independent of interpretation bias change), and direct and indirect effects in the change of dysfunctional attitudes.

**Conclusions.** This dissertation proves the existence of some of the Beck's categories of self-reported interpretation bias in depressed samples. It was not possible to individually meta-analyze each of the categories that he proposed in his cognitive model given the lack of research. However, this dissertation contributes to the partial validation of the extended use of his theory in research and clinical practice. Moreover, it also contributes to the development of the cognitive bias modification field by designing a new program that combines the focus and flexibility of CBM trainings and the long-validated CBT strategies to improve emotional symptoms. Furthermore, it shows evidence of the efficacy of this new program to improve negative interpretation biases and related variables, such as memory bias and dysfunctional attitudes. Finally, in this dissertation I provide further understanding of why CBM trainings

show weak effects to change symptoms and give some suggestions to improve these results in future studies.

## **RESUMEN**

**Introducción.** Al enfrentarnos ante información ambigua, los humanos a menudo tratamos de dar significado a la situación. La tendencia de crear interpretaciones negativas en cualquier momento y situación se conoce como sesgo negativo de interpretación. Este proceso cognitivo se ha encontrado consistentemente en trastornos emocionales y se propone como un factor precipitante y de mantenimiento de síntomas de depresión y ansiedad. Dadas las altas tasas de prevalencia y cronicidad de estos trastornos en la población, es necesario encontrar nuevas alternativas de tratamiento que alivien estos síntomas y mejoren la funcionalidad y el bienestar. La presente tesis doctoral tiene tres objetivos principales. Primero, analizar sistemáticamente la presencia de las categorías del sesgo de interpretación propuestas en el modelo cognitivo de Beck, medidas con auto-informes. Segundo, introducir el diseño de un nuevo programa para modificar el sesgo de interpretación negativo, comúnmente encontrado en depresión y ansiedad. Por último, pretende probar la eficacia de este nuevo programa y descubrir sus mecanismos de acción para producir cambios.

**Método.** La tesis está dividida en cuatro estudios. El Estudio 1 es una revisión sistemática y meta-análisis en el que se compara, con la diferencia de medias estandarizada como tamaño del efecto, los niveles de sesgo de interpretación en muestras con depresión frente a muestras sanas. El Estudio 2 explica el razonamiento y desarrollo de un ensayo clínico aleatorizado para evaluar un nuevo programa de modificación de sesgos cognitivos (CBM-IClin) para reducir el sesgo de interpretación y otras variables relacionadas. El Estudio 3, tras la aplicación de este protocolo, analiza el cambio en el sesgo de interpretación y en síntomas de depresión, estrés y ansiedad en estudiantes universitarios en comparación con un grupo control en lista de espera. Finalmente, el Estudio 4 incluye modelos de mediación para analizar cómo el cambio en el sesgo de interpretación, tras la intervención, media el cambio en otras variables relacionadas, como los sesgos de atención y memoria, las actitudes disfuncionales, la rumiación y el bienestar.

**Resultados.** El Estudio 1 reveló, con la inclusión de 63 estudios primarios, tamaños del efecto grandes al comparar los niveles de catastrofización y el sesgo general de interpretación en depresión y muestras sanas. Estos tamaños del efecto se caracterizaron por altos niveles de heterogeneidad, lo cual se pudo explicar con variables moderadoras como la distribución de género de la muestra, la localización geográfica, los instrumentos de medida y el diseño de los estudios. El Estudio 3 de la tesis mostró que el nuevo CBM-IClin (descrito en el Estudio 2) mejoraba significativamente el sesgo de interpretación negativo, pero no los niveles de depresión, estrés o ansiedad. Sin embargo, el Estudio 4 mostró que el cambio en el sesgo de interpretación mediaba el cambio en los síntomas de depresión, lo cual explica que la intervención fue capaz de mejorar los niveles de depresión sólo a través de la mejora del sesgo de interpretación. Además, se encontró que el programa tenía un efecto directo en el cambio en el sesgo negativo de memoria (es decir, independientemente del cambio en el sesgo de interpretación) y efectos directos e indirectos en el cambio de actitudes disfuncionales.

**Conclusión.** La presente tesis doctoral prueba la existencia de algunas de las categorías, medidas con auto-informes, de los sesgos cognitivos propuestos por el modelo cognitivo de Beck. No fue posible meta-analizar cada una de las categorías que propuso debido a la falta de

estudios primarios. Sin embargo, la tesis contribuye a la validación parcial del uso extendido de su teoría en investigación y en la práctica clínica. Además, este trabajo también ayuda en el desarrollo del cambio de la modificación de sesgos cognitivos con el diseño de un nuevo programa que combina el objetivo y la flexibilidad de los entrenamientos CBM con las estrategias altamente validadas de la CBT para mejorar síntomas emocionales. Por otro lado, se muestra la eficacia de este nuevo programa para reducir el sesgo de interpretación negativo y variables relacionadas como son el sesgo negativo de memoria y las actitudes disfuncionales. Finalmente, en la tesis proporciono un mayor entendimiento de por qué los entrenamientos de modificación de sesgos cognitivos muestran efectos bajos en la mejora de síntomas y doy algunas sugerencias para mejorar estos resultados en futuros estudios.

“If our thinking is bogged down by distorted symbolic meanings, illogical reasoning and erroneous interpretations, we become, in truth, blind and deaf”<sup>1</sup>

Aaron T. Beck (1921-2021)

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<sup>1</sup> From *Love Is Never Enough: How Couples Can Overcome Misunderstandings, Resolve Conflicts, and Solve Relationship Problems Through Cognitive Therapy* (1988, p.12). New York: Harper and Row Publishers, Inc.

## **INTRODUCTION**

### **CHAPTER 1. The relationship between cognition and emotion**

The interpretation of a situation could be defined as the meaning given by the person who observes it. When this situation contains ambiguous information, meaning-making can result in a positive, negative, or neutral resolution. For example, if your boss asked to speak to you later at her office, you may think that she wants to compliment your job (positive), fire you (negative), or just review your progress (neutral). Of course, each of these interpretations would lead to very different emotions. Although this variety of interpretations are part of normal processing when the information is not clear, the tendency to always choose the negative meaning can be damaging. This tendency to make a negative interpretation independent of the context, situation or any other additional information is what we call a negative interpretation bias. This bias is common in people with depression and anxiety and has an impact on mood and behavior, being a potential risk factor for the development and maintenance of symptoms (Hirsch et al., 2016).

Depression and anxiety disorders are highly prevalent in the population. The World Health Organization (2017) estimates that depressive disorders affect more than 300 million people and anxiety disorders affect around 265 million people worldwide. This situation leads to high social and economic costs due to the dysfunction caused by their symptoms (McIntyre & O'Donovan, 2004; Vos et al., 2016). Moreover, these disorders are characterized by high levels of relapse, being around 40–50% for depression (Forte et al., 2015) and 23.5% for anxiety disorders (Scholten et al., 2013). These numbers highlight the urge to find variables that lead to the appearance and maintenance of symptoms, as well as the vulnerability factors that may explain the high levels of recurrence (Ingram et al., 1998; Vázquez et al., 2008). Another

characteristic of depressive and anxiety disorders is their high levels of comorbidity (Olfson et al., 2017), with rates of 63% for comorbid generalized anxiety disorder and other emotional disorders in life prevalence (Ruscio et al., 2017). In fact, during the last years, the scientific community has embraced the disengagement from traditional categorization systems and supported that different diagnoses do not necessarily reflect ontological different disorders (Cramer et al., 2010; Insel et al., 2010). This situation highlights the need to place the focus of both research and clinical practice on common symptoms (e.g., repetitive negative thinking, McEvoy et al., 2019), and not on the differences between disorders (Brown & Barlow, 2009; Fried et al., 2017). There are several studies reporting symptom improvement of two different diagnoses when applying treatment for only one of them (e.g., Allen et al., 2010). Also, it has been shown that a unified protocol for emotional disorders can be, at least, as effective in the improvement of symptoms as a protocol specifically designed for anxiety (Barlow et al., 2017; Carlucci, Saggino, & Balsamo, 2021) and recent studies point to an increased benefit of transdiagnostic therapies compared with treatment as usual in some cases (Jeppesen et al., 2021).

The high prevalence of these disorders and their elevated relapse rates, even 12 months after treatment (van Dis et al., 2020), indicate that traditional therapies may not be effective for every patient (Cuijpers et al., 2018). Therefore, it seems necessary to continue with the research of new therapeutic procedures that aim to change variables empirically related to the development and maintenance of symptoms. An example of these variables is negative cognitive biases.

### **1.1. Theoretical foundations: Cognitive models of emotional disorders**

Several cognitive theories were proposed with the arrival of the ‘cognitive revolution’ during the 70s of the twentieth century which aimed to identify the aspects of emotional disorders that were difficult to explain from the more biological or behavioral perspectives.

One of the most influential of these theories was the one proposed by the late Aaron Beck (Beck, 1967; Beck, 1976; Beck et al., 1979). According to this model, people with depression or anxiety would present cognitive schemas characterized by dysfunctional attitudes and rigid, unrealistic beliefs framing their perspective of reality. These schemas would remain latent until facing a vital stressor. Once active, they would trigger a biased type of processing information characterized by catastrophizing (automatic anticipation of negative results), personalization (automatic attribution of blame), or dichotomous thinking (interpretation in terms of all-or-nothing), among others (i.e., arbitrary inferences, selective abstraction, overgeneralization, minimization, labeling, mind-reading, or emotional reasoning). While this information processing would be oriented to guilt or low self-esteem in depression, these biases would have content of danger or individual threat in anxiety (Beck, 1963; McNally, 1994). These biases constitute a key element in the development of depression and anxiety as, although many variables interact, the distortion of reality coming from this type of processing could eventually lead to symptoms (see Figure 1). With this filtered view of reality, people with depression would develop negative mental products of themselves, the world, and the future (*cognitive triad*), which would finally lead to clinical symptoms (Beck et al., 1979). In anxiety, these biases would trigger fear emotions, physiological processes of hyperactivation of the autonomous nervous system, and behaviors of escape and avoidance, which are maintenance factors of the disorder (Clark & Beck, 1988).

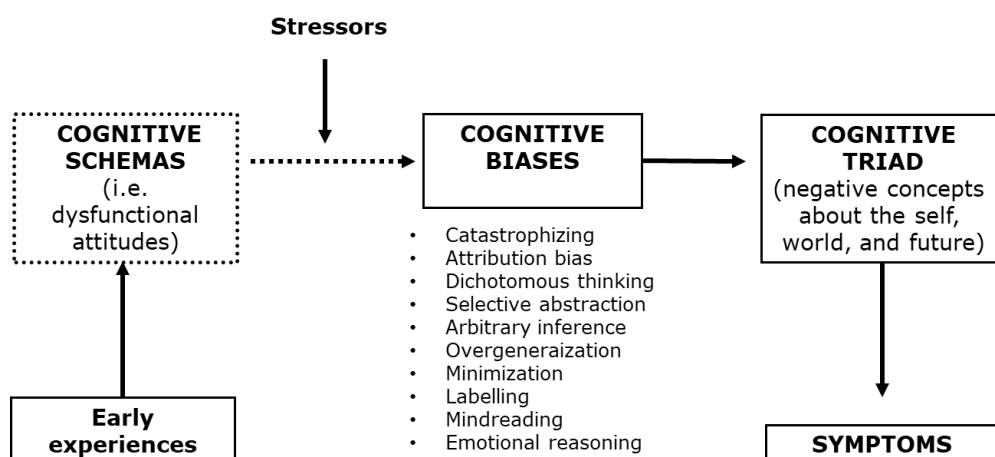


Figure 1. Schema of Beck's cognitive model. Adapted from Vazquez, Hervás, Hernangomez & Romero (2011).

Beck's model is considered to be within the framework of diathesis-stress models, which support the idea that emotional disorders are more likely to appear in those people with latent vulnerability factors (diathesis) which would activate in the face of a stressor. Following this idea, Bower (1981) proposed that cognition works like a network of semantic nodes which are interconnected and activate with external signals. When a node activates, it sends a signal to the rest of the network, being this signal stronger to those which are closer and share semantic content. In this way, the activation of nodes close to each other would require less external stimulation to activate. This was a significant conceptual advance for the study of the interaction between cognition and emotion, as the model focuses on understanding how processes such as attention, interpretation, or memory can influence and be influenced by emotions (Joorman, 2019). Two other cognitive theories of depression emerged from this network perspective of cognition. Both, Ingram and Teasdale, proposed that the biased processing of information would play an important role in the appearance, maintenance, and recurrence of symptoms. Ingram (1984) stated that people have a series of beliefs that determine the interpretation of external events. A negative interpretation would activate the depressed mood. If no more stimulation is received, this activation would decline. But, in the case of depression, there would

be a cognitive loop in which a low mood makes it easier to access negative thoughts and memories that would keep the depressed mood active. Teasdale's (1988) theory proposes a similar feedback loop between negative information processing and a negative mood, making fleeting feelings of sadness turn into a persistent depressive mood. Furthermore, Teasdale's differential activation hypothesis added the concept of cognitive reactivity to previous models. He explained that a depressive mood would be required to activate negative information processing, increasing the accessibility to negative interpretations of one self and personal events, and contributing to the maintenance of symptoms. However, in the absence of a depressive mood that activates these patterns of thinking, the spiral into depression would not develop (Lau et al., 2004). Finally, Abramson et al.'s (1978) theory focused on the attributions that people with depression make to success and failure. These authors proposed that people with depression attribute success to external factors, while the attributions for failure would be internal, global, and stable, which would maintain symptoms.

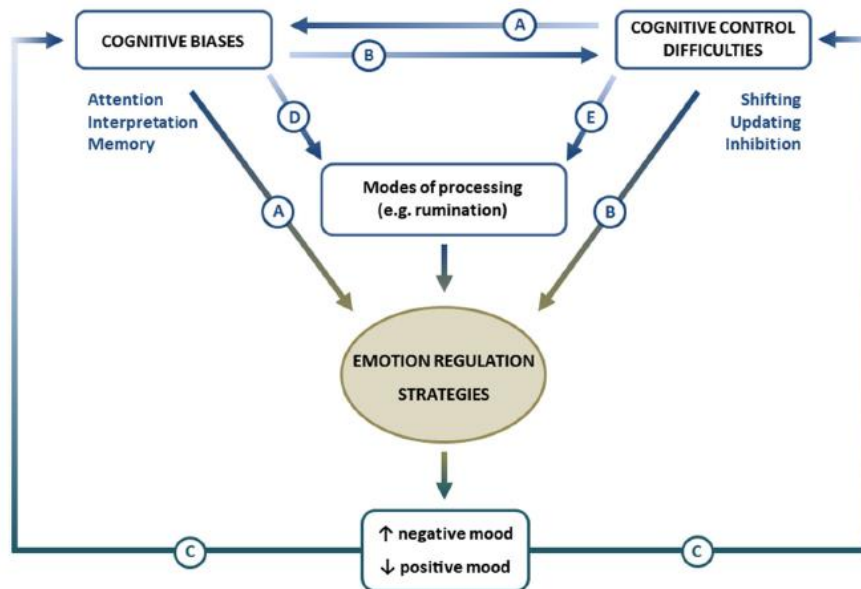
These circular processes and the view of cognition as interconnected nodes of a network have also been proposed in theories of anxiety. Mathews (1990) theorized that those people with higher levels of state anxiety tend to pay more attention to threatening stimuli, which causes a greater encoding of information about potential dangers, promoting feedback between anxious mood and selective information processing. Later on, Williams, Mathews, and MacLeod (1996) proposed that, in anxiety, those nodes (mental representations of stimuli) with the label of 'threatening' would have greater weight, either by biological inheritance or by learning, than those without the label. This would make them get activated more easily than the rest of nodes, automatically redirecting the cognitive resources (attention in particular) to them. Öhman (1993) proposed that humans unconsciously process threatening stimuli because they

are dangerous for survival. However, the rest of stimuli would pass to a conscious evaluation (“conscious perception system”) in which we generate meaning in line with stored memories. If the interpretation of these stimuli is threatening, the autonomous central system would be put into operation. This excitation would cause a greater sensitivity in the unconscious filter to detect similar information in the future, generating a biased attention processing. Finally, Mathews and Mackintosh( 1998) proposed that the difference in people with anxiety is not determined by a greater direction of attention towards threatening stimuli but by their greater difficulty in inhibiting this type of information. Similar to the previous models, the authors explain that there is an Automatic Threat Evaluation System (TES) whereby attention is directed to threatening stimuli to ensure survival. When emotional states of fear or anxiety appear, the threat detection threshold is lowered and the vigilant response appears. This process would be facilitated in people with high trait anxiety due to 1) a genetic lower baseline threshold and 2) a more frequent activation of the vigilant response causing more stimuli to be associated to threat. As we can see, cognitive theories of anxiety have been focused on attentional processes. In fact, Mathews and MacLeod (1994) proposed that anxiety states promote biases in early processing, favoring attention to threatening stimuli, while depressive states promote negative self-referential biases in memory, that is, in a subsequent elaboration of meaning.

## **1.2. Empirical evidence of the relationship between cognition and emotion in emotional disorders**

Following these classical models, numerous investigations have been developed to reveal the relationship between cognition and emotion. There is sound empirical evidence showing that emotional disorders are associated with cognitive biases, which is the focus of this dissertation. However, depression and anxiety are also associated with cognitive processes such as dysfunctional emotion regulation, and deficits in cognitive control. Figure 2 presents a recent model including these interactions.

It seems difficult to understand the nature of emotional disorders without considering all these factors. Therefore, this section is divided in three different parts to give a comprehensive overview of the most relevant findings in the field. The first part focuses on the relevance of the negative interpretation bias in depression and anxiety. The second part explains the combined cognitive bias hypothesis, which introduces the interaction between interpretation, attention and memory biases. Finally, the third part includes some of the most recent findings on the interplay between emotion regulation, cognitive control, and information processing in emotional disorders.



*Figure 2.* Proposal for an integrative interplay model among cognitive control, cognitive biases, and emotion regulation in depression (Villalobos et al., 2021).

### 1.2.1. Interpretation bias

As previously mentioned, the direction in which ambiguity is solved in a situation may have a great impact on mood (Wisco, 2009). There is ample evidence for the presence of negative interpretation bias in people with depression and anxiety disorders. Specifically, a tendency to interpret ambiguous information negatively has been demonstrated, in contrast to the optimistic tendency of people without symptoms (Hirsch et al., 2016). This result has been

found using a wide variety of measurement paradigms (for a review see Schoth & Lioffi, 2017). For example, in homophone-words tasks, people with depression and anxiety write more negative meanings than people without symptoms when listening to words that sound the same but have two possible meanings, one negative and another neutral (for example, die / dye) (Mogg et al., 2004, 2006). Perhaps one of the most frequently used paradigms to measure interpretation bias are those including ambiguous scenarios or sentences. For example, when asking adolescents with an anxiety disorder to freely write an interpretation of an ambiguous situation such as "You see the principal walking the hallways of the school and he has been asking other students where you are", it has been found that they generate more threatening interpretations than healthy adolescents (Waite et al., 2015). Using brain measurements (event-related potentials) it has been shown that people with social phobia, depression, or both do not expect positive resolutions of ambiguous scenarios (e.g., "As you give a speech, you see a person in the crowd smiling, which means that your speech is ..."), as opposed to healthy participants (Moser et al., 2012).

Despite these findings, some studies have failed to find evidence of interpretation bias in both depression (Bisson & Sears, 2007) and anxiety (Hirsch & Mathews, 2000). Meta-analytic studies explain that the type of measure used to assess interpretation bias can moderate these relationships (Chen et al., 2020; Everaert et al., 2017). Specifically, studies suggest that interpretation biases are captured by direct measures in which the instructions to interpret ambiguous information are explicit (for example, "[...]Imagine each scenario happening to you personally. [...] Then rate how pleasant your image is[...]", Berna et al., 2011), but not by indirect measures, such as reaction times or neurophysiological measures. Although direct measures are subject to demand, selection, and response biases (Hirsch et al., 2016), they allow for elaborate and thoughtful processing, which might be the nature of the interpretation bias. A

recent study has shown that the correlation between depression symptoms and direct measures of interpretation bias is higher than with indirect measures, although the Scrambled Sentences Task was the only one that explained part of the variance of the symptoms (O'Connor et al., 2021). The use of self-referential stimuli also has a moderating role in the relationship between interpretation bias and depression, but not other variables such as the type of sample (clinical, in remission, subclinical) or instructions to create mental images during measurement (Everaert et al., 2017). These findings warn about the possibility that all these instruments are measuring different constructs or, at least, different subcomponents of a construct. The direct comparison between the results obtained with these behavioral measures and other neurological indicators could help to clarify these differences (e.g., Auerbach et al., 2016). This problem deserves careful attention in experimental research. We aim to reach comparable conclusions between studies by using proxies that lack perfect convergent validity, and this makes it difficult to interpret research findings (Carlson & Herdman, 2012).

Empirical results have revealed a difference in the content of the interpretation process of people with depression and anxiety. While the emotional interpretation bias in anxiety seems to be more linked to the content of threat and danger, it shows a more general nature and is oriented to self-referent information in depression (Voncken et al., 2007). A recent meta-analysis supports the existence of a correlation between the specific content of anxiety symptoms and the content of the interpretation bias in anxiety samples (e.g., social threat bias in social anxiety disorder) (Subar et al., 2021). However, the presence of a negative interpretation bias has been shown in both disorders with clinical and subclinical samples (Chen et al., 2020; Everaert et al., 2017). For example, people with high levels of anxiety (according to the cut-off point in social anxiety questionnaires) interpret both ambiguous scenarios and

ambiguous facial expressions as threatening to a greater degree than participants with low levels of social anxiety (Chen et al., 2019). Also, there are significant differences in the number of negative interpretations generated by groups with a diagnosis of generalized anxiety or major depression compared to a group without a diagnosis (Krahé et al., 2019). The same authors also found that the levels of bias were associated with negative repetitive thinking patterns, characteristic of both diagnoses (rumination and worry). All these results suggest that the negative interpretation bias is a transdiagnostic variable that could play a role in both disorders.

Cognitive diathesis-stress theories propose that emotional biases are not only found in people with present symptoms but also in people vulnerable to develop a first episode or relapse. Several studies have compared different types of samples to address this issue. Dearing and Gotlib (2009) studied the interpretation bias in daughters of mothers with recurrent depression compared to girls without vulnerability, whose mother had never suffered an episode. The results supported cognitive vulnerability models since the first group generated more negative interpretations in the face of ambiguous information than the second one. Rude et al. (2003) found that a measure of interpretation under cognitive load (Scrambled Sentences Test, Wenzlaff & Bates, 1998) predicted diagnoses of major depression 18 to 28 months later, controlling for symptoms from the first evaluation. Something similar was found with a sample of young women who filled in an interpretation bias measure with ambiguous scenarios at two points in time. A negative interpretation bias was found to predict the onset of panic disorder 17 months later, controlling for sensitivity to anxiety and fear of physical sensations at the first assessment (Woud et al., 2014). These results emphasize the importance of understanding the mechanisms by which interpretation bias exerts its influence on the development and maintenance of both depression and anxiety symptoms. A new line of research proposes the lack of cognitive flexibility as the key to explain the influence of interpretation processes

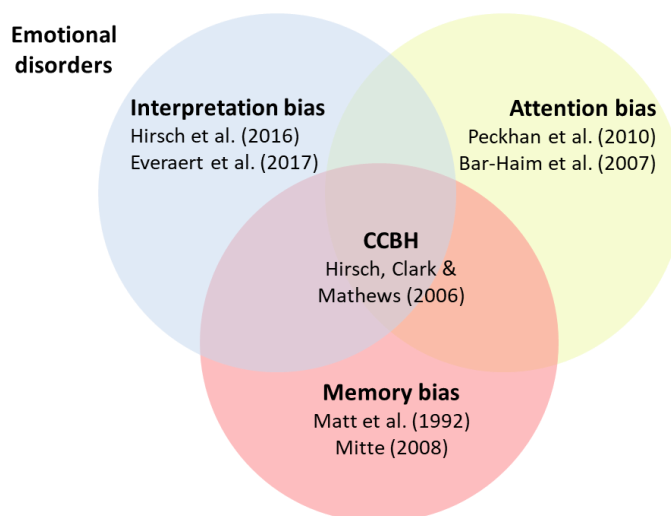
(Everaert et al., 2018). Cognitive flexibility refers to the ability to adapt information processing to each context to promote a more adaptive behavior (Kashdan & Rottenberg, 2010). It has been found that people with major depression show lower levels of flexibility in several facets of cognition. Among others, they show difficulty to adapt explanations to different events, emotion regulation strategies to each situation, or attention resources depending on the requirements of the moment (Stange et al., 2017). For example, recent studies with participants with major depression have shown that they not only have more negative expectations about their performance on an experimental task but are also less able to change those expectations in the face of positive feedback on their performance (Kube et al., 2018). Similarly, it has been shown that both the symptoms of depression and social anxiety correlate with the lack of flexibility to modify the interpretation of a situation when faced with information that contradicts it (Everaert et al., 2018).

The association between the interpretation bias and emotional symptoms has also been studied in relation to cognitive mediators. Specifically, there has been an increased interest to understand their interaction with attention and memory biases. Since the process of generating interpretations in the face of ambiguous information involves higher-order processing, it may require more basic operations such as attention and memory (Everaert, 2021). Neuropsychological evidence seems to support this view. It has been shown that there is enhanced activity in bottom-up circuits in emotional disorders, which could influence higher-order cortical regions and, therefore, the more effortful processing of information (Drevets, 2001). This idea directly connects with the combined cognitive bias hypothesis, which is presented in the next section.

### 1.2.2. The Combined Cognitive Bias Hypothesis (CCBH)

Cognitive theories of emotional disorders already raised the interconnection between different cognitive processes such as memory and attention (Becker & Vrijzen, 2017). The *combined cognitive bias hypothesis, CCBH* (Hirsch, Clark, & Mathews, 2006) continued with this idea and proposed that cognitive biases do not act in isolation but 1) they influence each other and 2) this interaction affects the influence of each bias on all other variables (for example, symptoms). Therefore, this theory suggests that the interaction between cognitive biases makes their effect stronger than if acting separately.

Despite this comprehensive proposal, standard research in the field has focused on studying cognitive biases in isolation (Sanchez-Lopez et al., 2017)- see Figure 3.



*Figure 3.* Main review and meta-analytic studies on the presence of cognitive biases in emotional disorders. Hirsch, Clark and Mathews introduced the Combined Cognitive Bias Hypothesis in 2006 in their work “Imagery and interpretations in social phobia: Support for the combined cognitive biases hypothesis”.

Attentional bias in emotional problems has been extensively studied. It has been found that people with depression and/or anxiety show attentional processes that favor the processing of negative information. Specifically, it has been found that people with anxiety tend to pay

more attention to threat-related stimuli (Hallion & Ruscio, 2011) and people with depression tend to attend more to self-referent stimuli and stimuli concerning negative mood (Armstrong & Olatunji, 2012; De Raedt & Koster, 2010). This type of negative processing is also accompanied by the tendency to avoid positive information, which is more conclusive in people with depression than in people with anxiety (Winer & Salem, 2016). Moreover, there is evidence, using eye-tracker technology, that depressed participants have difficulty to stop paying attention to negative stimuli in comparison to a healthy group (Sanchez et al., 2013). Peckham et al.'s (2010) meta-analysis on attentional bias in depression suggested that this relationship depends on the measurement method. They found a significant relationship when using the dot-probe test, but not the Stroop task. Some studies suggest that depressed individuals may be better characterized by the difficulty to disengage their attention from negative stimuli than by the first orientation toward negative information (Gotlib & Joormann, 2010). However, Peckham et al. (2010) did not find stimuli presentation duration as a significant moderator and neuroscience research has found differences between depressed and healthy control when processing negative in comparison to positive words in stages as early as the P100 and P200 ERP signals (Auerbach et al., 2015; Shestyuk & Deldin, 2010). This controversy does not exist for the relation between negative attention bias and anxiety, where the result seems to be more robust (Bar-Haim et al., 2007). Again, it would be important to clarify which specific subcomponents (e.g. early unconscious attention, selection of response, elaboration of the information) of cognition are being measured when using different paradigms.

Regarding memory bias, it refers to the preference to remember information congruent with the negative mood characteristic of emotional disorders. It has been proposed that those

persons with anxiety symptoms might show a tendency to recall threatening information (Clark, 1999; Eysenck, 2004). However, there is no conclusive evidence in this regard (Mathews & MacLeod, 2005; Mitte, 2008). On the contrary, it has been shown that people with depression tend to remember more negative information than positive or neutral information, which contrasts with the positive bias normally present in people without any symptoms (Matt, Vázquez, & Campbell, 1992). This negative bias has been found both in explicit memory processes (i.e. directly asking the participant to remember) and in implicit memory processes (i.e. remembering without being conscious) (LeMoult & Gotlib, 2019). In addition, there also seems to be slower access to positive memories (Gupta & Kar, 2012). However, it remains unknown whether memory bias resides on the encoding stage of information or the retrieval stage. In the first case, findings of a negative bias on memory would be more likely pointing to a bias on attention or interpretation processes (Köhler et al., 2015). In the second case, a bias on the retrieval would be more directly related to memory processes and its possible dependence on the person's mood. (LeMoult & Gotlib, 2019). To clarify this distinction, it would be necessary to use paradigms able to discern between early and late states of information processing.

In addition to the preference to recall negative information and a faster recollection of these memories, depression is characterized by an overgeneralized memory, i.e. the tendency to remember general autobiographical information instead of the details related to it. For example, people with emotional disorders report a greater number of categorical memories, that is, types of events (e.g., “all the times I have been to a wedding”) and a greater number of extended memories, that is, memories that refer to long periods of time (e.g., "my first semester at university") compared memories of a specific, short-duration moment (e.g., "I had a good

time on my sister's wedding day two years ago") (Raes et al., 2007; Williams et al., 2007). This bias has been found both in people with current symptoms of depression and in people in the recovery period, marking a possible risk factor (Peeters et al., 2002; Werner-Seidler & Moulds, 2012). The change of overgeneralized memories in older patients with depression was found to mediate the association between the intervention and the change in mood (Serrano et al., 2004). Also, there is meta-analytic evidence that a higher number of categorical memories and a lower number of specific ones are predictors of the course of depression over baseline levels (Sumner et al., 2010).

In support of the CCBH, it has been increasingly common to study the interaction between these three types of bias with both correlational and experimental designs (see Everaert & Koster, 2020, for a review). Correlational studies have shown the positive relationship between attention to negative stimuli (for example, words or faces) and negative memory and interpretation bias, both in dysphoric participants and in clinical samples with comorbidity of depression and anxiety (De Raedt & Koster, 2010; LeMoult & Joormann, 2012; Sanchez-Lopez et al., 2017). Experimental studies took one step further and focused on the manipulation of these processes to try to elucidate whether the change in processing bias had an impact on the change of emotional symptoms. This approach is now known as Cognitive Bias Modification (CBM) and aims to get closer to causality. The evidence coming from this field seems to point to the causal role of attention and interpretation bias on memory processes. Results have revealed that memory bias in depression and anxiety is affected by both training of attention bias (Blaut et al., 2013; Daches et al., 2019) and interpretation bias (Joormann et al., 2015; Salemink & Hertel, 2010). However, the relationship between attention and interpretation biases remains unclear. It has been shown that training interpretation away from negative stimuli decreases negative attention bias in socially anxious individuals, but also that training

attention towards threat stimuli increases the tendency to interpret information negatively in people high in anxiety (Amir et al., 2010; White et al., 2011). In depression, changes in attention bias or in interpretation bias have not always led to changes in interpretation or attention, respectively (e.g., Everaert et al., 2015; LeMoult et al., 2017). However, there is some evidence that attention biased towards negative stimuli predicts a higher proportion of negative interpretations, but not vice-versa. (Sanchez et al., 2015).

Moving forward in the field, some different approaches have been used to complement the findings from the correlational and experimental studies. Mediation analyses provide a way to more closely evaluate the mechanisms through which the change in one process can alter another one. For example, some cognitive models of depression propose that selective attention to negative information determines how it will be remembered because it leads to a negative interpretation of the situation (Joormann et al., 2007; Williams et al., 1988). Everaert et al. (2013) found empirical evidence of this idea using a mediation model which showed that the relationship between attention and memory bias mediated by the interpretation bias, i.e. how emotional information was attended had an effect on the interpretation of that information and then affected how it was remembered. Finally, some authors have approached the interaction of interpretation, memory, and attention biases using the network theory and analysis, recently incorporated in the field of psychopathology (Contreras et al., 2019). The network theory proposes that systems can be represented in a network topology with nodes as non-overlapping elements and edges as the relationships between them (Borsboom & Cramer, 2013). Although the incorporation of the network theory is new in this **field**, it some of the classical models reviewed in the previous section. Moreover, the use of the network analysis to study the CCBH hypothesis fits especially well since it not only allows to study the interaction between biases but is also able to evaluate whether this interaction has a greater influence on other variables in

the network than if working alone. Taking this into account, Parsons et al. (2021) found that, in adolescents, there is a connection between negative memory bias and negative interpretation bias, being a moderator of this connection the variable of general mental health.

### **1.2.3. Cognitive biases, cognitive control, and emotion regulation**

In sum, it is necessary to acknowledge that cognitive biases do not only interact with one another but are part of an even more complex cognitive (and emotional) system. Specifically, research on emotional disorders has been focused on studying the relationship between negative biases and the processes of cognitive control and emotion regulation (LeMoult & Gotlib, 2019).

Cognitive control is one of the main components of executive function and it is defined as the ability to redirect attention to new stimuli, inhibiting those more salient in a given situation (Joorman, 2019). As previously mentioned, the negative attention bias is characterized by the constant direction of attention to negative stimuli and the difficulty to disengage from this type of information. Therefore, both processes seem to be closely related. In fact, research has found that patients with depression and anxiety disorders show an impaired executive control network (Liu et al., 2021; Pacheco-Unguettia et al., 2011). Disner et al., (2011), in their neurobiological cognitive model of depression, proposed that cognitive biases are allowed to act when levels of cognitive control are low (hypoactivation of top-down processes), leading to the constant activation of brain emotional areas (hyperactivation of bottom-up processes). This model has been supported by meta-analytical findings indicating that major depression is characterized by lower connectivity within the *frontoparietal network* (involved in cognitive control of attention and emotion regulation) and between neural systems involved in processing emotion and midline cortical regions mediating top-down regulation of such functions (Kaiser

et al., 2015). There is also evidence that lower connectivity within the cognitive control network (related to executive function) and higher connectivity within the affective network correlate with symptom severity in adolescents with depression (Pan et al., 2020). Similarly, dual-systems theories, based on the distinction between associative processes (rapid spreading activation of concepts) and rule-based processes (rational analysis of the association between concepts), have been applied to the understanding of cognitive biases in anxiety (Ouimet et al., 2009). These models propose that associative processes may have a higher impact in individuals low in cognitive control, which is a mechanism directly linked to the capacity to regulate automatic attention to and interpretation of threatening information. It has been shown in samples of adolescents and young adults that working memory and regulatory control, as parts of the cognitive control system, moderate the relationship between anxiety and threat-related interpretation bias (direction dependent on the implicit or explicit nature of the measures of symptoms) (Salemink et al., 2013; Salemink & Wiers, 2012).

Cognitive control is closely related to emotion regulation. While cognitive control is the ability to adapt cognitive and behavioral processes to the specific goals of each situation (Friedman & Miyake, 2017), emotion regulation is defined as the “processes by which individuals influence which emotions they have when they have them, and how they experience and express these emotions” (Gross, 1998, p. 275). Past research has shown the link between both processes (see Pruessner et al., 2020, for a recent review). For example, some studies have found a positive relationship between cognitive control and the use of reappraisal of negative personal events (Cohen & Mor, 2018), while there seems to be a negative relationship between inhibition and rumination frequency (De Lissnyder et al., 2011). Neuroimaging data supports this relationship by showing that both cognitive control (Niendam et al., 2012) and emotion regulation (Ochsner et al., 2012) are sustained in the frontoparietal network. At the same time,

there is evidence that people with depression and anxiety present a specific pattern of emotion regulation strategies, i.e. lower levels of acceptance and reappraisal, and higher levels of suppression and rumination (Schäfer et al., 2017; Visted et al., 2018).

From a broader picture, cognitive biases have also been studied in relation to both impairments in cognitive control and specific emotion regulation strategies. For example, it has been found that the tendency to interpret ambiguous information negatively prevents the positive reappraisal of the event (Mogg & Bradley, 2018). Also, the tendency to attend and the difficulty to inhibit negative information could promote the use of repetitive negative thinking (Linville, 1996). Even Gross's (1998) model of emotion regulation suggested that cognitive biases could play a causal role in the use of some emotion regulation strategies. Some results have shown that emotion regulation strategies common in emotional disorders (e.g., rumination or suppression) mediate the relationship between cognitive biases and symptoms of depression both in adults and in children and adolescents (Sanchez-Lopez et al., 2019; Sfarlea et al., 2021). There are also some findings indicating that the influence of overgeneralized memory on interpretation bias is different for people with high and low levels of rumination (Raes et al., 2006) and that the association between overgeneralized memory and rumination is found in people with high levels, but not low levels, of depression (Romero et al., 2014; Sutherland & Bryant, 2007).

Some models have tried to bring all these processes together. The CaR-FA-X model (Williams et al., 2007) explains the interaction between overgeneralized memory bias, rumination, and low cognitive control. It proposes that autobiographical memory in people with emotional disorders, captured (Ca) by depressogenic themes, activates rumination (R) together

with functional avoidance (FA) of negative details of those memories, leading to an overgeneralization of the information. Moreover, the limitations in the executive function (X) would not inhibit this dysfunctional process, all leading to cognitive and behavioral symptoms. Another theoretical model focuses on the difficulty to disengage from negative information, which would be promoted by difficulties in executive function and would at the same time promote rumination over self-referent information (Koster et al., 2011). There is meta-analytic evidence that repetitive negative thinking is related to difficulties discarding information that is no longer relevant from the working memory but not to other cognitive control functions (Zetsche et al., 2018). All together points to a cycle in which attentional biases towards negative information, together with a lower ability to disengage or inhibit it, would lead to higher levels of rumination and negative memories. Recently, an integrative interplay model has brought together all these processes concerning depression (Villalobos et al., 2021). The authors propose different pathways that could explain these interactions. One of them supports previous models by proposing that cognitive control difficulties could cause biases in processing, leading to dysfunctional emotion regulation and symptoms of depression. However, these types of interactions need to be tested with specific research designs such as experimental or longitudinal data, which allow an approximation to causality.

## **CHAPTER 2. Cognitive bias modification in emotional disorders**

The clinical relevance of studying cognitive biases concerning emotional disorders lies in their potential causal role in the development and maintenance of symptoms. There is neurological evidence that psychological techniques can elicit changes in frontal brain regions related to information processing (Browning et al., 2010). Also, different meta-analyses show that cognitive-behavioral therapy (CBT), partly focused on modifying cognitive variables, leads to improvement in symptoms of anxiety and depression (Cuijpers et al., 2016; van Dis et al.,

2020). Some authors propose that changes in cognitive biases may be the working mechanism through which antidepressant medication and CBT lead to further improvement in symptoms of depression and anxiety (Harmer & Cowen, 2013; Reinecke et al., 2013).

The study of the specific role of cognitive biases as causal mechanisms started with Mathews and Mackintosh's (2000) research of interpretation bias and anxiety. They used an experimental design in which they presented university students with descriptions of situations that remained ambiguous until the final word (see Table 1). The training consisted of leaving a cue for participants to complete this final word leading to a positive or a negative resolution of the situation. Then, participants had to answer a comprehension question about the situation followed by feedback congruent with the training they had been assigned to (positive or negative). They found that those participants trained to complete the scenarios most of the times with a negative resolution showed increases in anxiety levels. This was the start of a new research area known as *Cognitive Bias Modification (CBM)*, which later on has been studied as a potential clinical mechanism (Blackwell, 2020).

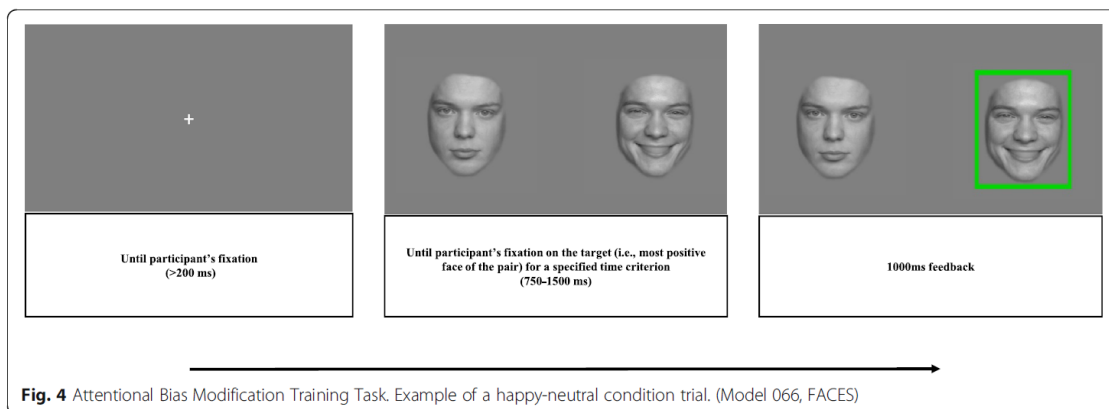
Table 1. *Example of interpretation bias training with 64 scenarios (adapted from Mathews & Mackintosh, 2000).*

Ambiguous scenario	<i>Your partner asks you to go to an anniversary dinner that their company is holding. You have not met any of their work colleagues before. Getting ready to go, you think that the new people you will meet will find you ...</i>
	↓
Negative/Positive resolution	<i>bo---g/fri---y.</i>
	↓
Comprehension question	<i>“Will you be disliked by your new acquaintances?” Yes/No</i>
Feedback	<i>Correct answer / Incorrect answer</i>

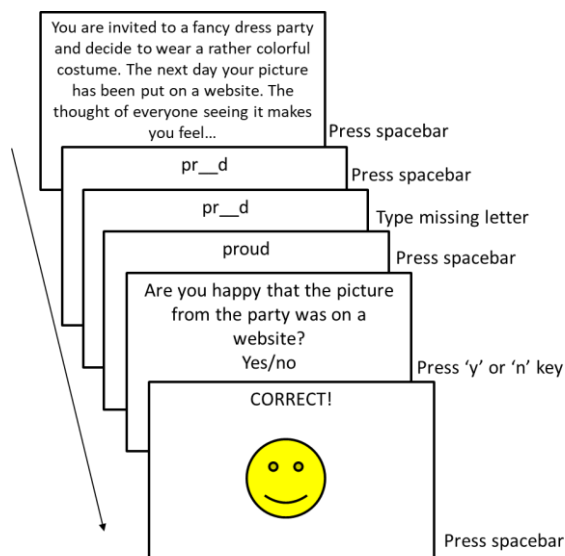
CBM training has focused on the modification of attention (ABM) and interpretation bias (CBM-I). The former consist of the presentation of numerous trials where negative stimuli

appear (for example, an angry face) together with neutral or positive stimuli (for example, neutral or happy emotional faces), while the person is asked to attend to the least negative stimulus (e.g. Vazquez et al., 2016) (see Figure 4). Similarly, in CBM-I, participants have to positively solve different trials where ambiguous information is presented in the form of homographs or homophones, incomplete sentences (see Figure 5), images with mixed emotional expressions, or ambiguous situations in image, video, or written formats (Schoth & Lioffi, 2017). The underlying rationale of these approaches is that repeated practice would lead to a change in automatic processing towards less negative stimuli.

*Figure 4.* a) Example of positive attentional bias training with 576 trials (adapted from Vazquez, Blanco, Sanchez, & McNally, 2016).



*Figure 5.* Example of positive interpretation bias training with 42 trials (adapted from de Voogd et al., 2017).



Regarding the modification of memory bias, there have been several approximations, although not covered by the term ‘Cognitive Bias Modification’. For example, *concreteness training* aims to reduce overgeneralized memory (Watkins et al., 2009) and *positive memory enhancement training* is focused on improving the quality of positive memories to fight against negative mood (Hall et al., 2018). Similarly, the new area of ‘memory therapeutics’ focuses on the application of empirical findings of basic science concerning memory into the clinical practice with emotional disorders (Dalgleish & Werner-Seidler, 2014). Among others, it includes the MEmory Specificity Training (MEST) which aims to modify overgeneralized memory in depression by activating negative autobiographical memories in neutral or positive contexts so that they change its valence allowing the person to access the specific details (Köhler et al., 2015). This training has proved to be effective in depressive symptoms and cognitive processes such as rumination, cognitive avoidance, and problem-solving (Neshat-Doost et al., 2013; Raes et al., 2009). In general, it is assumed that memory is not a stable structure but a part of cognition that changes with context and time. Some authors have recently suggested the use of the ABC functionalist approach to modify autobiographical memory taking into account the antecedents and consequents, and improve well-being (Vanaken et al., 2021).

CBM effectiveness has been studied both from its *near-transfer-effect* to the targeted bias and from its *far-transfer-effect* to other related variables such as symptoms, and the debate about its utility remains open (Beevers, 2015; Richards et al., 2016). Meta-analyses suggest that training interpretations could be more effective than training attention, for both bias (Hallion & Ruscio, 2011) and symptom change (Cristea et al., 2015). Menne-Lothmann et al. (2014) found that CBM-I training improved interpretation processes and mood states, which was moderated by the use of imagery instructions, gender, number of sessions, and type of sample (although mixed results have been found regarding the two last moderators, Cristea et al., 2015; Hallion & Ruscio, 2011). A recent meta-analysis supports the efficacy of CBM-I in comparison to wait-list and sham training control groups and some studies suggest that these programs are as effective as computerized CBT for emotional disorders (Bowler et al., 2012; Fodor et al., 2020). In fact, the higher efficacy of CBM-I than ABM trainings could be explained by the use of techniques resembling the CBT cognitive restructuring approach, in which a more conscious, elaborated type of thinking is enhanced (Fodor et al., 2020). However, the high levels of heterogeneity among CBM studies makes it difficult to uncover the mechanisms through which these trainings can improve cognitive bias and symptoms. Steinman et al. (2021) recently identified until 13 variations of brief, one-session CBM trainings and compared them to no-task and neutral control conditions. The authors found that all of them, but three, were able to reduce negative and increase positive interpretations of ambiguous information (near-transfer), but only three of them were able to change stress and anxiety responses after training (far-transfer). One of the key aspects to improve symptoms seems to be targeting flexibility related to emotional materials and not only teaching to systematically process positive information or increasing flexibility in relation to non-emotional material (Parsons et al., 2016; Steinman et al., 2021). Also, although it might seem straightforward, for CBM programs to be able to

improve symptoms, they need first to be able to improve the cognitive bias they aim to modify. Cristea et al. (2015) conducted a meta-analysis to examine the efficacy of CBM to improve clinically relevant outcomes and concluded that these interventions only showed small effects. However, some years later, Grafton et al. (2017) reanalyzed these data arguing that CBM effectiveness for clinical outcomes should be examined only when the training has been successful, i.e. when it has managed to change the targeted cognitive bias. In fact, the authors found that only those CBM trainings which successfully modified negative biases were also able to reduced emotional vulnerability. All together leads to the conclusion that CBM programs are a promising clinical tool as long as we manage to discover the factors that make them effective.

## GENERAL OBJECTIVES AND HYPOTHESES

Given the important role of interpretation bias in emotional disorders, the first aim of this dissertation was to systematically analyze its presence in samples with depression in comparison to other groups. The framework used for this purpose was Beck's cognitive model. Despite the importance of Beck's theory and its influence in both research and the clinical practice (Beck, 1976; Weissman & Beck, 1978), the specific cognitive biases that he framed within the spectrum of depression (catastrophizing, dichotomous thinking, selective abstraction, arbitrary inference, overgeneralization, minimization, labeling, mindreading, and emotional reasoning) had never been systematically studied before. A previous meta-analysis (Everaert et al., 2017) revealed a medium effect size for both the presence of a negative interpretation bias and lack of a positive interpretation bias at different levels of depression symptoms (clinical, subclinical, and in remission). However, this research focused mainly on studies using experimental tasks to measure interpretation bias. Although experimental tasks are highly used in research and provide important benefits to study cognitive processes (e.g., minimization of response biases or control of extraneous variables), in clinical practice the use of questionnaires is still the standard. Moreover, the authors found high levels of heterogeneity, partly explained by the variety of paradigms used. Thus, it was necessary to complement these findings with a systematic study of interpretation bias measured with questionnaires and with a reduced content scope (i.e. Beck's classification of cognitive distortions).

Therefore, the first study presented in this dissertation is a systematic review and meta-analysis on the presence of Beck's cognitive biases, as measured by self-reports, in samples with depression in comparison to any other groups. The main hypothesis of this study was that there would be significantly higher levels of Beck's categories of interpretation bias in depression groups in comparison to other control groups. Moreover, it was hypothesized that

this effect could be moderated by different factors, such as year of study, geographic location of the author of correspondence, sample size, percentage of women, type of sample (subclinical or clinical, general population, students), the measure of depression symptoms, and the characteristics of the measure of cognitive bias.

The second aim of this work, given the clinical potential of CBM-I, was the design a new program to modify interpretation bias using a novel approach in which the focus is on promoting more elaborate than automatic processing. The new program, called ‘Relearning how to think’ or CBM-IClin, is the result of combining the clinical techniques for cognitive change used in cognitive-behavioral therapy, together with the focus and the flexibility of the traditional CBM procedures. The design and protocol for the evaluation of this new intervention are presented in the second study of the dissertation.

The third and final aim was to evaluate the effectiveness of the new program. This was done in two different studies. Study 3 evaluated whether the program could successfully reduce negative interpretation bias (near-transfer-effect) in participants with different levels of emotional symptoms. Study 4 addresses the efficacy of the program to change other related variables, such as memory biases and symptoms (far-transfer-effect), and evaluates the mediating role of the change in interpretation bias in the change of these other related variables.

### **CHAPTER 3. Study 1. Self-reported cognitive biases in depression: A meta-analysis**

As mentioned above, Beck's cognitive theory has been and continues to be one of the most influential in both research and clinical practice of emotional disorders. This theory has inspired the study of the relationship between cognitive constructs and symptoms of depression in different cultures, sexes, and ages (Cristea et al., 2015; Hu et al., 2016; Vîslă et al., 2016). It has also led to the development of commonly used measures, such as the Beck Depression Inventory (BDI-II, Beck et al., 1996) or the Dysfunctional Attitudes Scale (Weissman & Beck, 1978). In addition, Beck's theory resides in the underlying logic of the cognitive behavioral therapy, one of the most commonly used therapies today, in which the treatment of biased thinking is one of the main ways to improve symptoms such as anhedonia or negative mood (Joormann & Gotlib, 2010).

Despite the apparent validity of Beck's model and the extensive use of cognitive-behavioral interventions, the specific cognitive biases that Beck described in his work (see Figure 1) have not been systematically studied, except for the causal attribution bias (Hu et al., 2015). Therefore, it seems necessary to validate these modes of processing in people with symptoms of depression.

The first article included in the dissertation (Nieto, I., Robles, E., & Vazquez, C., 2020. Self-reported cognitive biases in depression: A meta-analysis. *Clinical Psychology Review*, 82 101934. <https://doi.org/10.1016/j.cpr.2020.101934>) addresses this objective. Given the lack of studies, it was not possible to analyze all the bias categories separately. Two different meta-analyses were carried out showing high effect sizes in the relationship between catastrophizing and depression ( $k = 23$ ,  $g = 0.95$ , 95% CI [0.64; 1.26]) and general interpretation bias and depression ( $k = 40$ ,  $g = 0.78$ , 95% CI [0.43; 1.13]). High levels of heterogeneity were found, which were explained by moderator variables such as the gender distribution of the sample, the

geographic location of the corresponding author, the instruments to measure depression and cognitive biases, and the design of the study.

## Self-reported Cognitive Biases in Depression: A Meta-analysis

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### Abstract

Despite the influence of Beck's cognitive models of depression, the presence and magnitude of the specific proposed cognitive biases have not been systematically investigated. After a systematic search in PsycInfo and PubMed, studies reporting self-reported outcomes on cognitive biases and depressive symptoms in depressed and/or healthy groups were included. From a total of 4,840 records, two different meta-analyses were conducted. 23 studies on 4,865 participants provided data about catastrophising and depression ( $g = 0.95$ , 95% CI [0.64; 1.26]) and 40 studies on 4,678 participants provided data about interpretation bias in depression ( $g = 0.78$ , 95% CI [0.43; 1.13]). Moderation analyses showed that the relationship between catastrophising and depression was higher in studies with more women, when the corresponding author was from a Western country, and when the instrument to measure depression was the DSM criteria, the SCL-90, the BDI, or the DASS. The relationship between interpretation bias and depressive symptoms was significant only in studies comparing depressed and healthy groups, and when using specific instruments to measure symptoms (DSM/RDC criteria plus a scale cut-off score) and cognitive bias (CDQ/CBQ, SCT, AST-D, other). Some limitations are acknowledged, but risk of publication bias was found to be low, and these results support the utility of some self-reported measures of cognitive biases in depression.

Trial registration: This systematic review and meta-analysis was prospectively registered on the 20th of November 2018 with PROSPERO number CRD42018115365.

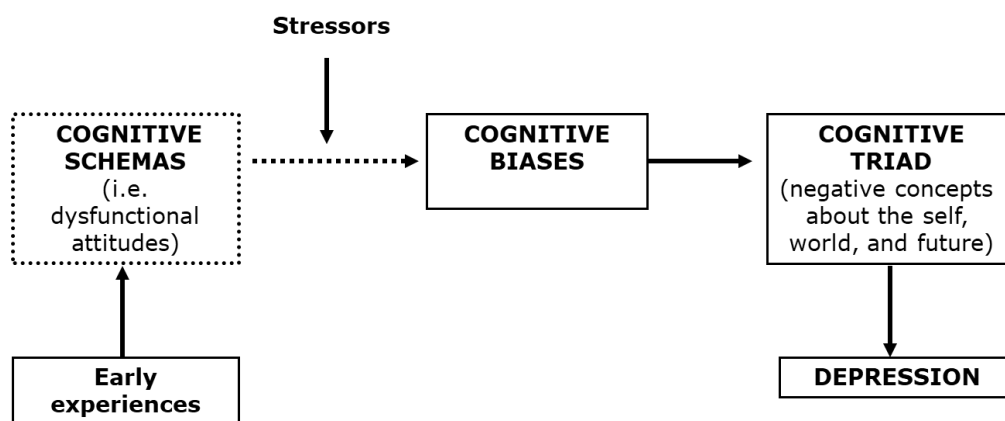
Keywords: cognitive bias; depression; cognitive model; catastrophizing; interpretation bias

## **Introduction**

Depression is considered one of the leading causes of disability in the world and is associated with great social and economic costs (Whiteford et al., 2013). More than 200 million people suffer from major depression (World Health Organization, 2017) and the relapse rate is around 85% (McIntyre & O'Donovan, 2004). Given the impact of this disorder, it is important to understand the variables that influence its development, maintenance and recurrence. Several theories have been proposed to explain the causes of this disorder (Gotlib & Hammen, 2014). Among them, cognitive theories have been very influential both in research and applied fields. These theories point out to dysfunctional thinking as a key causal factor related to the onset and maintenance of these emotional disorders (Beck, 1967, 1976; Barlow et al., 2011).

Beck's seminal cognitive model of depression (1967, 1976) provided some of the concepts and explanatory heuristics that have been incorporated in most of the current cognitive models of depression. According to this model (see Figure 1), individuals may develop, early in life, latent cognitive schemas that get activated when facing environmental stressors that are pertinent to the contents of those schemas (e.g., themes of loss). Cognitive schemas are rather abstract representations of the world and determine the way in which information is processed and how events and stimuli are interpreted in a given context (Dalglish & Power, 2000). When the negative contents of these cognitive schemas are triggered by internal or external events, psychological processes (i.e., memory, interpretation, and attention) operate following negative cognitive biases, like dichotomous thinking or arbitrary inferences (see Table 1). These processes then lead to biased mental products or thoughts about the self, the world and the future (i.e. the cognitive triad). It is important to note the difference between cognitive schemas and cognitive biases. Following Ingram and Kendall's (1986) cognitive taxonomy, cognitive

schemas would be structural variables of the system (i.e., broad cognitive frames through which information is filtered, represented and organized), whereas cognitive biases would function as operational variables, or mechanisms, by which cognitive structures work. Although schemas would be the most distal causes of depression (Panzarella, Alloy & Whitehouse, 2006), biased cognitive operations would also have a critical causal role as they are the action mechanisms used to support and validate the schemas. Overall, this cognitive machinery might be considered as an antecedent of the presence of negative automatic thoughts, negative beliefs (about oneself, the world and/or the future), and ultimately depressive symptoms, which would all be the products (i.e., the tangible outputs) with which clinicians typically work with their clients.



*Figure 1.* Beck's cognitive model. See further descriptions in the text.

Beck's theoretical account has had a profound impact on both clinical and research fields. For instance, cognitive-behavior therapy (CBT) for depression follows the rationale of the cognitive model (Beck et al., 1979; Greenberg & Padesky, 2015). One of the main aims in CBT is to modify biased thinking (Beck, 1976) as a path to improve symptoms such as negative affect and anhedonia (Joorman & Gotlib, 2010). Also, extensive research on cognition and depression has analysed the relationships between these constructs and depressive symptoms in a variety of samples regarding culture, gender, age and diagnostic severity (e.g. Hu et al., 2016; Cristea et al., 2015; Višlā et al., 2016). Moreover, Beck's proposal has inspired the

creation of widely used instruments to measure both symptoms (e.g., the Beck Depression Inventory-II, BDI-II, Beck, Steer, & Brown, 1996) and cognitive constructs like the Cognitive Errors Questionnaire (CEQ, Lefebvre, 1981) or the Cognitive Bias Questionnaire (CBQ, Krantz & Hammen, 1979). In sum, Beck's model has been extraordinarily influential both in research and applied fields in clinical psychology.

### **The role of cognitive biases in Beck's model**

Beck's original theory has been further developed during recent decades. Empirical research has supported and refined the model by clarifying the nature of stressors contributing to form early negative schemas (Hammen, 2005), distinguishing different subtypes of schemas (Clark & Beck, 1991), or lately adding new mechanistic processes, like rumination (Nolen-Hoeksema, Wisco & Lyubomirsky 2008) or overgeneral autobiographical memory (Williams et al., 2007), that have been incorporated in the depression literature for some decades after Beck's initial formulation. Likewise, there have been efforts to inquire into the neurological basis of Beck's theoretical account (Beck, 2008). For instance, researchers have found that cognitive biases seem to be characterized by a maladaptive bottom-up system at the subcortical level, which is reinforced by an attenuated cortical cognitive control unable to regulate them (Disner et al., 2011).

Despite the relevance of Beck's cognitive model of depression, the specific cognitive biases proposed in it (see Table 1) have not been subjected to a systematic review, except for causal attribution bias (Hu, Zhang & Yang, 2015). Although the model is still inspiring research on cognitive processes (Gotlib & Joormann, 2010) and has become one of the best validated and most frequently used therapeutic interventions (Cuijpers et al., 2019), the validity of the cognitive biases explicitly formulated in the model is relatively unknown.

Table 1. *Cognitive biases of depression according to Beck's cognitive model.*

Cognitive Biases	Definition	Example
Catastrophizing or Fortune telling	Anticipating negative extreme events and outcomes.	“I am going out of my mind”
Personalization or Internal causal attribution	Always interpreting events from a self-point of view. Exaggerated guilt.	“He is disgusted by me” “When something goes wrong, it is my fault”
Dichotomous thinking	Extreme thinking where things are interpreted like all-or-nothing, black-or-white.	“If I can’t do it perfect, I won’t do it at all”
Selective abstraction	Paying attention in a selective manner to negative events or outcomes and missing the rest of the information.	“She only said the job was ‘good’”
Arbitrary inference	Making negative interpretations with no evidence that supports them, or with contrary evidence.	“It will go bad for sure”
Overgeneralization	Making general interpretations and conclusions taking into account only one piece of information.	“Everything will always be this bad”
Minimization/Discounting positives	Disqualifying positive events or experiences as non-relevant	“Winning the price was not that good”
Labelling	Naming negatively the self and others based on the occurrence of just one mistake.	“I am a loser”
Mindreading	Systematically thinking that others are reacting negatively to you.	“He thinks I am a failure”
Emotional reasoning	Assuming negative emotions represent how things are in reality.	“I feel guilty. Therefore, I must have done something bad”

Note. These categories of cognitive bias have been proposed in different books and articles by Beck and collaborators. For the present meta-analysis the following documents were revised: Beck (1963, 1967, 1976, 1979) and Burns (1980).

Whereas some meta-analyses have approached the study of cognitive constructs such as irrational beliefs, dysfunctional thinking, or automatic thoughts (Cristea et al., 2015; Višlă et al., 2016), the magnitude of most cognitive biases in depressed individuals has not been synthesised in the literature. Also, it remains unclear whether these processes are exclusive for

depressed individuals, which makes it important to study their relationship with depressive symptoms itself (dimensional studies) but also to compare different types of populations (categorical studies). Thus, the aim of this study was to conduct a meta-analysis of those cognitive biases of depression, as specified in Beck's cognitive model, that have not been meta-analysed in previous studies (i.e. those presented in Table 1 except for Personalization/Internal causal attributions). Random-effect models were used (since sampling variability was expected, Riley, Higgins, & Deeks, 2011) to meta-analyse each cognitive bias, using the standardized mean difference with Hedge's correction ( $g$ ) as the effect size (ES). The meta-analysis was pre-registered in PROSPERO (CRD42018115365). The first hypothesis was that there would be significantly larger levels of cognitive biases in depression groups than in other comparison groups, such as healthy participants, or individuals with other psychological symptoms, or subclinical levels of depression. Also, it was expected that several variables could moderate this effect. The year of the study and geographic location of the corresponding author were coded to study potential spatial and temporal effects. Based on previous findings, sample characteristics such as age (Reed, Chan, & Mikels, 2014), gender (Kessler & Bromet, 2013), or type of sample (Clark, Beck & Alford, 1999) were investigated although the direction of these potential moderation effects was not anticipated. Finally, methodological variables such as sample size, type of measure, and the psychometric characteristics of the instruments were also included as potential moderators given previous meta-analytic results (Everaert, Podina, & Koster, 2017).

## **Method**

### **Eligibility and search criteria**

A systematic search was conducted on the databases of PsycINFO and PubMed, until February 2020, combining terms related to the spectrum of depression (depress\* OR dysphor\*

OR mood OR “affective disorder” OR “sad mood” OR sadness), comparison groups based on DSM-5 (American Psychology Association, 2013) categories and type of population (delirium OR dementia OR "neurodevelopmental disorder" OR schizophrenia OR "psychotic disorder" OR "delusional disorder" OR "bipolar disorder" OR "anxiety disorder" OR "somatoform disorder" OR "factitious disorder" OR "dissociative disorder" OR "obsessive-compulsive disorder" OR "trauma-related disorder" OR "stressor-related disorder" OR "somatic symptom disorder" OR "eating disorder" OR "elimination disorder" OR "sleep disorder" OR "sexual dysfunction" OR "gender identity disorder" OR "disruptive disorder" OR "impulse-control disorder" OR "conduct disorder" OR "substance-related disorder" OR "addictive disorder" OR "alcohol-use disorder" OR "neurocognitive disorder" OR "personality disorder" OR "paraphilic disorder" OR "intellectual disability" OR "developmental disorder" OR "autistic disorder" OR "oppositional defiant disorder" OR "attention deficit-hyperactivity disorder" OR "normal population" OR "general population" OR student\* OR control OR healthy OR group\* OR nondepressed OR nondysphoric OR “never depressed” OR compar\* OR differ\*) and the list of cognitive biases described in Beck’s model of depression: catastrophizing, dichotomous thinking, selective abstraction, arbitrary inference, overgeneralization, minimization, labelling, mindreading, and emotional reasoning. This selection was made after revising different documents by Beck and collaborators (Beck, 1963, 1967, 1976, 1979; Burns, 1980). Different terms were used to search for the results of each specific cognitive bias (e.g. “polarized thinking” OR “dichotomous thinking” OR “bipolar thinking” OR “all-or-nothing thinking”) given that these constructs have been named heterogeneously in the literature. Moreover, more general terms (‘negative thinking’, ‘interpretation bias’, ‘thinking error’, and ‘cognitive distortion’) were also included in the search to fully cover the research in the area. Samples with physical or medical conditions were excluded. Also, personalization, or causal attribution

bias, were not included in the search as it has already been meta-analysed (Hu et al., 2015). Two complementary approaches were used to complete the inclusion of studies. First, all the studies cited in the meta-analyses found in our search were individually inspected to add possible relevant references. Second, a complementary search was performed using the terms (cognitive distortion\* OR “cognitive bias” OR cognitive style\* OR cognitive intrusion\* OR cognitive error\* OR maladaptive cognition\* OR thinking error\* OR heuristic\*) AND ti("meta-analysis" OR "meta-analyses" OR "review") to find meta-analyses and reviews in the area and inspect the primary studies included.

The inclusion criteria were a) empirical categorical and dimensional studies; b) measuring cognitive biases and depression symptoms; c) with self-report questionnaires; d) in adults (> 18 years); e) published in English; f) peer-reviewed; and g) providing the necessary data to calculate effect sizes. Studies were excluded if they measured cognitive constructs different from cognitive biases (e.g. Dysfunctional Attitude Scale, DAS, Hammen & Krantz, 1976; Automatic Thoughts Questionnaire, ATQ, Hollon & Kendall, 1980), or measured cognitive biases with experimental tasks, interviews or non-quantitative methods. Studies including only samples with comorbidity or with disorders other than depression were also excluded. Multiple measures of the same cognitive bias or depressive symptoms were handled either by choosing the most common instrument among the included studies (to improve comparison) or by calculating the mean for that result.

### **Data collection process**

The search, selection and codification processes were made by two different PhD students (IN and ER) independently. The inter-rater agreement for the selection of studies was excellent ( $\kappa=0.80$ ,  $k=274$ ). All the potential variables relevant to the analyses were coded (see Table 1 in Supplementary Material). The following moderators were included: year of the

study, geographic location of the author of correspondence -Western (Europe, North-America, Australia and New Zealand), non-Western (Asia)- sample size, percentage of women in the total sample, type of sample (subclinical or clinical, general population, students), measure of depression symptoms (used to select the groups in categorical studies and to calculate the correlation with cognitive bias in dimensional studies), measure of cognitive bias (no pre-specified categories), number of items, and reliability of the cognitive bias measure. The first and second authors coded all studies independently, being kappa inter-rater reliability 0.77. Disagreements were discussed to reach consensus among all the authors.

## **Analytic plan**

### **Summary measures**

Random-effects meta-analyses for all the included cognitive biases were conducted, in SPSS 20 and R 3.5.0 (metafor package Viechtbauer 2010), using the standardized mean difference ( $d = \frac{\bar{X}_1 - \bar{X}_2}{S_{pooled}}$ ) with Hedge's correction ( $g = c(m) * d$ ) as the effect size (ES). Positive values reflect a higher level of cognitive bias in the experimental group compared to the control group. Hedge's  $g$  values can be categorized as small (0.2–0.5), medium (0.5–0.8), or large (>0.8) (Cohen, 1988). All studies were included in the analyses. Thus, the ES was calculated based on data comparing groups (depressed group vs. any other condition) and correlations between cognitive biases and quantitative measures of depression symptoms. This strategy allowed us to include a larger number of studies and make the results more reliable. Means, standard deviations, sample sizes and correlations were used to calculate the ES. If between-group data were not available, then reported  $t$ -values or between-group  $F$ -values and sample sizes were used. For dimensional studies, Pearson correlations were first standardized using Fisher transformation ( $Z_r = 1/2 * \ln * ((1+r)/(1-r))$ ). Then, these values were converted to standardised mean differences ( $d = 2r / \sqrt{1 - r^2}$ ;  $v_d = 4v / (1 - r^2)^3$ ), followed by Hedge's correction

(g). In all cases the pooled standard deviation was used to calculate  $g$ , the method to weight studies was the inverse of the sampling variance of  $g$ , and confidence intervals (CI) were used as reflection of the estimate precision, both within and between studies.

### **Homogeneity**

Homogeneity was assessed using two indicators: the  $Q$ -value of the test of heterogeneity, and the  $I^2$  index. When the  $Q$  value has a significance level lower than .05 the null hypothesis of homogeneity is rejected, leading to the conclusion that all the studies are not estimating the same parameter. Regarding the  $I^2$  values, categorization is established as follows: 0% = no heterogeneity; equal to or higher than 25% = low heterogeneity; equal to or higher than 50% = moderate heterogeneity; and equal to or higher than 75% = high heterogeneity (Borenstein et al., 2009).

### **Moderation analyses**

For moderation analyses, mixed-effects models were used to test categorical variables and meta-regression (DerSimonian-Laird's estimator) was used to test continuous variables (Borenstein et al., 2009).

### **Risk of bias**

Publication bias was analysed using different methods. First, the Orwin's (1983) fail-safe number ( $N_s$ ) was calculated to know the number of studies with a medium effect equal to zero that would make the ES in the meta-analysis become non-significant. The threat is considered to be real when  $N_s \leq (5k + 10)$ . Second, the funnel plot was inspected. It represents the precision of each primary study (standard error, SE) against its individual effect size. Without publication bias, the shape and density should be symmetric. Two different methods can be used to test the symmetry of the funnel plot. Kendall's Rank correlation tests the null hypothesis that the ES and the SE are independent. The Eger's regression test for funnel plot

asymmetry (Sterne, Becker, & Egger, 2006) tests the null hypothesis that there is perfect symmetry in the plot (starting point of the regression line equal to 0). Finally, the trim-and-fill procedure (Duval & Tweedie, 2000) is used as a sensitive analysis to calculate the ESs and confidence intervals of the individual studies accounting for the missing values reflected in the asymmetry of the funnel plot.

All the analyses were repeated after removing outliers. These were defined as those primary studies with both sides of their 95% confidence interval outside the 95% confidence interval of the pooled studies.

### **Quality of studies**

The quality of primary studies was assessed using an adaptation of the Downs and Black's checklist (Downs & Black, 1998). This scale has previously been used in a meta-analysis on interpretation biases (Everaert et al., 2017) and evaluates standards of methodological quality, such as quality of report (e.g., "*Is the hypothesis/aim/objective of the study clearly described?*"), external validity (e.g., "*Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*"), bias and confounding variables (e.g., "*If any of the results of the study were based on "data dredging", was this made clear?*", "*Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*"), and statistical power ("*Did the study have sufficient power to detect an effect where the probability value for a difference being due to chance is less than 5%?*"). Ratings were made by the first and second author independently and an inter-rater agreement of kappa = 0.94 was reached. Disagreements were resolved with discussion until reaching consensus. The quality of the meta-analysis itself was also assessed following standard sets of recommendations (Moher et al., 2015; American Psychology Association, 2018).

## Results

### Study selection

The process of selection and inclusion of studies is shown in Figure 2. From a total of 4,840 records (1,320 duplicates), 3,131 were excluded based on the screening of the title or abstract, while 461 were excluded after a full-text reading. The main reason for exclusion was the lack of a measure of bias (i.e., many studies were focused on constructs different from cognitive biases, such as cognitive schemas or automatic thoughts -see Figure 1). Many studies were also excluded because they did not use self-report questionnaires to measure cognitive biases. Finally, a total of 63 studies were included in the quantitative analyses. 21 studies fulfilled the inclusion criteria but could not be included in the meta-analysis. This was due to the lack of commonality in the type of comparison group and the type of cognitive bias measured by a large enough number of studies (see Table 2 in Supplementary Materials).

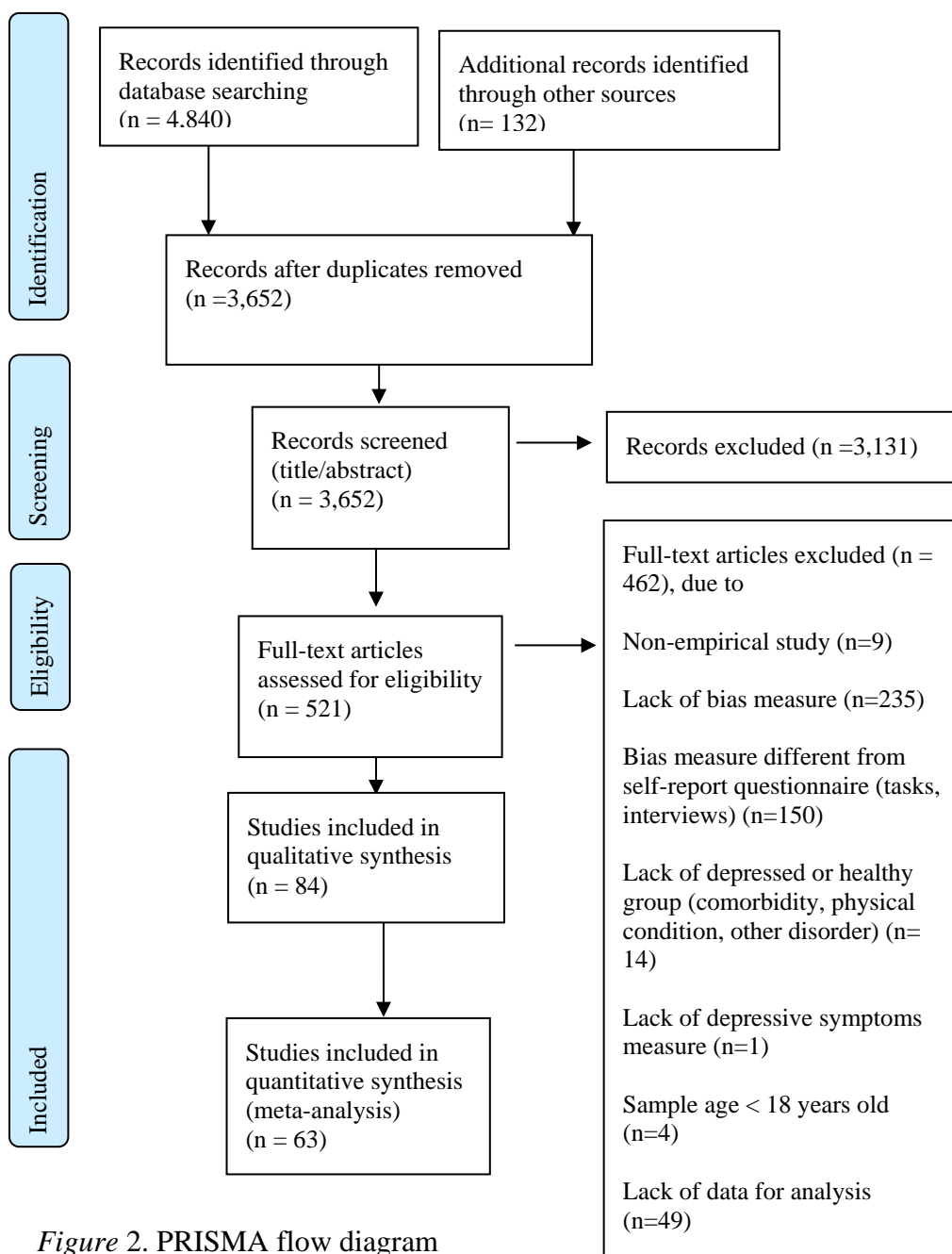


Figure 2. PRISMA flow diagram

### Study characteristics

Studies included in the meta-analysis were published from 1979 to 2017, covering almost four decades of research. Total sample size ranged from 19 to 611 participants, with mean percentage of female participants being 64.4% (from 28.1% to 100%) and a mean age of 32.5 years old (18.9-71.6).

From the different searches that were performed (one per specific cognitive bias name plus the different searches with general terms), studies fulfilling all inclusion criteria were only

found in five of them: ‘catastrophizing’, ‘negative thinking’, ‘interpretation bias’, ‘thinking error’ and ‘cognitive distortion’. Given the lack of studies in the other categories, the content of the instruments used to measure cognitive bias in the selected studies was examined. It was found that only a small group of studies provided results for a specific type of cognitive bias (i.e. catastrophizing). All the other articles provided results for the general concept of biased cognition. Thus, two different analyses were conducted. The first one (k=23) included results evaluating catastrophizing bias in relation to depression. Some of these studies conceptualized catastrophizing as an emotion regulation strategy and used the Cognitive Emotion Regulation Questionnaire (CERQ) to measure it; other series of studies conceptualized it as the probability of occurrence of negative events (e.g., Corcoran et al. (2006) and measured catastrophizing by asking participants to predict the likelihood that some negative events happened to them. The second analysis included 40 studies using a broader conceptualization of biased processing. The measurement methods used in this second group of studies was varied, but all of them instructed participants to interpret ambiguous information applied to themselves. For instance, the Cognitive Bias Questionnaire presents potentially problematic daily life situations and participants are asked to select from four response options the one that best represents their interpretation of the situation; the Ambiguous Scenarios Test-D is composed by ambiguous scenarios which participants imagine that they have happened to them and are asked to rate how pleasant they perceive it, based on their interpretation of such scenarios; and the Sentence Completion Test presents participants with short sentence stems formed by agent–verb combinations (e.g. ‘I think ...’) or simple nouns (e.g. ‘the world ...’) which participants need to complete based on their first interpretation).

Only a small number of categorical studies (i.e. studies with groups or subgroups of individuals) included more than one comparison group, making the analyses comparing

depressed participants and other diagnostic groups not possible. Thus, all the analyses were performed based on the comparison of depressed individuals with healthy individuals. The group of studies measuring catastrophizing bias included 7 categorical studies: 6 with a clinical sample and 1 with subclinical individuals (Beck Depression Inventory, BDI, Beck et al., 1996, total score  $\geq 16$ ). The group of studies measuring general cognitive bias included 28 categorical studies: 18 with a clinical sample diagnosed with major depression, 2 with a clinical sample diagnosed with either major depression or dysthymia, 8 with a subclinical sample (using BDI cut-off scores), and 1 study performing a sad mood induction in the experimental group. All the dimensional studies ( $k=16$  for catastrophizing and  $k=11$  for interpretation bias) were based on healthy, or general population participants, in which depression symptoms were measured with a self-report instrument.

### **Quality of primary studies**

The average quality of primary studies was low (53.34%,  $SD = 8.83$ ) when compared with Everaert et al. (2017) meta-analytic study on interpretation bias where the average quality, also using the Downs and Black's checklist, was 75.68% ( $SD=9.43$ ). Items measuring external and internal validity (e.g. representativeness of the sample, reliability and validity of the measures, time of recruitment, or randomization) and power (item 19) showed the lowest quality scores. Table 3 (in Supplementary Material) presents the mean and standard deviation for each item of the adapted version of the scale.

### **Synthesis of results**

#### **Overall effect sizes**

Effect sizes for catastrophizing bias and interpretation bias (see Figure 3 and Figure 4) were large and moderate ( $g=0.95$ ,  $p < 0.001$  and  $g=0.78$ ,  $p < 0.001$ , respectively). Heterogeneity was significant and high in all cases, with the  $I^2$  value around 90% (see Table 2 and 3).

Significant effect sizes were maintained after the removal of 6 outliers for the catastrophizing bias analysis, and 13 for interpretation bias. These sensitivity analyses also showed a reduction in heterogeneity. Details for sensitivity analyses can be found in the Supplementary Material (Tables 4 and 5).

### **Moderator analyses**

*a) Catastrophizing bias.* For the analyses on catastrophizing and depression (see Table 2), it was found that the variables year of study, sample characteristics (size, type or mean age) and measure of bias (type, number of items or reliability) did not significantly moderate the ES.

Percentage of women, nationality of the corresponding author, and instrument to measure depressive symptoms significantly moderated the ES. The relationship between catastrophizing bias and depression was higher in those studies with a higher percentage of women (meta-regression  $estimate= 0.04$ ,  $SE=0.01$ ,  $p=0.001$ ). Also, the ES was significant for Western but not for non-Western nationality of authors of correspondence and also in studies using DSM criteria, the Symptom Checklist-90, the Beck Depression Inventory or the Depression, Anxiety and Stress Scale. The ES did not reach significance for those studies using the Self-rating Depression Scale or the Centre for Epidemiological Studies–Depression scale. The ‘Other’ category for the moderator type of depressive symptoms measure also showed a large and significant effect. However, due to the lack of studies, it was not possible to make independent groups to clarify the direction of this significant effect. The instrument to measure depressive symptoms was the only significant moderator in the sensitivity analyses (see Supplementary Material, Table 4).

Table 2. *Analyses on catastrophizing and depression.*

<b>Catastrophizing</b>	<b>N</b>	<b>k</b>	<b>g [95%CI]</b>	<b>p</b>	<b>Q (df)p</b>	<b>I<sup>2</sup></b>
<b>Overall ES</b>	4,865	23	0.95 [0.64; 1.26]	< 0.001	311.67 (22) < 0.001	92.94%
<b>Moderators</b>			Beta coefficient/ Mean ES [95%CI]			
<i>Year</i>	4,865	23	0.00 [-0.05; 0.05]	.96	0.0031 (1) .96	
<i>Nationality</i>	4,865	23			4.08 (1) .04	
Western		17	1.15 [0.78; 1.52]	< 0.001	16.03 (16) .45	
Non-western		6	0.41 [-0.21; 1.02]	.19	13.26 (5) .02	
<i>N</i>	4,865	23	0.00 [-0.001; 0.003]	.18	1.84 (1) .18	
<i>% women</i>	3,204	17	0.04 [0.01; 0.06]	< 0.01	10.56 (1) < 0.01	
<i>Mean age</i>	3,204	17	0.00 [-0.03; 0.03]	.95	0.00 (1) .95	
<i>Sample type</i>	4,603	22			1.59 (2) .45	
GP		4	1.02 [0.24; 1.80]	.01	1.35 (3) .72	
Students		12	0.75 [0.30; 1.20]	<0.001	17.21 (12) .14	
GP and CP		6	1.25 [0.60; 1.89]	<0.001	13.21 (5) .02	
<i>Measure of depression</i>	4,865	23			12.93 (6) .04	
DSM		6	1.24 [0.66; 1.82]	< 0.001	15.56 (5) .01	
SCL-90		2	1.37 [0.37; 2.37]	.01	0.04 (1) .84	
SDS		2	0.79 [-0.17; 1.74]	.11	0.41 (1) .52	
BDI		5	1.23 [0.62; 1.84]	< 0.001	0.11 (4) .10	

CES-D		3	-0.40 [-1.23; 0.42]	.34	6.95 (2) .03
DASS21		2	1.03 [0.04; 2.01]	.04	0 (1) .99
Other <sup>1</sup>		3	0.98 [0.17; 1.79]	.02	3.15 (2) .21
<i>Catastrophizing bias measure</i>	4,865	23			3.03 (1) .08
CERQ-C		15	1.14 [0.78; 1.51]	<0.001	4.92 (14) .99
Other <sup>2</sup>		8	0.57 [0.05; 1.09]	.03	28.58 (7) <0.01
Number of items	4,865	23	0.01 [-0.04; 0.07]	.63	0.23 (1) .63
Reliability	4,078	18	3.64 [-0.61; 7.89]	.09	2.82 (1) .09

N=number of participants. k=number of studies. *g* [95% CI] = standardized mean difference with Hedge's correction with confidence interval. Beta coefficient/Mean ES [95% CI] = estimate values for meta-regression analyses with continuous variables, and mean effect sizes for mixed models with categorical variables in moderation analyses. *Q* (df) *p*= test of homogeneity statistic, degrees of freedom and *p*-value. *I*<sup>2</sup> = percentage in which the observed variability exceeds the expected by chance. Type of sample: CP = clinical population; GP = general population. Measure of depression: BDI = Beck Depression Inventory; CES-D = Centre for Epidemiological Studies–Depression; DASS21 = Depression Anxiety Stress Scale; DSM = Diagnostic and Statistical Manual of Mental Disorders criteria to select, at least, the experimental group in categorical studies; SCL-90 = Symptom checklist-90; SDS = Self-rating Depression Scale. Catastrophizing bias measure: CERQ-C= Cognitive Emotion Regulation Questionnaire-catastrophizing.

<sup>1</sup>Other measures of depression: Brief Symptom Inventory; Patient Health Questionnaire-9; Profile of Mood Scale.

<sup>2</sup>Other catastrophizing bias measures: Cognitive Error Questionnaire-catastrophizing subscale; Future Events Questionnaire (FEQ)-estimate the likelihood-negative subscale; Grief cognitions questionnaire-catastrophic misinterpretations subscale; Likelihood estimation measure- negative events-self subscale; Probability-Cost-Questionnaire (PCQ)-depression-probability subscale; Refraining from catastrophic thinking; The availability test-negative future-self subscale.

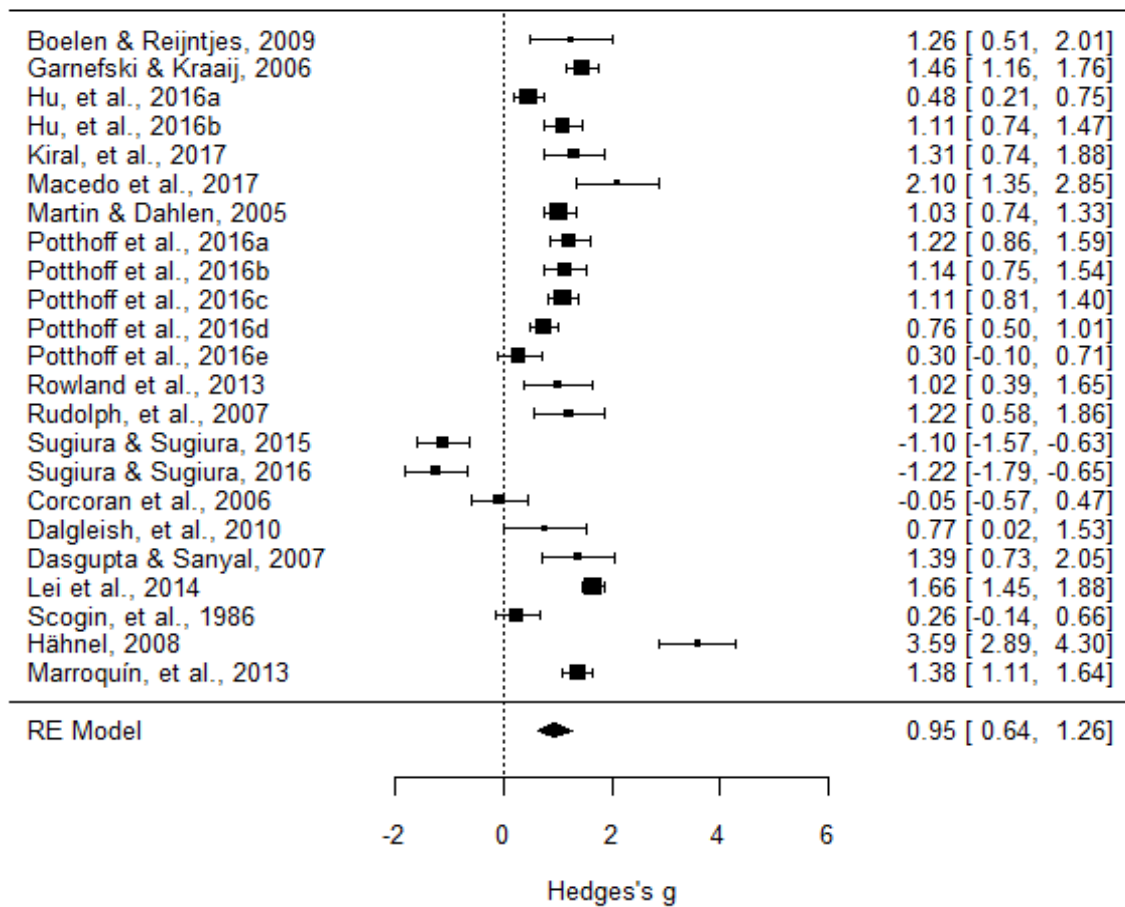


Figure 3. Forest plot for catastrophizing studies.

*b) Interpretation bias.* Meta-regression and mixed-effects models showed that the variables year of study and the nationality of corresponding author did not significantly moderate the relationship between interpretation bias and depressive symptoms (see Table 3).

Regarding the characteristics of the sample (size, percentage of women and mean age) they did not have a moderating effect, but the type of sample did. Categorical studies comparing depressed and healthy groups were the only category of type of sample with a significant mean ES. The effect in student samples (categorical studies comparing groups above and below a cut-off score, or dimensional studies with only healthy or (sub)clinical groups) or dimensional studies with only a clinical population did not show a significant relationship.

Finally, the type of instruments used to measure interpretation bias and depression seemed to be relevant. ES was significant only in categorical studies using both a diagnostic instrument (based on DSM or RDC criteria) and a cut-off point in a questionnaire (BDI, Hamilton Depression Rating Scale (HDRS), LSAS), or using just a diagnostic instrument based on DSM criteria but not in those using only RDC criteria or questionnaires (i.e., Beck Depression Inventory, Centre for Epidemiological Studies–Depression). Regarding the measure of interpretation bias, ES was significant and large when using the Cognitive Distortion/Bias Questionnaire, the Sentence Completion Test and the Ambiguous Scenarios Test for Depression but not when using the Cognitive Error Questionnaire, or the Interpretation Bias Questionnaire. The group of other measures of distortion also had a significant moderating effect, but the small number of studies using each of these instruments did not allow for the conducting of further analyses within the category. Number of items or reliability of the bias measure did not have a significant effect on ES.

None of these moderation effects were significant in the sensitivity analyses after the removal of outliers (see Supplementary Material, Table 5).

Table 3. *Analysis on interpretation bias and depression.*

<b>Interpretation bias</b>	N	k	g [95%CI]	P	Q (df)p	<i>I</i> <sup>2</sup>
<b>Overall ES</b>	4,678	40	0,78 [0.43; 1.13]	<0.0001	742.45 (39) <0.0001	94.75%
Beta coefficient/ Mean ES[95%CI]						
<b>Moderators</b>						
<i>Year</i>	4,678	40	-0.02 [-0.05; 0.01]	.11	2.53 (1) .11	
<i>Nationality</i>	4,678	40			0.25 (1) .62	
Western		38	0.76 [0.40; 1.12]	<0.001	90.18 (37) <0.0001	

Non- Western	2	1.17 [-0.35; 2.69]	.13	0.53 (1) .47	
<i>N</i>	4,678	40	0.00 [-0.00; 0.00]	.32	0.98 (1) .32
<i>% women</i>	3,983	34	0.00 [-0.02; 0.02]	.10	0.00 (1) .10
<i>Mean age</i>	2,847	26	0.02 [-0.01; 0.06]	.19	1.69 (1) .19
<i>Sample type</i>	4,678	40			9.49 (3) .02
Other	2	-0.07 [-1.57; 1.43]	.93	7.19 (1) .01	
Students	17	0.34 [-0.12; 0.92]	.13	12.95 (16) .68	
GP and CP	19	1.34 [0.83; 1.85]	<0.001	60.74 (18) <0.001	
CP	2	-0.33 [-2.05; 1.39]	.71	1.89 (1) .17	
<i>Measure of depression</i>	4575	39			15.13 (4) <0.01
DSM or RDC criteria + cut-off point	9	1.30 [0.58; 2.03]	<0.001	11.78 (8) .16	
DSM interview	4	2.49 [1.33; 3.64]	<0.001	41.36 (3) <0.001	
RDC	5	0.86 [-0.14; 1.96]	.09	1.58 (4) .81	
BDI	17	0.36 [-0.17; 0.89]	.18	17.51 (16) .35	
CES-D	4	-0.04 [-1.08; 1.01]	.94	5.31 (3) .15	
<i>Interpretation bias measure</i>	40				30.59 (5) <0.001
CEQ	6	0.49 [-0.25; 1.22]	.19	8.34 (5) .14	
CDQ/CBQ	12	0.90 [0.37; 1.44]	<0.001	3.23 (11) .99	
SCT	3	1.53 [0.46; 2.59]	.001	7.24 (2) .03	
AST-D	3	-1.25 [-2.28; -0.21]	.02	0.18 (2) .91	
IBQ	2	-1.07 [-2.31; 0.17]	.09	2.71 (1) .10	

Other	14	1.33 [0.83; 1.84]	<0.001	64.57 (13) <0.001
Number of items	3143	33	-0.01 [-0.05; 0.03]	.72
Reliability	1580	11	-3.64 [-11.53; 4.26]	.37

N=number of participants. k=number of studies.  $g$  [95%CI] = standardized mean difference with Hedge's correction with confidence interval. Beta coefficient/Mean ES [95% CI] = estimate values for meta-regression analyses with continuous variables, and mean effect sizes for mixed models with categorical variables in moderation analyses.  $Q$  (df)  $p$ = test of homogeneity statistic, degrees of freedom and p-value.  $I^2$  = percentage in which the observed variability exceeds the expected by chance. Type of sample: CP = clinical population; GP = general population; Other =one dimensional study with a sample of students and university staff and one categorical study with groups of the general population divided based on a BDI cut-off score. Measure of depression: BDI= Beck Depression Inventory, CES-D=Centre for Epidemiological Studies–Depression; DSM = Diagnostic and Statistical Manual of mental disorders; RDC = Research Diagnostic Criteria; cut-off point = using questionnaires Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HDRS) or Liebowitz Social Anxiety Scale (LSAS). Measure of interpretation bias: AST-D = Ambiguous Scenarios Test for Depression-pleasantness rating; CEQ = Cognitive Error Questionnaire; CDQ/CBQ (Krantz & Hammen, 1979) = Cognitive Distortion/Bias Questionnaire-depression distortion subscale; IBQ = Interpretation Bias Questionnaire; SCT = Sentence Completion Test for Depression-negative statements subscale.

<sup>1</sup>Other measures of interpretation bias: Ambiguous Social Situations Interpretation Questionnaire (ASSIQ); Ambiguous/Unambiguous Situations Diary (AUSD); Sentence Completion Test for Depression-total score; Cognitive Bias Questionnaire-total score; Cognitive Distortion Questionnaire (Burns, Shaw, & Croker, 1987); Cognitions Questionnaire; Interpretations of Depression Questionnaire (IDQ); Interpretation of Events Measure (IEM); Interpretation Inventory (II); Interpretation and Judgmental Questionnaire (IJQ)-multiple choice-cross situations subscale; Interpretation Questionnaire for Social Phobia and Depression (IQSD)- depression distortion subscale; Negative and Positive Cognitive Error Questionnaire-negative (NPCEQ); and two measures without name (Drennen, 1991; Nunn, Mathews, & Trower, 1997).

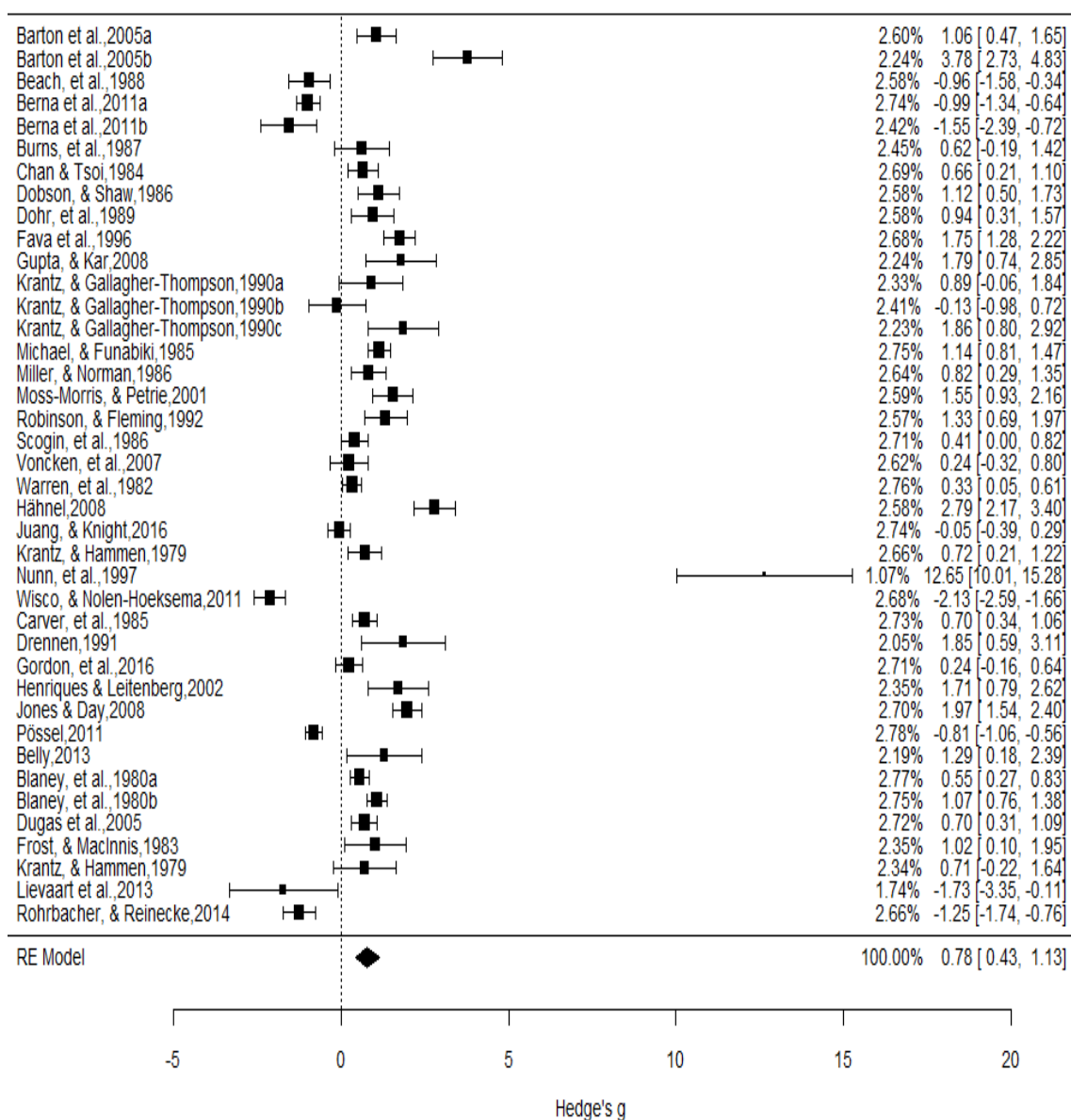


Figure 4. Forest plot for interpretation bias studies.

### Risk of bias.

a) *Catastrophizing studies.* First, the Orwin's fail-safe number was 421, showing no threat of publication bias ( $N_s = 421 > 5k+10$ ). Second, an inspection of the funnel plot (see Figure 5) showed that the shape and density of the funnel plot seemed to be symmetric, which was confirmed with the rank correlation test (Kendall's tau = 0.00,  $p = 1$ ) and the Eager's

regression test ( $z = 0.81$ ,  $p = 0.42$ ). Given that asymmetry was not found, the trim-and-fill procedure was not conducted.

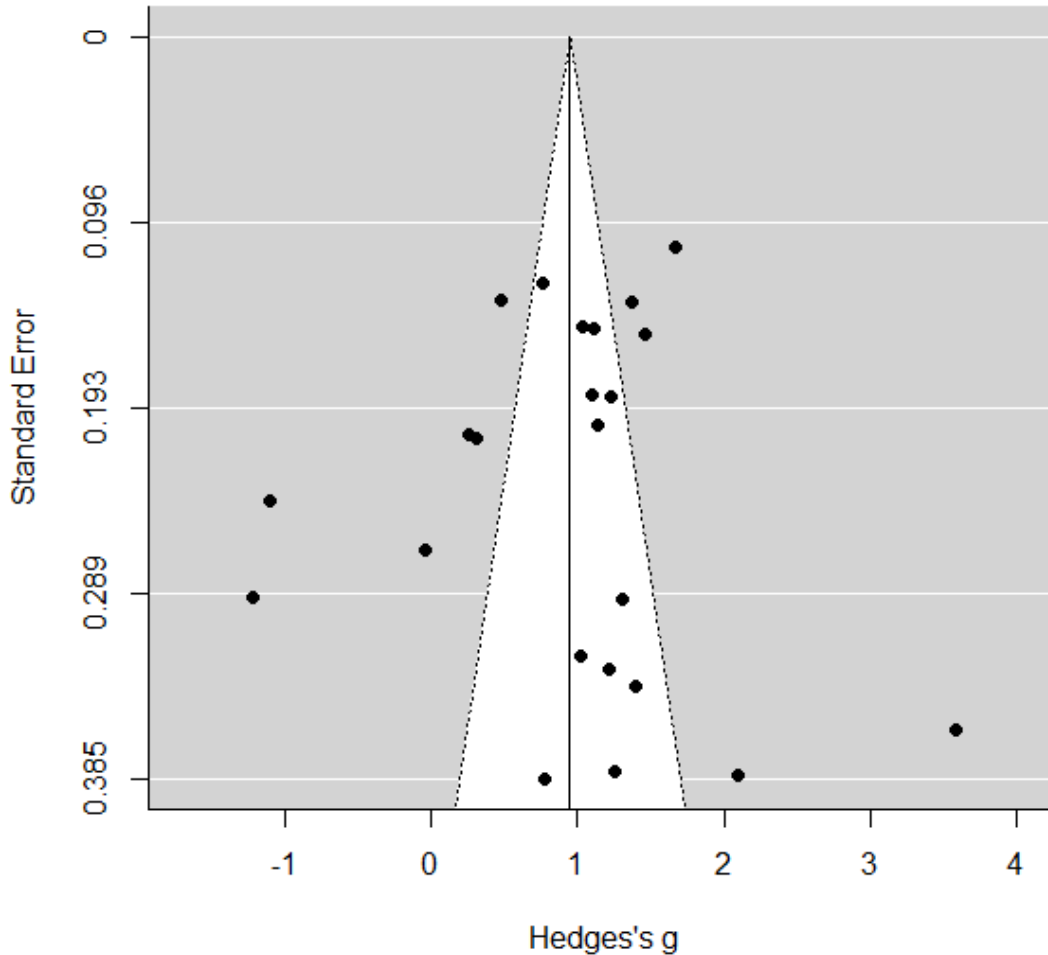


Figure 5. Funnel plot for catastrophizing studies.

*b) Interpretation bias studies.* First, the Orwin's fail-safe number showed there was not a threat of publication bias ( $N_s = 780 > 5k + 10$ ). Second, the funnel plot was inspected with and without the outlier (see Figure 6).

The rank correlation test indicated a lack of publication bias (Kendall's tau = 0.19,  $p = 0.08$ ), while the regression test for funnel plot asymmetry was significant ( $z = 5.50$ ,  $p < .0001$ ). However, sensitivity analyses showed that both the rank correlation test (Kendall's tau = 0.15,

$p = 0.18$ ) and the regression test for asymmetry ( $z = 1.80$ ,  $p = 0.07$ ) indicated the absence of publication bias when removing the outlier.

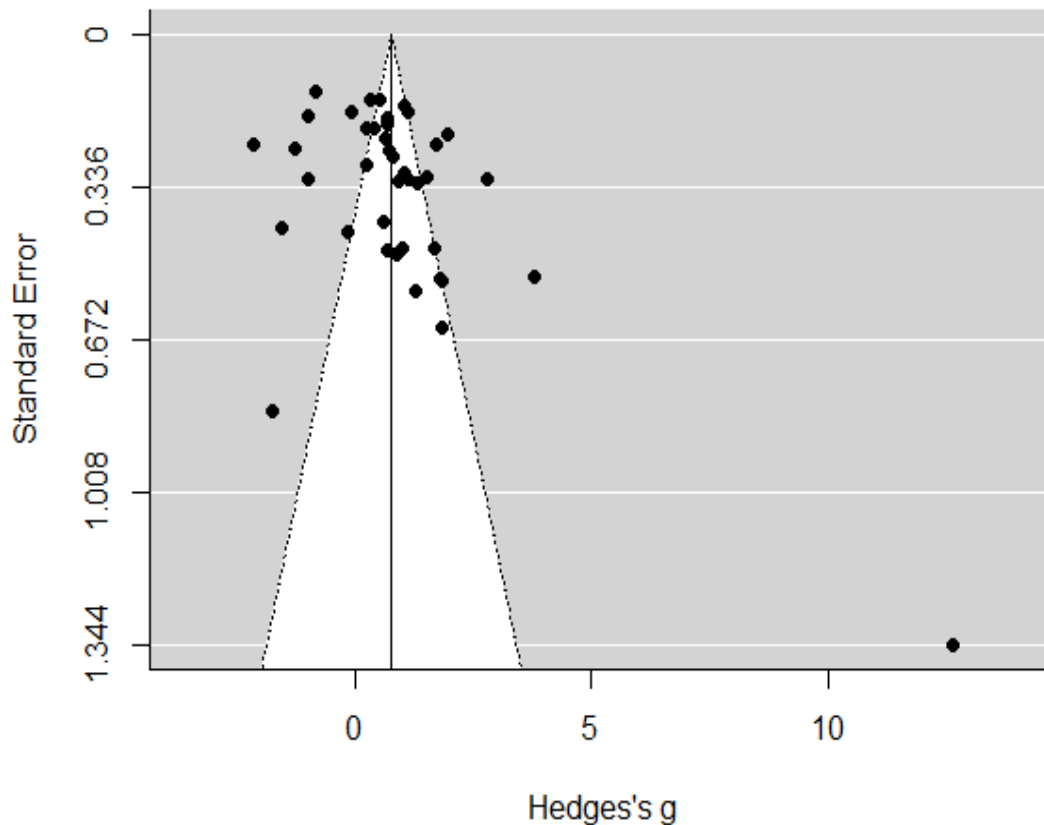


Figure 6. Funnel plot for interpretation bias studies.

## Discussion

The aim of this study was to quantify the evidence of self-reported cognitive biases in depressed individuals as compared to other groups of participants. Based on the relatively scarce amount of empirical studies found in our search ( $k = 63$ ), analyses only included two categories of bias (catastrophizing and interpretation bias) and comparisons between groups of depressive participants and non-symptomatic groups.

Given that the search covered a large period of time (no limit-2020), it seems surprising that only 63 studies could be included in the final review. For example, Hu et al. (2015), in their

meta-analysis on attribution bias and depression, reviewed 86 studies in the past 20 years. One of the main reasons for this relatively small number of studies is that the majority of articles initially screened for inclusion focused on cognitive constructs such as maladaptive cognitive schemas and negative automatic thoughts, which do not reflect the concept of information processing biases proposed in Beck's cognitive conceptualization (Beck, 1967, 1979). Yet, a clear distinction among different components of cognitive psychopathology seems to be crucial to further understand the nature of depression (Ingram & Kendall, 1986) and therefore, efforts should be aimed at clarifying the role of different mechanisms and pathways in psychopathology. In this respect, our study focuses on the notion of cognitive biases as defined in Beck's model. Also, the number of studies was limited due to the exclusion of studies using experimental tasks. Despite some recent criticisms on the reliability of tasks commonly used in experimental psychopathology (Hedge, Powell, & Sumner, 2018; Price et al., 2015), there is a vast amount of research consistently showing cognitive biases in a diversity of domains of processing like attention (Peckham, McHugh & Otto, 2013; Winer & Salem, 2016), memory (Matt, Vázquez & Campbell, 1992), and interpretation (Everaert et al., 2017) using experimental tasks. In fact, Everaert et al. (2017) conducted a meta-analysis on interpretation bias in depression using experimental tasks. They included a total of 84 studies and found an overall ES of  $g=0.72$  (95%-CI: [0.62;0.82]), which is very similar to the result of this meta-analysis. Yet, the aim of our study was precisely to focus on self-report methods as these are still the basic instruments that are used in clinical research and applied settings. There has also been no systematic review on these widely used clinical tools in depression.

The results supported the idea that cognitive biases are stronger in depression when compared to healthy groups. Specifically, we found a large effect for catastrophizing ( $g = 0.95$  [0.64; 1.26] ( $p<0.001$ )) and medium effect ( $g = 0,78$  [0.43; 1.13]  $p<0.001$ ) for interpretation

bias. The large effect associated with catastrophic thoughts may reveal that depression is strongly related to negative expectations of the future, although this type of negative anticipatory thought seems to also be present in other conditions like chronic pain (Crombez et al., 2013), health anxiety (Todd et al., 2018) or pathological worrying (Dash, Meeten & Davey, 2013). In the case of depression, this catastrophic bias might lead to building an overall negative view of oneself, the future and one's own experience, a cognitive product known as the 'cognitive triad' (Beck, 1976). Regarding interpretation bias, results indicate a higher level of negative interpretation bias in depression when compared to healthy individuals. Specifically, depressive groups present a higher tendency to interpret ambiguous scenarios negatively when putting themselves in that situation. This finding is in line with previous findings showing that depression is characterized by an interpretation bias when using self-referential stimuli (Everaert et al., 2017).

Despite the restriction of including only self-report instruments, a high degree of heterogeneity was found. Geographic location, percentage of women and the measure of depressive symptoms explained part of the variability in catastrophizing results, while type of sample, and the instruments to measure both depression and bias moderated the ES in interpretation bias.

Regarding sample characteristics, the percentage of women moderated the relationship between catastrophizing and depression (i.e., the higher the percentage of women, the higher the effect), which could be related to a small but significantly higher presence of cognitive factors, like rumination, in women than in men (Johnson & Whisman, 2013). Although this result is also in line with previous findings showing that depression is more prevalent in women than men (Kessler & Bromet, 2013), the moderation effect of gender for the analysis of interpretation bias was not significant. This difference could be influenced by the variance in

the number of studies included in the analysis for catastrophizing bias ( $k=17$ ) and for interpretation bias ( $k=34$ ). Also, this result should be taken with caution given that the moderation effect disappeared in the sensitivity analysis when removing outliers. Thus, the result related to gender could have been biased by extreme values. Moreover, type of sample significantly explained part of the variance when measuring interpretation bias. The effect was only found in categorical studies comparing clinical and non-symptomatic groups. Neither categorical studies with subclinical samples, nor dimensional studies measuring symptoms of depression in healthy individuals, showed an effect. This finding points out to the possibility that interpretation bias is associated with other unique characteristics of clinically depressed patients. For example, emotion regulation strategies such as rumination are associated with depression and have also been proposed to be influenced by cognitive biases (Joormann & Vanderlind, 2014). Yet, these results should be carefully interpreted since the categories of general population and clinical patients included only one and two primary studies, respectively.

The geographic location of the corresponding author and the measure of depressive symptoms also explained part of the variance in the analysis of catastrophizing bias. The effect was significant only when the corresponding author was from a Western country. It should be noted that this result does not necessarily reflect the relationship between depression and catastrophizing in different country populations since we could only code the nationality of the corresponding author, and not of the sample, which was unfrequently specified in the primary studies. Also, this result should be interpreted with caution since heterogeneity was high within the non-Western group of studies ( $Q\text{-within}=13.26$ ,  $p=0.02$ ) and the moderating effect disappeared when excluding outliers (see Supplementary Material). In fact, the only variable left to explain heterogeneity in this analysis was the type of measure of depressive symptoms.

This moderation effect should not come as a surprise as there is a controversy on which are the best instruments to identify depression (Choi et al., 2014). Finally, the type of measure of interpretation bias also has a moderating effect, which could be explained by the high variability in the instruments used. For example, some of them allow open-ended responses (SCT, IBQ, Burns's CDQ, IJQ), while others provide multiple choice answers (CDQ/CBQ, IDQ, ASSIQ) or Likert scales to rate how often or how likely participants would respond to the situation in a given manner -CEQ, IQSD, II (Warren, Stake & McKee, 1982), Nunn et al., 1997- or how positively/negatively they perceive the situation (ASTD, IEM, AUSD). Nevertheless, these effects also disappeared when excluding outliers (see Supplementary Material). This variability was also reflected in the instruments measuring catastrophizing. Although this variable did not moderate the ES for catastrophizing bias, it is remarkable the difference in the result obtained by studies using the CERQ-C ( $g=1.14$ , 95CI [0.78; 1.51]) in comparison to the rest of the instruments ( $g=0.57$ , 95CI [0.05; 1.09]). This finding could actually reflect the heterogeneity in the instructions and contents of the instruments used in the rest of the studies (see Supplementary Table 6 for more details). Congruently with our findings, Everaert et al. (2017) found that the significant ES of interpretation bias in depression was moderated by the type of measurement used, i.e. only significant when measured with direct, but not with indirect, measures. These results may question the validity of some instruments to measure cognitive biases. Although we coded the psychometric features of the different measures used to analyse cognitive biases, very few studies provided data regarding the reliability and validity of the instruments. Also, in many cases, the subscales, and not the results for the whole questionnaire, were considered to calculate effect sizes (see Supplementary Table 6 for details). All these aspects collectively may have influenced the results. Further research on the convergences and

discrepancies of the modalities of measurement are needed to clarify the issue of finding gold standards of measurement of cognitive biases both in the clinical and experimental fields.

While the risk of publication bias was found to be low, the overall quality of primary studies was not optimal. More than one third of studies (26/63) met less than half the criteria evaluated. 'Quality' is a multi-faceted construct and it is likely that some of these criteria, like those referred to the quality of report (e.g., *Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001 or 0.05?*), may have had a minor impact on the resulting effect sizes. However, criteria evaluating aspects related to the external and internal validity of the studies may have had a direct impact on the findings. For example, representativeness of the sample is a criterion directly affecting the conclusions that can be drawn from quantitative results. Also, the psychometric characteristics of the measures in each sample is essential to know the reliability of the findings. This is a matter of concern in the assessment of self-reported cognitions in the clinical field (e.g. Samtani & Moulds, 2017), and it could have contributed to the heterogeneity of the results of this meta-analysis. Moreover, power calculations to detect the effects are almost absent in the literature selected for this study, and both too large and too small sample sizes can lead to erroneous statistical results. However, it is important to remark that the year of publication range from 1979 to 2019, demonstrating one third of the studies published in the last century. While it is still a warning signal for future investigations, quality of research has also increased during recent decades with the development of new standards such as APA standards (APA, 2018) or PRISMA (Moher et al., 2015). Also related to the year of publication, it is surprising that only 12 of the studies have been conducted during the last five years, which could be related to the tendency to use experimental procedures rather than self-report questionnaires as a more appropriate way to analyse cognitive biases. Nevertheless, it must be kept in mind that the use

of questionnaires is still the default choice in clinical practice and clinical trials comparing therapies, which makes it highly important to keep scrutinizing the validity of these assessment methods.

Based on the findings of this meta-analysis, some recommendations to move this field forward are suggested. The assumption that some specific cognitive biases are present in depression still needs empirical evidence. While processes such as selective abstraction or overgeneralization were theoretically established based on clinical practice (Beck, 1963), this meta-analysis was not able, several decades later, to address its magnitude given the lack of empirical data. As mentioned before, the analysis was split into two categories. While the first one allowed us to conclude that catastrophizing bias exists and is stronger in depression groups than in healthy individuals, the second group of studies focused on a broader concept of cognitive biases that can be understood under the general umbrella of ‘interpretation’ biases. The limited number of studies within this category has made it impossible to draw conclusions about the specific categories of bias proposed in Beck’s model (see Table 1).

While experimental research in the field of cognitive bias has developed refined methodologies to measure specific cognitive biases related to interpretation (Holmes, Lang & Shah, 2009), attention (Duque & Vazquez, 2015), and memory (Matt et al., 1992), and the interplay between these processes (Everaert, Koster & Deraksh, 2012), main clinical models are still anchored on theoretical concepts and assessment methods (e.g., self-report questionnaires) that require further support. Fortunately, there is evidence that both the development of theoretical models of depression (e.g., Gotlib & Joormann, 2010), and interventions aimed at correcting biases (e.g., Jones & Sharpe, 2017), benefit from those newer experimental psychopathology approaches. Although clinical cognitive models of depression, and in particular Beck’s model, are still invaluable as heuristic tools, some of their ingredients,

like ‘cognitive biases’, have been addressed using self-report questionnaires which is problematic. On the one hand, as the present meta-analysis has revealed, there has been no consensus on the most reliable and valid self-report instruments to assess these biases. In some cases, the instruments have only been used occasionally, or only by their original authors; in other cases, the instruments require a laborious correction process by independent coders (e.g., the SCT) which is not practical for clinical purposes. On the other hand, and more importantly, self-report methodologies are likely inadequate indicators of true underlying cognitive processing biases, a problem that was identified several decades ago (Nisbett & Wilson, 1977). Also, theoretical models of cognition and the accompanying experimental methods have significantly evolved since Beck’s model was formulated (Chipman, 2017) and the field is much more mature and sophisticated than when initial cognitive models of depression were formulated. For instance, experimental research on selective attention in depression (which is conceptually related to the ‘selective abstraction’ bias in Beck’s model, see Table 1), has shown that depressed individuals have difficulties in some, but not others, modalities of attention, which were not described at the time when Beck’s model was formulated. In particular, depressed individuals have difficulties to disengage from negative stimuli once they have fixated their attention on them, but they have no difficulties in orienting their initial attention towards emotional stimuli (Armstrong & Olatunji, 2012).

Whilst this is the first study to systematically investigate the presence of the self-reported cognitive biases proposed in Beck’s theory, several limitations should also be mentioned. Our study has not addressed some other types of cognitive biases related to depression, such as thought action fusion (Berle & Starcevic, 2005) or jumping to conclusions (Wittorf et al, 2012) that have also been described in the literature although not included in Beck’s seminal theory. Yet, taking Beck’s proposal as the theoretical framework of reference

seemed to be a good approach for different reasons. First, authors using other cognitive theories (e.g., the hopelessness model of depression) acknowledge the conceptual similarities between models (Panzarella et al., 2006). Second, Beck's model of depression is one of the most used in clinical practice (Greenberg & Padesky, 2015) and empirical results supporting the theory are essential for optimal treatment. Third, the lack of empirical studies fulfilling the inclusion criteria has limited the number of cognitive biases included in the review and the variety of group comparisons to analyse. Another limitation of our results is that it is unknown whether catastrophizing and interpretation bias are specific to depressive individuals or also related to other disorders. Given the surprisingly low number of studies found in our search comparing groups with different psychopathologies, the specificity of these biases could not be assessed, which is a major proposition in cognitive models of depression (Beck & Perkins, 2001).

In sum, this systematic review has found a clear support for the existence of some self-reported cognitive biases in depression as described in Beck's theory, which particularly appear under certain circumstances (e.g., selection of samples using DSM criteria and questionnaires like the CERQ-C). Yet, the rather general low quality of the studies and the lack of sound psychometric properties of the instruments utilized allows for an understanding that the conclusions must be taken with caution. Also, given the scarce number of studies comparing samples with different psychological problems, the specificity of the findings is unknown. Yet, these findings may shed some light on the robustness of some cognitive biases in depression and the best ways to explore them.

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**SUPPLEMENTARY MATERIALS**

Self-reported Cognitive Biases in Depression: A meta-analysis

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Supplementary Table 1. *Characteristics of included studies.*

	Author	TE (g)	Year	Type of study	Geographic location	N	% women	Mean age (years)	Type of sample	Measure of depression	Measure of cognitive bias
<b>Catastrophizing bias</b>											
					The Netherlands						
1	Boelen & Reijntjes	1.26	2009	D	Netherlands	79	83.5	21.5	S	SCL-90	GCQ-c
2	Corcoran et al.	-0.05	2006	C	UK	57	28.07	38.7	CG	DSM	AT
3	Dalgleish et al.	0.77	2010	C	UK	29	58.62	48.55	CG	DSM	LEM
4	Dasgupta & Sanyal	1.39	2007	C	India	48	47.92	49.2	CG	DSM	CERQ-c
5	Garnefski & Kraaij	1.46		D	The Netherlands	611	60%	41.92	GP	SCL-90	CERQ-c
6	Hähnel	3.59	2008	C	The Netherlands	84	100	22.45	CG	DSM	PCQ
7	Hu et al. a	0.48	2016	D	China	255	32.94	21.9	S	SDS	CERQ-c
8	Hu et al. b	1.11	2016	D	China	262	52.67	21.8	S	SDS	CERQ-c
9	Kirall et al.	1.31	2015	D	Turkey	141	77%	59.74	GP	BDI	CERQ-c
10	Lei et al.	1.66	2014	C	China	458	55.02	38.37	CG	DSM	CERQ-c
11	Macedo et al.	2.10	2017	D	Portugal	258	79.8	19.26	S	POMS	CERQ-c
12	Martin & Dahlen	1.03	2005	D	USA	362	79.01	20.46	S	DASS21	CERQ-c
13	Marroquín et al.	1.38	2013	C	USA	262	-	-	S	BDI	FEQ

Author	TE (g)	Year	Type of study	Geographic location	N	% women	Mean age (years)	Type of sample	Measure of depression	Measure of cognitive bias	
<b>Catastrophizing bias (cont.)</b>											
14	Potthoff et al. a	1.22	2016	D	UK	301	81.80	21.69	S	BDI	CERQ-c
15	Potthoff et al. b	1.14	2016	D	UK	235	50.20	24.19	S	BDI	CERQ-c
16	Potthoff et al. c	1.11	2016	D	UK	394	82.20	29.9	S	BDI	CERQ-c
17	Potthoff et al. d	0.76	2016	D	UK	367	62.10	22.24	S	BSI	CERQ-c
18	Potthoff et al. e	0.30	2016	D	UK	102	63.70	28.38	GP	PHQ-9	CERQ-c
19	Rowland et al.	1.02	2013	D	Australia	81	54.3	44.65	GP	DASS21	CERQ-c
20	Rudolph et al.	1.22	2007	D	Canada	100	92	20.2	S	CES-D	CERQ-c
21	Scogin et al.	0.26	1986	C	USA	96	58.33	71.6	CG	DSM	CEQ-c
22	Sugiura & Sugiura	-1.10	2015	D	Japan	157	45.86	19.5	S	CES-D	CCS-Ref
23	Sugiura & Sugiura	-1.22	2016	D	Japan	126	55	18.9	S and GP	CES-D	Ref

	Author	TE (g)	Year	Type of study	Geographic location	N	% women	Mean age (years)	Type of sample	Measure of depression	Measure of cognitive bias
<b>Interpretation bias</b>											
1	Barton et al. a	1.06	2005	C	UK	50	70	39	CG	RCA and BDI	SCD
2	Barton et al. b	3.78	2005	C	UK	40	55	37.8	CG	RCA and BDI	SCD
3	Beach et al.	-0.96	1988	C	USA	45	100	38	CG	DSM and BDI	CEQ
4	Belli	1.29	2013	D	UK	40	57.5	20.2	S	BDI	ASSIQ
5	Berna et al. a	-0.99	2011	C	UK	144	69.44	22	S	BDI	AST-D
6	Berna et al. b	-1.55	2011	C	UK	33	45.45	23	S	BDI	AST-D
7	Blaney et al. 1	0.55	1980	D	USA	255	49.8	-	S	BDI	CBQ
8	Blaney et al. 2	1.07	1980	D	USA	350.5	53.56	-	S	BDI	CBQ
9	Burns et al.	0.62	1987	C	USA	25	100	40	CG	RDC	CDQ
10	Carver et al.	0.70	1985	D	USA	175	52	-	S	BDI	CBQ
11	Chan & Tsoi	0.66	1984	C	China	82	50	-	S	BDI	CDQ
12	Dobson & Shaw	1.12	1986	C	Canada	52	61.54	41	CG	RDC	II
13	Dohr et al.	0.94	1989	C	USA	44	56.82	42.5	CG	RDC and HDRS	IEM
14	Drennen	1.85	1991	D	USA	67	50.75	-	S	BDI	CD
15	Dugas et al.	0.70	2005	D	Canada	148	77.03	22.5	S	BDI	AUSD
16	Fava et al.	1.75	1996	C	USA	123	52.84	41.8	CG	DSM	CQ

Author	TE (g)	Year	Type of study	Geographic location	N	% women	Mean age (years)	Type of sample	Measure of depression	Measure of cognitive bias	
<b>Interpretation bias (cont.)</b>											
17	Frost & MacInnis	1.02	1983	D	UK	40	100	-	S	BDI	CBQ
18	Gordon et al.	0.24	2016	D	Australia	103	56	19	S	MASQ	SCT
19	Gupta & Kar	1.79	2008	C	India	30	-	42	CG	DSM and HDRS	CBQ
20	Hähnel	2.79	2008	C	The Netherlands	84	100	22.45	CG	DSM and LSAS	IQSD
21	Henriques & Leitenberg	1.71	2002	D	USA	117	76 (64.96%)	18.8	S	BDI	NPCEQ
22	Jones & Day	1.97	2008	D	UK	231	183 (79.22%)	28.52 (10.27)	S and GP	CES-D	IDQ
23	Juang & Knight	-0.05	2016	C	USA	136	69.23	46.00	CG	CES-D	AST
24	Krantz & Gallagher-Thompson, a	0.89	1990	C	USA	19	-	-	CG	RDC	(EV) CBQ
25	Krantz & Gallagher-Thompson, b	-0.13	1990	C	USA	22	-	-	CG	RDC	(EV) CBQ
26	Krantz & Gallagher-Thompson, c	1.86	1990	C	USA	21	-	-	CG	RDC	(EV) CBQ
27	Krantz & Hammen, a	0.71	1979	D	USA	29	51,72	26	CP	DSM	CDQ
28	Krantz & Hammen, b	0.72	1979	C	USA	65	100	-	S	BDI	CDQ
29	Lievaart et al.	-1.73	2013	D	The Netherlands	36	63.89	41.7	CP	DSM	SCT-total

Author	TE (g)	Year	Type of study	Geographic location	N	% women	Mean age (years)	Type of sample	Measure of depression	Measure of cognitive bias	
<b>Interpretation bias (cont.)</b>											
30	Michael & Funabiki	1.14	1985	C	USA	555	-	-	S	BDI	CDQ
31	Miller & Norman	0.82	1986	C	USA	60	60	31,3	CG	DSM and BDI	CBQ
35	Moss-Morris & Petrie	1.55	2001	C	New Zealand	58	70.69	41,9	CG	DSM and BDI	CEQ
33	Nunn et al.	12.65	1997	C	UK	48	-	-	CG	DSM	IT
34	Pössel	-0.81	2011	D	USA	397	80,35	23,27	S	CES-D	CEQ
35	Robinson & Fleming	1.33	1992	C	Canada	47	68.09	-	CG	DSM	CEQ
36	Rohrbacher & Reinecke	-1.25	2014	D	UK	176	77.27	24	S	CES-D	AST-D
37	Scogin et al.	0.41	1986	C	USA	96	58,33	71,6	CG	DSM and HDRS	CEQ
38	Voncken et al.	0.24	2007	C	The Netherlands	53	62.26	42,3	CG	DSM	IJQ
39	Warren et al.	0.33	1982	C	USA	471	58,81	21,2	S	BDI	II
40	Wisco, & Nolen-Hoeksema	-2.13	2011	C	USA	110	61,3	21,8	GP	BDI	IBI

Note: Studies are ordered alphabetically based on the name of the first author. Geographic location: of the corresponding author. Type of study: C=categorical; D=dimensional. N = total sample size of the groups included in the analyses. % women = total percentage of women in the groups included in the analyses. Mean age in years of the groups included in the analyses. Type of sample: CG= different groups of clinical and general population; CP=clinical sample; GP= general population S=students. Measure of depression: BDI= Beck Depression Inventory; BSI= Brief Symptom Inventory; CES-D= Centre for Epidemiological Studies–depression; DASS= Depression Anxiety Stress Scale; DSM= Diagnostic and Statistical Manual of Mental Disorders instruments; PHQ-9= Patient Health Questionnaire-9; POMS= Profile Of Mood Scale; RCA= Routine Clinical Assessment; RDC= Research Diagnostic Criteria; SCL-90= Symptom checklist-90, SDS= Self-rating Depression Scale. Measure of cognitive bias: AST-D: Ambiguous Scenarios Test- Depression- pleasantness; AST =Ambiguous situation task adapted from the IBQ; ASSIQ= Ambiguous Social Situations Interpretation Questionnaire; AT= The availability test-Negative future self; AUSD= Ambiguous/Unambiguous Situations Diary; CBQ=Cognitive Bias

Questionnaire-depressed-distorted; (EV) CBQ= Elders' Valenced Cognitive Bias Questionnaire-depressed-distorted; CD= Burns' cognitive distortions definitions; CDQ= Cognitive Distortion Questionnaire; CDM= Cognitive Distortion Measure; CEQ= Cognitive Error Questionnaire; CERQ-c = Cognitive Emotion Regulation Quest (CERQ)-catastrophizing; CQ= Cognitions Questionnaire; FEQ= Future Events Questionnaire-estimate the likelihood-negative; GCQ-c= Grief cognitions questionnaire-Catastrophic misinterpretations; IBI= Interpretation bias imagery; IDQ= Interpretations of Depression Questionnaire-negative self-dispositional; IEM= Interpretation of Events Measure; II= Interpretation Inventory; IJQ= Interpretation and Judgmental Questionnaire-Part II (multiple choice)-across situations; IQSD= Interpretation Questionnaire for Social Phobia and Depression-depression-dysfunctional; IT= Interpretation Task; Likelihood estimation measure (LEM)-negative events-self; NPCEQ= Negative and Positive Cognitive Error Questionnaire-negative; PCQ= Probability-Cost-Questionnaire-depression-probability; Ref= Refraining from catastrophic thinking; SCD= Sentence Completion Test for Depression-negative statements; SCT-total= Sentence Completion Test-positive, negative, and neutral statements. Number items included in the measure of cognitive bias.  $\alpha$ = Cronbach's alpha for the measure of cognitive bias.

Supplementary Table 2. *Studies fulfilling the inclusion criteria but not included in the meta-analysis.*

<b>Reason for exclusion</b>	<b>Citation</b>
<b>a) Lack of studies to include comparison groups different from healthy participants</b>	
<i>Schizophrenia (current and in remission)</i>	Corcoran et al. (2006)
<i>Anxiety</i>	Dasgupta & Sanyal (2007)
<i>Suicide</i>	Marroquin, Nolen-Hoeksema, & Miranda (2013, st2)
<i>Bipolarity and depression in remission</i>	Wolkenstein, Zwick, Hautzinger, & Joormann, (2014)
<i>Anxiety</i>	Hähnel (2008)
<i>Marital discord</i>	Beach, Nelson, & O'Leary, (1988)
<i>General psychiatric population</i>	Dobson, & Shaw (1986)
<i>Depression in remission</i>	Dohr, Rush, & Bernstein (1989)
<i>Depression in remission</i>	Gupta, & Kar (2008)
<i>General psychiatric population</i>	Miller & Norman (1986). St1
<i>General psychiatric population</i>	Miller & Norman (1986). St2 Moss-Morris & Petrie (2001).
<i>Chronic fatigue syndrome (with and without depression)</i>	
<i>Bereavement (with and without depression) and general psychiatric population</i>	Robinson & Fleming (1992)
<i>Social phobia (with and without depression)</i>	Voncken, Bögels, & Peeters (2007)
<i>Anxiety</i>	Hähnel (2008).
<b>b) Lack of studies to conduct analyses on other cognitive biases<sup>1</sup></b>	
<i>Positive bias (SCT)</i>	Teasdale, Lloyd, & Hutton (1998) <sup>a</sup>
<i>Positive bias (SCT)</i>	Teasdale, Taylor, Cooper, Hayhurst, & Paykel (1995) <sup>b</sup>
<i>Overgeneralization</i>	Scogin, Hamblin, & Beutler (1986) <sup>c</sup>
<i>Overgeneralization</i>	Van den Heuvel, Derksen, Eling, & van der Staak (2012) <sup>d</sup>

*Overgeneralization*

Kernis, Whisenhunt, Waschull, Greenier, Berry,  
Herlocker, & Anderson (1998)<sup>e</sup>

*Overgeneralization*

Mitchell & Campbell (1988)<sup>f</sup>

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<sup>1</sup>The studies in this category were excluded because they measured a type of cognitive bias non-comparable to the ones included in the main analyses. The instruments were:

<sup>a,b</sup> Sentence Completion Test (SCT; Teasdale et al., 1995) provided an index of positive cognitive bias, which was outside the scope of this meta-analysis.

<sup>c</sup> Cognitive Error Questionnaire (CEQ; Lefebvre, 1981). This study provided data on the overgeneralization subscale alone but could not be included. However, the study also reported data on the catastrophizing subscale and the full scale separately, which were used in the main analyses.

<sup>d</sup> Overgeneralization subscale of the Attitudes Toward Self Scale (ATSS; Carver & Ganellen, 1983). Item example: *How I feel about myself overall, is easily influenced by a single mistake.* Overgeneralization test (OGT; Klar et al., 1997). Item example: *When you turned on the television yesterday, there was a break in transmission, as a result of which you couldn't watch your favorite show. How probable is it that the next time you want to watch that show there will be a break in transmission again?*

<sup>e</sup> Overgeneralization subscale of the Attitudes Toward Self Scale (ATSS; Carver & Ganellen, 1983). Item example: *Noticing one fault of mine makes me think more and more about other faults.*

<sup>f</sup> Cognitions Questionnaire (CQ; Fennell & Campbell, 1984) measures generalization across time and situations. Examples of items are not provided by the authors.

Supplementary Table 3. *Means and standard deviations for the adapted Downs and Black's Checklist for Measuring Quality.*

Item	M	SD
1 Is the hypothesis/aim/objective of the study clearly described?	1	0
2 Are all primary outcomes to be measured clearly described in the Introduction or Methods section?	0.87	0.34
3 Are the characteristics of the participants included in the study clearly described?	0.52	0.50
4 Are the measures of biases clearly described?	1	0
5 Are the distributions of principal confounders in each group of subjects to be compared clearly described?	0.71	0.46
6 Are the main findings of the study clearly described?	0.62	0.49
7 Does the study provide estimates of the random variability in the data for the main outcomes?	0.74	0.44
8 Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001 or 0.05?	0.38	0.49
9 Were withdrawals and dropouts reported in terms of numbers and/or reasons per group?	0.39	0.49
10 Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	0.23	0.42
11 Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	0	0
12 Were the main outcome measures used accurate (valid and reliable)?	0.15	0.36
13 Were the statistical tests used to assess the main outcomes appropriate?	1	0
14 If any of the results of the study were based on 'data dredging', was this made clear?	1	0
15 Were the participants recruited from the same population?	0.61	0.49
16 Were study participants recruited over the same time?	0.13	0.34
17 Was there adequate adjustment for confounding variables in the analyses?	0.65	0.48
18 Were study subjects randomized to groups?	0	0
19 Did the study have sufficient power to detect a clinically important effect?	0.02	0.13

## Sensitivity analyses

### Catastrophizing bias

Six outliers were found: Macedo et al., 2017; Sugiura & Sugiura, 2015; Sugiura & Sugiura, 2016; Corcoran et al., 2006; Lei et al., 2014; Hahnel, 2008. After their removal, sensitivity analyses still showed a large ES ( $g=1$  [0.81; 1.19]), while heterogeneity was reduced from 92.94% to 75.32% which was higher than expected.

For moderation analyses, nationality of corresponding author, percentage of women and bias measure became non-significant. The instrument to measure depressive symptoms was the only moderator left to explain the variability of the results. All the instruments included in the analysis showed a significant effect, being larger when using the SCL-90, the BDI or the DASS21. Regarding the two instruments that were found to have a non-significant effect in the main analysis, when removing outliers, the SDS showed a medium effect and the CES-D could not be included in the analysis since just one study used this measure.

Supplementary Table 4. *Analyses on catastrophizing and depression without outliers.*

Catastrophizing without outliers	N	k	g [95%CI]	P	Q (df)p	I <sup>2</sup>
<b>Overall ES</b>	3,725	17	1 [0.81; 1.19]	< 0.001	64.84 (16) < 0.001	75.32%
<b>Moderators</b>			Beta coefficient/ Mean ES [95%CI]			
<i>Year</i>	3,725	17	0.01 [-0.01; 0.04]	0.38	0.77 (1) 0.38	
<i>Nationality</i>		17			0.14 (1) 0.71	
Western		14	1.01 [0.80; 1.23]	< 0.001	11.48 (13) 0.57	
Non-western		3	0.92 [0.47; 1.37]	< 0.001	2.70 (2) 0.26	
<i>N</i>		17	0.00 [-0.00; 0.00]	0.17	1.92 (1) 0.17	
<i>% women</i>		11	0.01 [-0.01; 0.03]	0.19	1.72 (1) 0.19	

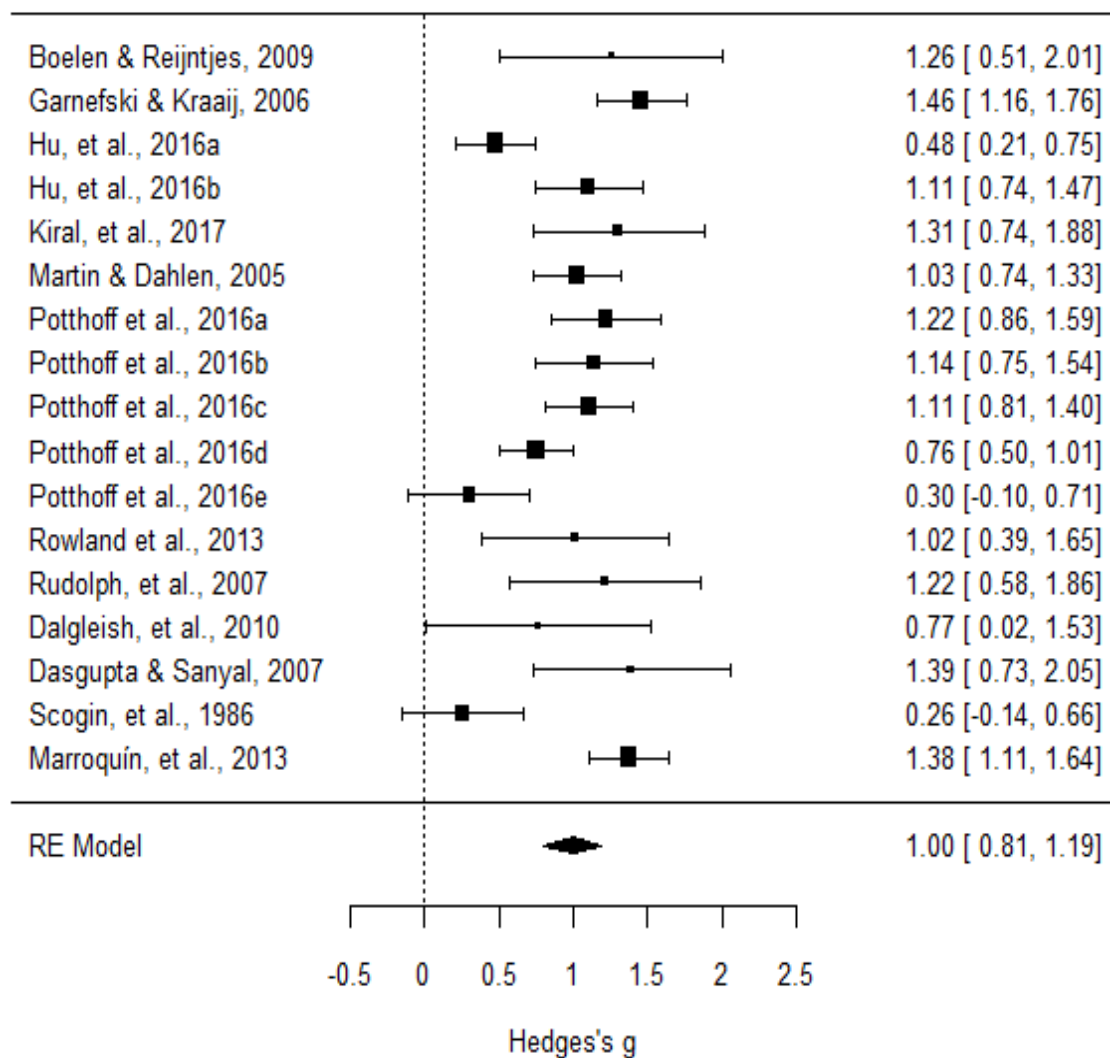
<i>Mean age</i>	11	0.00 [-0.02; 0.01]	0.57	0.32 (1) 0.57
<i>Sample type</i>	16			0.99 (2) 0.61
GP	4	1.02 [0.62; 1.42]	<0.001	5.28 (3) 0.15
Students	9	1.01 [0.75; 1.26]	<0.001	3.74 (8) 0.88
GP and CP	3	0.73 [0.22; 1.24]	<0.01	3.44 (2) 0.18
<i>Measure of depression*</i>	16			15.07 (5) 0.01
DSM	3	0.69 [0.28; 1.10]	0.001	5.16 (2) 0.08
SCL-90	2	1.41 [0.96; 1.85]	<0.001	0.16 (1) 0.69
SDS	2	0.76 [0.39; 1.13]	<0.001	2.65 (1) 0.10
BDI	5	1.23 [0.98; 1.48]	< 0.001	0.67 (4) 0.95
DASS21	2	1.03 [0.60; 1.46]	< 0.001	0 (1) 0.97
Other <sup>1</sup>	2	0.57 [0.19; 0.98]	<0.01	1.33 (1) 0.25
<i>Catastrophizing bias measure</i>	17			0.17 (1) 0.68
CERQ-C	13	1.02 [0.80; 1.24]	<0.001	8.53 (12) 0.74
Other <sup>2</sup>	4	0.92 [0.48; 1.35]	<0.001	4.58 (3) 0.21
Number of items	17	0.00 [-0.03; 0.03]	0.93	0.01 (1) 0.93
Reliability	13	1.47 [-1.04; 3.99]	0.25	1.32 (1) 0.25

N=number of participants. k=number of studies. *g* [95%CI] = standardized mean difference with Hedge's correction with confidence interval. Beta coefficient/Mean ES [95%CI] = estimate values for meta-regression analyses with continuous variables, and mean effect sizes for mixed models with categorical variables in moderation analyses. *Q* (df) *p*= test of homogeneity statistic, degrees of freedom and *p*-value. *I*<sup>2</sup> = percentage in which the observed variability exceeds the expected by chance. Type of sample: CP = clinical population; GP = general population. Measure of depression: BDI = Beck Depression Inventory; DASS21 = Depression Anxiety Stress Scale; DSM = Diagnostic and Statistical Manual of Mental Disorders criteria to select, at least, the experimental group in categorical studies; SCL-90 = Symptom checklist-90; SDS = Self-rating Depression Scale. Measure of catastrophizing bias: CERQ-C= Cognitive Emotion Regulation Questionnaire-catastrophizing.

<sup>1</sup>Other measures of depression: Brief Symptom Inventory, Patient Health Questionnaire-9 Profile Of Mood Scale.

<sup>2</sup>Other catastrophizing bias measures; Cognitive Error Questionnaire-catastrophizing subscale; Future Events Questionnaire (FEQ)-estimate the likelihood-negative subscale; Grief cognitions questionnaire-catastrophic misinterpretations subscale; Likelihood estimation measure- negative events-self subscale;

Probability-Cost-Questionnaire (PCQ)-depression-probability subscale; Refraining from catastrophic thinking; The availability test-negative future-self subscale.



Supplementary *Figure 1*. Forest plot for catastrophizing studies without outliers

### Interpretation bias

After removing 13 outliers (Barton et al. 2005b; Beach et al., 1988; Berna et al., 2011a; Berna et al., 2011b; Fava et al., 1996; Hahnel, 2008; Juang & Knight, 2016; Nunn et al., 1997; Wisco & Nolen-Hoeksema, 2011; Jones & Day, 2008; Possel, 2011; Lievaart et al., 2013; Rohrbacher & Reinecke, 2014), sensitivity analyses showed that the main ES remained significant, although it changed from medium  $g= 0.78$  to large  $g= 0.83$ . Heterogeneity was reduced from 94.75% to 60.40% of variability which was higher than expected.

The moderating effect of the variable type of sample, type of measure of depressive symptoms and measure of interpretation bias became non-significant. Thus, when excluding outliers, none of the variables explained the variability of the results. Some categories of the moderators (other and CP in sample type, CES-D in measure of depression, and AST-D and IBQ in measure of bias) could not be included in the analysis as just one study used this measure.

Supplementary Table 5. *Analyses on interpretation bias and depression without outliers.*

<b>Interpretation bias without outliers</b>	N	k	g [95%CI]	P	Q (df)p	$I^2$
<b>Overall ES</b>						
<i>All studies</i>	3,075	27	0.83 [0.67; 1.00]	<0.0001	65.66 (39) <0.0001	60.40%
<b>Moderators</b>						
			Beta coefficient/ Mean ES[95%CI]			
<i>Year</i>	3,075	27	0.00 [-0.01; 0.02]	0.74	0.11 (1) 0.74	
<i>Nationality</i>	3,075	27			0.21 (1) 0.65	
Western		25	0.82 [0.65; 1.00]	<0.001	24.96 (24) 0.41	

Non- Western		2	0.98 [0.32; 1.64]	<0.001	2.36 (1) 0.12
N	3,075	27	0.00 [-0.00; 0.00]	0.64	0.22 (1) 0.64
<i>% women</i>	2,428	22	0.00 [-0.01; 0.01]	0.57	0.32 (1) 0.57
<i>Mean age</i>	1,376	15	0.00 [-0.02; 0.02]	0.97	0.00 (1) 0.97
<i>Sample type</i>	3,046	26			0.44 (1) 0.51
Students		13	0.79 [0.56; 1.01]	<0.001	11.46 (12) 0.49
GP and CP		13	0.90 [0.64; 1.16]	<0.001	15.51 (12) 0.21
<i>Measure of depression</i>	2972	26			0.70 (3) 0.87
DSM or RDC criteria + cut-off point		6	0.99 [0.63; 1.35]	<0.001	5.62 (5) 0.34
DSM interview		2	0.75 [0.13; 1.36]	0.02	2.98 (1) 0.08
RDC		5	0.84 [0.37; 1.31]	<0.001	6.39 (4) 0.17
BDI		13	0.83 [0.60; 1.07]	<0.001	9.30 (12) 0.68

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<i>Interpretation bias measure</i>	3075	27			2.87 (3) 0.41
CEQ		4	1.12 [0.68; 1.56]	<0.001	5,67 (3) 0,13
CDQ/CBQ		13	0.85 [0.61; 1.10]	<0.001	10,69 (12) 0,56
SCT		2	0.59 [0.03; 1.15]	0.04	2 (1) 0,16
Other		8	0.73 [0.43; 1.03]	<0.001	6,80 (7) 0,45
Number of items	1874	23	-0.01 [-0.03; 0.01]	0.30	1.09 (1) 0.30
Reliability	1224	8	-1.95 [-6.93; 3.03]	0.44	0.59 (1) 0.44

N=number of participants. k=number of studies. g [95%CI] = standardized mean difference with Hedge's correction with confidence interval. Beta coefficient/Mean ES [95%CI] = estimate values for meta-regression analyses with continuous variables, and mean effect sizes for mixed models with categorical variables in moderation analyses. Q (df) p= test of homogeneity statistic, degrees of freedom and p-value. I<sup>2</sup> = percentage in which the observed variability exceeds the expected by chance. Type of sample: CP= clinical population; GP = general population. Measure of depression: BDI= Beck Depression Inventory; DSM = Diagnostic and Statistical Manual of mental disorders; RDC = Research Diagnostic Criteria; cut-off point = using questionnaires Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HDRS) or Liebowitz Social Anxiety Scale (LSAS). Measure of interpretation bias: CDQ/CBQ (Krantz & Hammen, 1979) = Cognitive Distortion/Bias Questionnaire-depression, distortion subscale; CEQ = Cognitive Error Questionnaire; SCT = Sentence Completion Test for Depression-negative statements subscale.

<sup>1</sup>Other measures of interpretation bias: Ambiguous Social Situations Interpretation Questionnaire (ASSIQ); Ambiguous/Unambiguous Situations Diary (AUSD); Cognitive Bias Questionnaire-total score; Cognitive Distortion Questionnaire (Burns, Shaw, & Croker, 1987); Cognitions Questionnaire (CQ); Interpretations of Depression Questionnaire (IDQ); Interpretation of Events Measure (IEM); Interpretation Inventory (II); Interpretation and Judgmental Questionnaire (IJQ)-multiple choice-cross situations subscale; Interpretation Questionnaire for Social Phobia and Depression (IQSD)- depression, distortion subscale; Sentence Completion Test for Depression-total score; and two measures without name (Drennen, 1991; Nunn et al., 1997).

**Supplementary Table 6. Description of the cognitive bias measures. (In italics, examples of items when made available by authors).**

<b>Measure</b>	<b>Instruction to participants</b>	<b>Item example</b>
<b>Catastrophising</b>		
<b>CEQ-C</b>	Rating the similarity of the catastrophising thought to the one that they would have had in a similar circumstance on a 5-point scale ranging from "almost exactly like I would think" to "not at all like I would think".	Daily scenarios followed by a catastrophising thought about that situation.
<b>CERQ-C</b>	Rating the use of catastrophising in response to threatening or stressful life events on a 5-point Likert scale ranging from 1 ((almost) never) to 5 ((almost) always).	<i>I often think that what I have experienced is much worse than what others have experienced.</i>
<b>FEQ-sub</b>	Estimation of the likelihood that a negative event will happen to them in the future, on a scale ranging from -5 (certain that it will not happen) to +5 (certain that it will happen).	<i>Being rejected by a significant other.</i>
<b>GCQ-sub</b>	Rating the tendency to make catastrophic misinterpretations of their own feelings after loss.	Examples are not provided by the author(s).
<b>LEM-sub</b>	Estimating the likelihood that a negative event will happen to them in the future, on a 9-point scale ranging from 'not at all likely' to 'extremely likely'.	<i>What is the likelihood that, if you surprised a burglar in your home, he would attack you?</i>
<b>PCQ- sub</b>	Estimation of the likelihood that a negative event will happen to them in the future, on a scale ranging from 0 (not at all) to 10 (extremely likely).	<i>You can't find any pleasure in your life anymore.</i>
<b>REF</b>	Rating of perceived ability to do what is described in each item when they feel anxious, on a 4-point scale from 1 (I absolutely cannot) to 4 (I definitely can).	<i>Even if bad consequences of a problem come to mind, I can reassure myself that they are nothing more than my imagination.</i>
<b>The availability test- sub</b>	Estimation of the likelihood that a negative event will happen to them in the coming week, on a scale ranging from 1 (not at all) to 7 (very likely).	Examples are not provided by the author(s).
<b>Interpretation bias</b>		

<b>ASSIQ</b>	Choosing what they think is the most likely explanation (negative, neutral, or positive) to a given situation. The total number of negative explanations chosen is summed.	<i>Someone you know passes you on the street and does not stop to greet you. Why not?</i> <i>(a) They were ignoring you</i> <i>(b) They didn't see you</i> <i>(c) They were in a rush and could not stop</i>
<b>AST-D</b>	Forming a mental image of a given situation, then they are asked to imagine that it was happening to them and rate how pleasant the image is.	<i>It's New Year's Eve. You think about the year ahead of you.</i>
<b>AUSD</b>	Rating the degree of concern for a given situation on a 5-point scale ranging from 'not at all concerned' to 'extremely concerned'.	<i>While on my way out tonight I was stopped in the street.</i>
<b>CEQ</b>	Rating the similarity of a type of biased thought (catastrophizing, overgeneralizing, personalization, or selective abstraction) to the one that they would have had in a similar circumstance on a 5-point scale ranging from "almost exactly like I would think" to "not at all like I would think".	<i>You hand in a report to your boss that has taken you four hours to write. Your boss, however, doesn't say anything about it. You think to yourself, '(S)he must think I did a lousy job'.</i>
<b>CDQ</b>	Writing down open thoughts and feelings in response to a certain situation. Then, score each response for the total number of distortions based on the definitions of Burns (1980): all or nothing thinking, overgeneralization, selective abstraction, disqualifying. the positive, mind-reading, fortune-telling, magnification or minimization, emotional reasoning, labelling and mislabeling, and personalization.	<i>Your spouse (or friend) is quieter than usual tonight.</i>
<b>CDQ/CBQ</b>	Choosing among four response options (depressed-distorted, depressed-non-distorted, non-depressed-distorted, or non-depressed-non-distorted) the one that would best represent their own response to a certain situation.	A character is depicted as a member of an organization who was encouraged by friends to run for the presidency of the organization. She (he) eventually lost. Participants are instructed to put themselves on the situation and think how they would think and feel. Then they are presented with this scenario: <i>When you first</i>

<b>CQ</b>	Choosing one of four options (two depressed, two non-depressed) about what they would think and feel given a certain situation.	<p><i>heard you'd lost, you immediately: 1) feel bad and imagine I've lost by a landslide (depressive-distorted) 2) shrug it off as unimportant (non-depressive distorted), 3) feel sad and wonder what the total counts were (depressive-non-distorted), 4) shrug it off, feeling I tried as hard as I could (non-depressive-non-distorted).</i></p> <p>Examples are not provided by the author(s).</p>
<b>IBQ</b>	Being in a certain situation, participants are asked to write down all explanations/interpretations that came to their mind and choose the most likely for them. Then, they rate the positivity and negativity of each on a Likert scale from 1 (not at all) to 5 (extremely). All responses were also coded by two independent coders as negative or positive.	<p><i>You call a good friend of yours and leave a message suggesting getting together later in the week. A few days pass, and you haven't heard from them. Why haven't they returned your call?</i></p>
<b>IDQ</b>	Different situations are followed by two options (negative self-dispositional and normalizing appraisals). Participants had to indicate (yes/no) whether they had experienced each situation in the preceding three months.	<p><i>If I felt cut off from other people, I would probably think it was because:</i></p> <p><i>-I am an insensitive person.</i></p> <p><i>-Things are difficult at the moment and I have little energy for other things.</i></p>
<b>IEM</b>	Imaging themselves in a certain situation, they are asked to rate their overall reaction on a 4-point Likert scale ranging from 1 = very positive to 4 = very negative.	<p><i>Your boss criticizes some aspects of your recent proposal but encourages you to keep working on what he considers to be a generally good idea.</i></p>
<b>II</b>	Indicating how often, on a 5-point scale ranging from "never think that way" to "always think that way", they would respond to a certain situation in a biased manner (arbitrary inference, selective abstraction, overgeneralization, magnification, minimization, personalization, and catastrophizing).	<p><i>A friend walks by and does not appear to see you. Do you think that your friend is just avoiding you? (arbitrary inference).</i></p>

<b>IJQ-sub</b>	Imagining themselves in a certain situation, participants rank four kinds of interpretations (profoundly negative, mildly negative, positive, and neutral) on a scale ranging from 4=most likely to 1=least likely.	<p><i>You made an appointment with an acquaintance to go to the cinema. Shortly before the appointment this person leaves a message on your answering machine that the appointment has to be cancelled. Why does this acquaintance cancel the appointment?</i></p> <ul style="list-style-type: none"> <li><i>a) This acquaintance doesn't like me (profoundly negative).</i></li> <li><i>b) This acquaintance has made another appointment and considers the appointment with me not important enough (mildly negative).</i></li> <li><i>c) This acquaintance likes to go to the cinema with me but couldn't cancel another, tedious, appointment (positive).</i></li> <li><i>d) This acquaintance feels sick (neutral).</i></li> </ul>
<b>IQSD-sub</b>	Rating, on a 5-point scale, how likely it is that different thoughts (one functional and two dysfunctional/depressogenic) would come to their mind in a certain situation.	<p><i>You lie in bed awake and can't fall asleep. What thoughts occur to you?</i></p> <ul style="list-style-type: none"> <li><i>a) This is how it always starts. Now nothing makes a difference anyway.</i></li> <li><i>b) A lot happened today. My mind has to process all this.</i></li> <li><i>c) This is terrible. I can't stop ruminating.</i></li> </ul>
<b>SCT</b>	Completing short sentence stems (agent-verb combinations or simple nouns) based on how they had been feeling within the previous week. Independent raters coded the responses as negative, positive, or neutral.	<p><i>I think...</i> <i>The world...</i></p>
<b>Drennen (1991)</b>	Rating how much each of the 10 different cognitive distortions apply to them on a scale ranging from 0= not like me to 4= extremely like me.	Definitions of 10 different Cognitive Distortions (Burns, 1980, pp. 40-41).
<b>Nunn, Mathews, &amp; Trower (1997)</b>	Imagining themselves in a certain situation, they must rate the similarity of each of the four options (one neutral filler, one	<i>A friend phones you about a trip to the cinema, but is unable to suggest a mutually convenient time:</i>

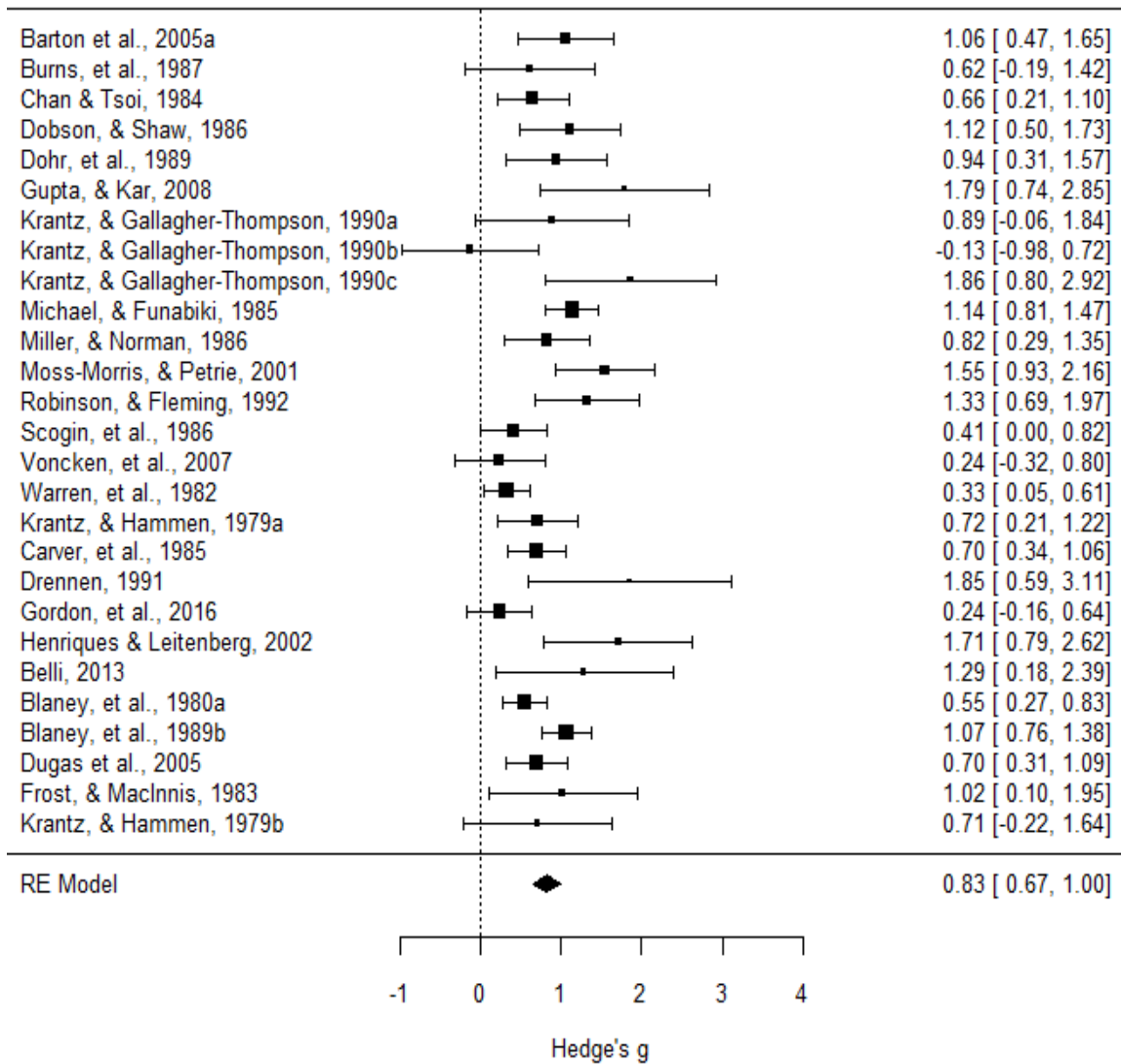
general description of an emotional reaction, and two distorted reactions) to how they would likely think and feel.

1. *People have better things to do than see you.*
2. *It's your fault for not being sufficiently organized.*
3. *General emotional reaction.*
4. *Neutral filler.*

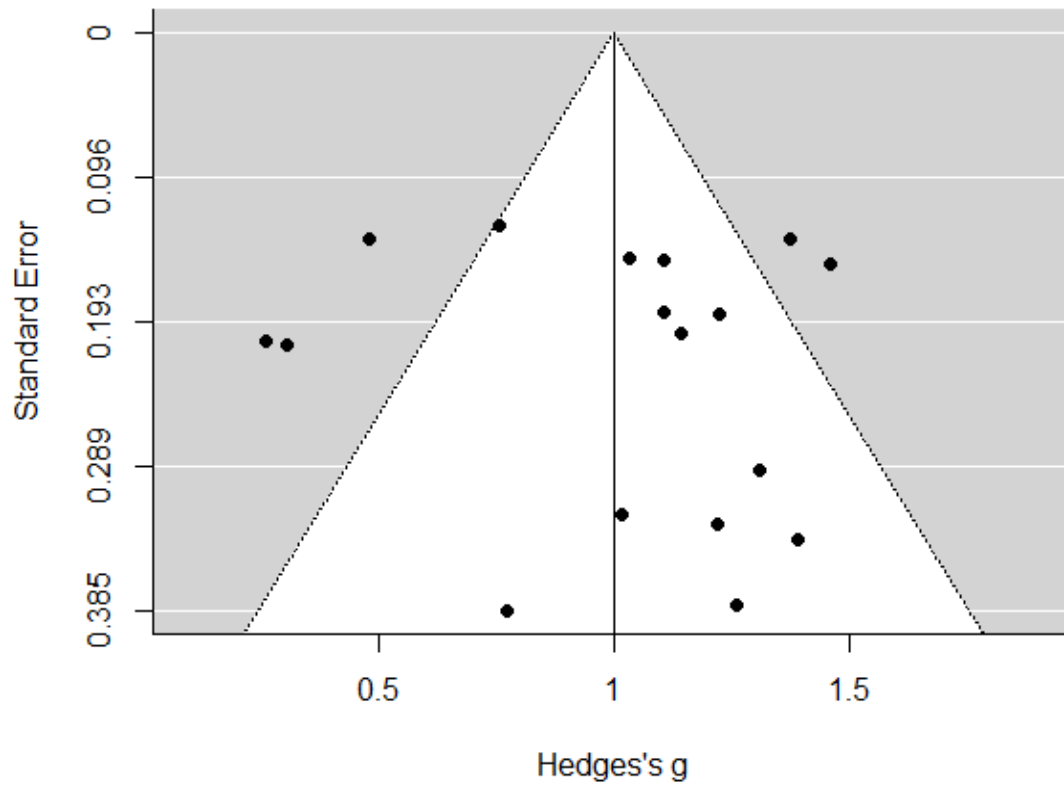
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**Measures of catastrophizing:** CERQ-C= Cognitive Emotion Regulation Questionnaire-catastrophizing; CEQ-C= Cognitive Error Questionnaire- catastrophizing; FEQ-sub= Future Events Questionnaire- estimate the likelihood-negative subscale; GCQ-sub=Grief cognitions questionnaire-catastrophic misinterpretations subscale; LEM= Likelihood estimation measure- negative events-self subscale; PCQ= Probability-Cost-Questionnaire-depression-probability subscale; REF= Refraining from catastrophic thinking scale; The availability test-negative future-self subscale.

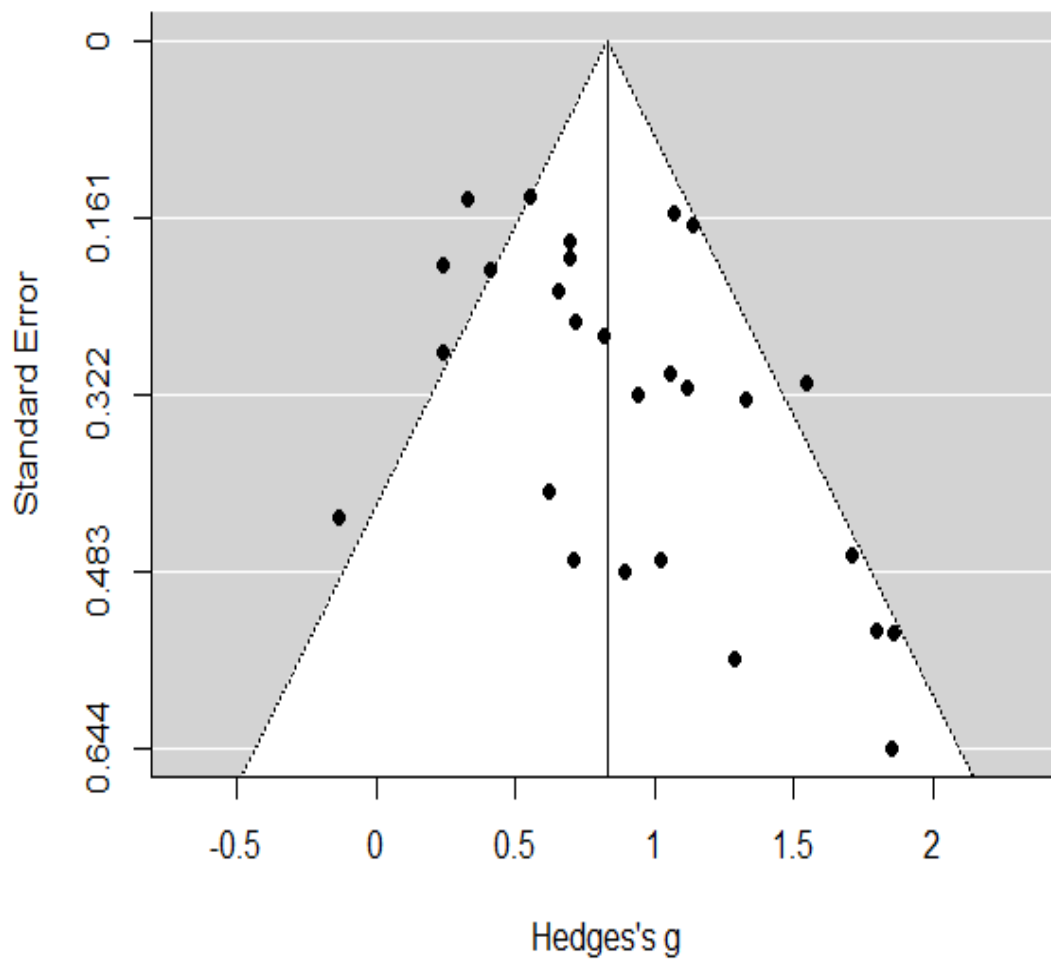
**Measures of interpretation bias:** ASSIQ= Ambiguous Social Situations Interpretation Questionnaire; AST-D = Ambiguous Scenarios Test for Depression-pleasantness rating; AUSD= Ambiguous/Unambiguous Situations Diary; CEQ = Cognitive Error Questionnaire; CDQ= Cognitive Distortion Questionnaire (Burns, Shaw, & Croker, 1987); CDQ/CBQ = Cognitive Distortion/Bias Questionnaire-depression distortion subscale (Krantz & Hammen, 1979); CQ= Cognitions Questionnaire; IBQ = Interpretation Bias Questionnaire; IDQ= Interpretations of Depression Questionnaire; IEM= Interpretation of Events Measure; II= Interpretation Inventory; IJQ-sub= Interpretation and Judgmental Questionnaire-multiple choice-cross situations subscale; IQSD-sub=Interpretation Questionnaire for Social Phobia and Depression- depression distortion subscale; SCT = Sentence Completion Test for Depression; and two measures without name (Drennen, 1991; Nunn, Mathews, & Trower, 1997).



Supplementary *Figure 2*. Forest plot for interpretation bias studies without outliers



Supplementary *Figure 3*. Funnel plot for catastrophizing studies excluding outliers.



Supplementary *Figure 4*. Funnel plot for interpretation bias studies excluding outliers.

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## **CHAPTER 4. New interpretation bias modification program for emotional disorders**

### **Study 2. ‘Relearning how to think’: A brief online intervention to modify biased interpretations in emotional disorders—study protocol for a randomized controlled trial**

Given the clinical potential of modifying negative interpretation biases and the room to improve some aspects of the training used to date, the second study of this dissertation focused on the design of the CBM-IClin program. This is a four-session online program that moves away from the traditional approach of CBM and focuses on the use of techniques commonly used in cognitive-behavioral therapies. The details of the program are presented in the article Nieto, I., Vazquez, C. (2021). ‘Relearning how to think’: A brief online intervention to modify biased interpretations in emotional disorders—study protocol for a randomized controlled trial. *Trials*. 22, 510. <https://doi.org/10.1186/s13063-021-05459-32.2>.

**‘Relearning how to think’: A brief online intervention to modify biased interpretations in emotional disorders. Study protocol for a randomised controlled trial**

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**Abstract**

**Background:** Cognitive biases play an important role in the development and maintenance of emotional disorders, such as depression and anxiety. Novel procedures, known as Cognitive Bias Modification (CBM), aim to reduce these dysfunctional information processing modes. This study develops a brief clinically-based online intervention program to modify biased interpretations in depression and anxiety (CBM-I<sub>Clin</sub>), overcoming some methodological issues that have been addressed in previous literature.

**Methods:** Volunteer participants will be recruited via social media, and posters at the university. They will be randomly assigned to an experimental group or a waiting list control group. Both groups will complete two assessment sessions, before and after the intervention, consisting of questionnaires measuring cognitive and emotional variables as well as experimental tasks measuring cognitive biases (i.e., attention, memory, and interpretation). After the first assessment session, only participants in the experimental group will receive a link to follow the four CBM-I<sub>Clin</sub> sessions at home. All participants will receive, via email, follow-up questionnaires two weeks and three months after the second assessment.

**Discussion:** This study will test an online program potentially beneficial to modify cognitive variables in disorders such as depression and anxiety. Several limitations of previous CBM procedures are addressed and the impact of the program both on cognitive performance and clinical symptoms will be explored.

**Trial registration:** This trial was prospectively registered on June 17, 2019, with the ClinicalTrials.gov NCT03987477

**Keywords:** Cognitive Bias Modification; Ambiguous Interpretations; Emotional Disorders

## **Background**

Anxiety and mood disorders are the most common mental disorders in the general population, showing an 18.1 % and 9.5% 12-month prevalence, respectively (Kessler et al., 2005). Both disorders are associated with high social and economic costs, as well as high rates of chronicity and relapse ( Collins et al., 2011; Whiteford et al., 2013).

High patterns of comorbidity between anxiety and mood disorders are consistent across studies (Kessler et al., 2005; Wittchen, 2002). This comorbidity could be due, at least in part, to the fact that these disorders share transdiagnostic factors such as rumination (McLaughlin & Nolen-Hoeksema, 2011), and are also likely to share some general risk factors (Barlow, Farchione, Sauer-Zavala, et al., 2017). Cognitive theories point to dysfunctional thinking as one of the main variables related to the onset and maintenance of these emotional disorders (Barlow, Farchione, Sauer-Zavala, et al., 2017; Beck, 1967, 1976). According to these influential theories, depressed and anxious individuals show specific cognitive dysfunctions that can ultimately lead to symptom

development (Mineka et al., 1998; Nieto, Robles, et al., 2020). Several types of dysfunctions have been distinguished in regard to the onset and maintenance of emotional disorders. A useful heuristic to clarify diverse types of cognitive activity intervening in psychopathology is the so-called “cognitive taxonomy”, initially proposed by Ingram & Kendall (Ingram & Kendall, 1986). This taxonomy differentiates between *structural* variables (i.e., broad cognitive schemas through which information is filtered, represented, and organised); *operational* variables (i.e., the mechanisms such as attentional, interpretation, or memory biases, by which cognitive structures work); *product* variables (i.e., the tangible outputs such as thoughts, images, and memories, with which clinicians typically work with their clients). In general, cognitive biases have been defined as errors or distortions related to the operational domain that occur systematically at different times and across distinctive situations, reflecting ‘irrational’ modes of perceiving and elaborating information (Haselton et al., 2005; Kahneman, 2012).

### **Cognitive Bias Modification (CBM)**

*Cognitive Bias Modification (CBM)* is a recent approach developed to alter cognitive biases and explore the link between them and symptoms development. CBM procedures have mainly been aimed at modifying attentional, memory, or interpretation biases. Besides their clinical utility, these procedures are theoretically ambitious as their rationale is that a causal link between cognition and emotion would be demonstrated if changes in cognition are accompanied by consequent changes in emotion. Thus, the efficacy of CBM would provide support to the etiological role of cognition in emotional disorders. Although it has been applied in different conditions, such as eating disorders, substance abuse, or anger-related problems (MacLeod et al., 2009), the main focus has

been on anxiety and depression (Cristea et al., 2015; Hakamata et al., 2010; Hallion & Ruscio, 2011; Jones & Sharpe, 2017).

Mathews and Mackintosh (Mathews & Mackintosh, 2000), in their pioneer study in the field of CBM for interpretation processes (CBM-I), used a paradigm to induce negative interpretation biases in healthy individuals and found a possible causal link to anxiety. Since then, studies using different training paradigms have found an association between change in interpretation bias and symptoms. Recent meta-analyses show evidence of a correlation between change in interpretation bias and negative mood (Menne-Lothmann et al., 2014), and significant differences between CBM training and control groups in anxiety and depression measures (Cristea et al., 2015). Some transdiagnostic factors, such as rumination, have also been found to improve with CBM-I (Hertel et al., 2014). A review of 12 meta-analyses of CBM procedures (Jones & Sharpe, 2017) revealed that there was a significant effect in 8 out of 10 meta-analyses for anxiety and 3 out of 7 meta-analyses for depression. Authors also found significant changes in attention biases in 8 out of 9 meta-analyses of studies using Attentional Bias Modification procedures (ABM), and changes in interpretation biases in the 3 meta-analyses on CBM-I. All this evidence reflects a possible causal link between cognitive biases and symptoms that, at least in the case of interpretation biases, might suggest the existence of a causal connection with a depressed mood in particular (Everaert et al., 2017).

Although results are promising, there are some limitations in the current CBM procedures (Koster & Bernstein, 2015; Lee et al., 2015). First of all, some variables could affect the efficacy of CBM but remain unexplored. For example, although some studies are indicating that the use of mental imagery during CBM procedures could

have a beneficial impact on CBM (Duque et al., 2015; Hitchcock et al., 2017; Holmes et al., 2008), it is still unclear whether this factor is relevant (Cristea et al., 2015; Menne-Lothmann et al., 2014). Also, most CBM procedures are based on the idea that repetitive exposure to a specific way of processing information leads to its automatic use later in daily life (Schartau et al., 2009). Yet, the theoretical support to this mechanistic and repetitive procedure (that typically involves hundreds or even thousands of trials) is still not clear. In fact, it could be possible that CBM procedures focused on enhancing elaborative rather than automatic processing modes could be more beneficial for disorders like depression where those elaborative mechanisms seem to be more affected than automatic ones (Duque et al., 2015).

Another methodological recommendation to improve CBM paradigms is the use of direct and indirect measures to evaluate cognitive change (Everaert et al., 2017; MacLeod et al., 2009). This involves asking participants to directly respond to a series of interpretations (e.g. plausibility ranking or the scrambled sentence task) together with non-conscious measures of interpretations (e.g. reaction time or jumping to conclusions measure). The evaluation of long-term benefits, when participants may have faced possible stressors in real life, has also been encouraged by previous research (Vazquez et al., 2016). Also, cognitive biases at different processing levels (attention, interpretation, and memory) have traditionally been studied independently from each other but some authors now state the need to know how they interact with each other (Everaert et al., 2014; Sanchez-Lopez et al., 2017).

### **Objectives and hypotheses**

The purpose of the study is to design a brief online intervention aimed at reducing the interpretation of negative emotional cognitive biases. The intervention will

be applied to an experimental group to analyse its impact on cognitive and emotional variables in comparison to a waiting-list control group. More specifically, the intervention is framed within the field of CBM-I but, instead of using repetitive training, it is based on the techniques frequently used in cognitive-behavioural therapies (e.g., Beck et al., 1979; Everaert et al., 2014; Greenberger & Padesky, 2015). Thus, while original CBM studies (e.g., Mathews & Mackintosh, 2000) were designed to train participants to change automatic processing of information with repetition of trials, the current intervention aims to teach participants the meaning and consequences of emotional cognitive biases, plus how to modify them.

This study also aims to improve with regard to the procedures used in previous CBM procedures. First, based on previous evidence (Lang et al., 2012), mental imagery is used in order to shed some light on its role when modifying cognitive processes. Second, direct and indirect measures of cognitive performance are used to complement the information provided by self-report questionnaires. Moreover, these measures evaluate the three different domains proven to be affected by them (attention, interpretation, and memory) (Gotlib & Joormann, 2010), giving the need to explore their interplay (Everaert et al., 2012). Finally, given that it is not clear the maintenance of CBM effects, a longitudinal follow-up was used to explore the continuation of benefits in time and the dynamics of the different processing biases (attention, interpretation, and memory).

It is hypothesised that there will be a significant change in interpretation bias (less negative or more positive/neutral) from pre-intervention to post-intervention in the experimental group in comparison to the control group. It is also expected that changes in interpretation biases will also be associated with significant changes in attention and

memory biases (less negative or more positive/neutral) from pre-intervention to post-intervention in the experimental group in comparison to the control group. Finally, it is hypothesised that the intervention will help the experimental group to reduce symptoms of depression and anxiety and increase well-being from pre-intervention to post-intervention in comparison to the control group. Due to the lack of conclusive findings from previous studies, it is explored whether these changes are maintained over time (after 2 weeks and 3 months) and the temporal dynamics of the different cognitive bias processes (attention, interpretation, and memory).

## **Methods**

### **Participants and recruitment**

Participants will be volunteer students from the Complutense University of Madrid who will be recruited via social media channels associated with the university and posters at the Faculty of Psychology. Inclusion criteria will be 1) aged 18 years or older, and 2) being interested in the intervention, announced as a free online program to ‘learn how to control the influence of thoughts on emotional reactions.’ The announcement will include the name and email address of one of the researchers. Volunteers will be instructed to contact the researcher for more information and academic course credits will be offered to those interested within the context of an official faculty program that aims to promote the students’ involvement in academic training events. Exclusion criteria will include 1) having any form of visual and/or auditory disability that makes participants unable to follow online sessions, and 2) lack of internet access. No restrictions will be placed regarding concomitant treatment during the study, although this information will be monitored during the assessment sessions. When participants first contact the researcher, they will be explained the main purpose

of the intervention. Inclusion and exclusion criteria will be evaluated by asking about their ability to correctly complete the program (i.e., no disabilities and internet access). Further information about the procedure will be given during their first visit to the laboratory in a printed document format before they are asked to sign the consent form.

### **Randomisation and blinding**

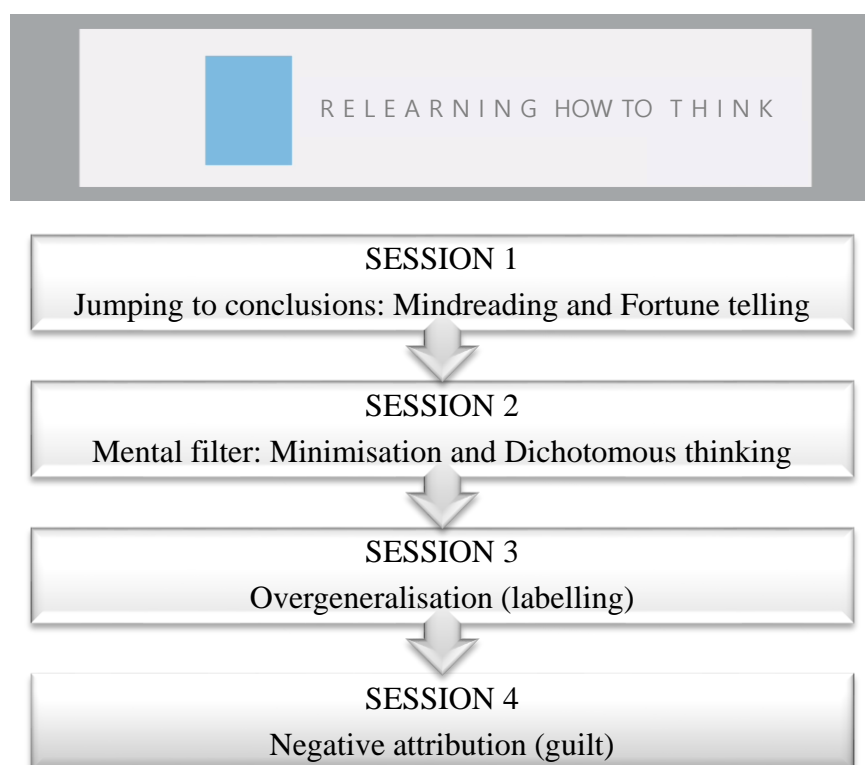
This study is a randomised superiority trial with two parallel groups and a 1:1 allocation ratio. Participants will be randomly allocated to the experimental group (cognitive bias intervention) or a control waiting list group. This control group was chosen due to the novelty of the intervention, for which a waiting list is recommended to get a first impression of its effects (Gold et al., 2017). Randomisation will be conducted by the main investigator using an Excel macro. This method assigns a different code to each group, which will only be known by the researchers. In this trial, solely participants will be blinded to their allocation and the meaning of codes.

### **Sample Size**

The sample size was calculated based on the estimated effect size of the change in interpretation bias before and after a CBM-I intervention ( $d = .43$ ) according to a recent meta-analysis on the field (Menne-Lothmann et al., 2014). Following G\*Power calculations (Faul et al., 2009), the minimum sample size ( $\alpha$  set at 0.05, power at 0.95) to find a difference in a repeated-measures multivariate analysis of variance with one within-subjects factor (two-time points) and one between-subjects factor (two groups) was 73 participants. Due to expected attrition (Crutzen et al., 2015), 20% more participants will be recruited, reaching a total sample size of 88 participants.

### **Intervention: ‘Relearning how to think’ program**

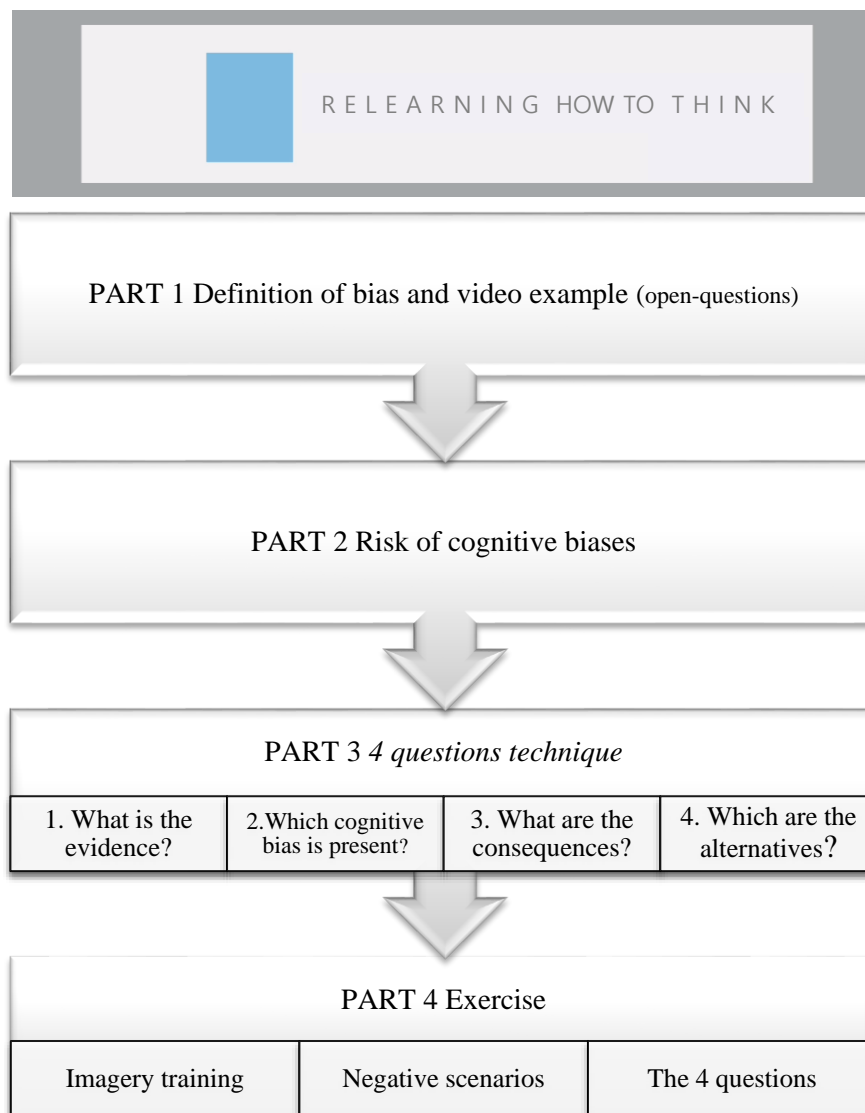
This is a brief online intervention designed to modify negative emotional interpretation biases. The intervention is composed of four different sessions in audiovisual format with psychoeducational content, open-answer questions and exercises to be completed by users. Different cognitive biases, such as jumping to conclusions, mental filter, overgeneralisation, and negative attributions are targeted in each session following classical descriptions of biases (Beck, 1976; Burns & Beck, 1999)- see Figure 1. The organisation of the content of the sessions was based on the Cognitive Error Rating Scales (CERS) (Drapeau et al., 2010), a manual created for therapists to evaluate cognitive errors during clinical sessions, and the CBM-errors (Lester et al., 2011), a clinical strategy to promote more benign interpretations following Beck's theory (Lee et al., 2015).



*Figure 1.* Classification of the specific cognitive biases targeted in the four online sessions of the program.

Each session of ‘Relearning how to think’ is composed of four different parts (see Figure 2). In part 1, participants receive information about specific interpretation biases and are given examples in video format. Some of these videos are daily life scenes where professional actors represent examples of cognitive biases (following clinical vignettes described elsewhere) (Barlow, Farchione, Sauer-Zavala, et al., 2017). During each video (before the resolution of the scene), and to increase active involvement, participants have to complete an open-ended question about what could happen in those ambiguous situations. In the second part, users are informed about the risks of using negative interpretations and it is followed by an explanation of the strategies to avoid them (part 3). These strategies are based on “the 4 questions technique” (Beck, Emery, & Greenberg, 1985), widely used in clinical practice. This technique involves 4 steps to re-evaluate the negative interpretation of a given situation: finding evidence for the negative thoughts, uncovering the cognitive bias present in the situation, identifying the negative consequences, and creating alternative ways of thinking. Finally, during part 4, participants have the opportunity to practice the strategies in an exercise composed of imagery training (Holmes et al., 2009) followed by negative scenarios in an audio format aimed to be reinterpreted. Figure 3 shows the steps of the exercise. It starts with an imaginary training (Holmes et al., 2009) aimed to make scenarios more vivid to users. Participants are presented with a screen saying ‘Close your eyes. Imagine.’ for 1 second followed by a black screen during which a negative scenario is played in audio format with a female voice (e.g. *Your partner travels to work by car and normally arrives home promptly every day. Today you notice that they are over an hour late. Your first thought is that there must have been a crash*). Audio scenarios are daily life situations where negative interpretations arise, and participants are asked to imagine themselves in those situations. A beep is played for users to open their eyes and start

with the exercise questions. First, they have to rate their mood (sadness, happiness, anxiety, and anger) on a 10-point VAS scale based on the most frequent emotions experienced in daily life (Cowen & Keltner, 2017; Trampe et al., 2015). Then, they are guided to apply the 4 questions technique to each scenario. Finally, users evaluate the degree to which they believe in the new alternative thoughts and emotions generated by the new scenario (sadness, happiness, anxiety, and anger).



*Figure 2.* Structure of each session of the program.

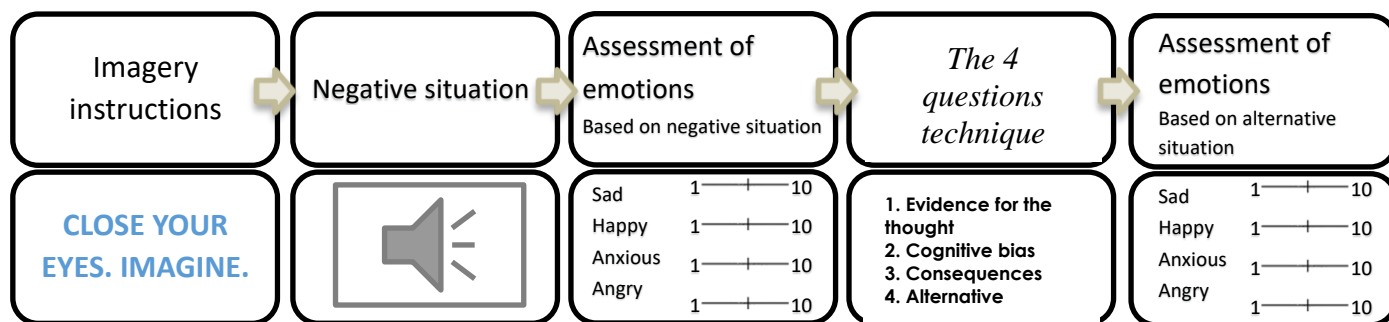


Figure 3. Practice exercise of each session of the program.

### Cognitive bias measures

*Ambiguous Scenarios Test for Depression-II.* The AST-D-II (Rohrbacher & Reinecke, 2014) is a self-report measure of interpretation biases. It consists of 15 ambiguous scenarios which participants have to rate on a scale from -5 (very unpleasant) to 5 (very pleasant). Participants are asked to imagine each scenario as vividly as possible and as if it was happening to them (e.g. *As you enter the room, the commission welcomes you and begins with the oral examination. After just a few minutes you know intuitively how the examination will go*). Two parallel versions are used in counterbalanced order at baseline, post-treatment, and follow-ups. Participants' responses to the items were transformed into a total sum score by adding up the values of each item, rescaled from 1 to 11 (higher scores represent more positive interpretations). Internal consistency is good ( $\alpha = 0.87$ ) for the general scale and also for its two short versions A ( $\alpha = 0.77$ ) and B ( $\alpha = 0.78$ ).

*Mouse-based (gaze) Contingent Attention Task (MCAT)* (Sanchez-Lopez et al., 2019). A variant of the original Scrambled Sentence Test (SST) (Wenzlaff & Bates, 1998) is used to measure interpretation bias while monitoring attention towards emotional stimuli, based on the same principles as in the Eye-gaze Contingent Attention Training (ECAT) (Sanchez et al., 2016). At the beginning of the task, participants have

to click a fixation cross at the left side of the screen to elicit natural left-to-right reading patterns. Then, the *reading screen* is presented with a six-word emotional scrambled sentence (e.g., “am winner born loser a I”) where each word is hidden with a blank mask. Participants are instructed to move the mouse cursor over each mask to read the hidden word and mentally form a grammatically correct sentence using five of them. They are given a time limit of 14 seconds per sentence. This procedure is used to objectively measure attention biases toward emotional words (negative or positive). Then, the *answer screen* is presented with the six words unmasked for participants to click the order of the sentence they had mentally formed. In this section, participants are given a time limit of 7 seconds. Two are calculated from this procedure. First, the time spent (in ms) reading negative words divided by the total time spent (ms) reading positive and negative words is the index of overall negative attentional bias. Second, the resulting ratio of correctly unscrambled negative sentences and correctly unscrambled positive and negative sentences is considered to be the index of automatic negative interpretation bias (Sanchez et al., 2016). In both cases, higher scores indicate higher negative cognitive biases. To maximise the appearance of biases, at the beginning of the task participants are presented a six-digit number for 5 seconds and told to keep that number in mind during the entire task as they will be asked to retrieve it at the end of the task. This procedure will be completed by participants at both pre-and post-intervention evaluations.

*Memory task.* As a measure of memory biases, participants are given 5 minutes to remember the sentences they constructed during the MCAT procedure. Following Everaert et al.’s procedure (Everaert et al., 2014), the ratio between negative sentences and the total number of emotional sentences recalled will be used as an index of

negative memory bias. This procedure will be completed by participants at both pre- and post-intervention evaluations.

*Computerised beads task*<sup>2</sup> (Huq et al., 1988). The beads task is a measure of probabilistic reasoning which was initially designed to measure jumping to conclusion (JTC) bias in schizophrenic patients (Garety et al., 2005). The adapted version used in this study has two parts. The first part consists of presenting two jars with beads of two different colours in different ratios (e.g. 60 orange/40 purple, and 60 purple/40 orange). Participants are told that the program selects one of the jars to take beads randomly out of it and then return them. The instruction is to decide which jar is being used, based on the number of beads of each colour. The second part follows the same procedure with the difference being that the beads are all in white but present two different ratios of positive and negative adjectives (60 positive/40 negative, and 60 negative/40 positive). The number of beads viewed before reaching a decision is considered to be an index of jumping to conclusion bias. This procedure will be completed by participants at both pre- and post-intervention evaluations.

### **Symptom measures**

*Depression, Anxiety and Stress Scale-21*. The DASS (Lovibond & Lovibond, 1995) is a 21-item self-report questionnaire measuring symptoms of depression, anxiety, and stress. Each of the three subscales contains 7 items which, by adding up their values,

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<sup>2</sup> The results of this task were not included in the following publications of the dissertation given space constraints. The results for the 2 (Time: pre-intervention vs. post-intervention) x 2 (Condition: experimental vs. control) repeated measures ANOVA showed that there was a main effect of Group  $F(1,118) = 5.10, p = .03, \eta^2 = 0.04$  showing that the experimental group had higher levels of JTC bias than the control group. There were no other significant effects for this task: Time  $F(1,118) = 0.13, p = .72, \eta^2 = 0.001$ , Time x Group  $F(1,118) = 0.13, p = .72, \eta^2 = 0.001$ .

provide a score for the three constructs. This questionnaire has shown good reliability with the following Cronbach's alpha values for the Depression, Anxiety, and Stress scales, respectively: 0.84, 0.70, and 0.82 (Bados et al., 2005). This procedure will be completed by participants at both pre- and post-intervention evaluations.

*Patient Health Questionnaire-9.* The PHQ-9 (Spitzer et al., 1999) is a 9-item self-report questionnaire to assess any present episodes of depression according to the DSM-IV diagnostic criteria. Each item is rated in frequency on a four-point scale from 1 (Not at all) to 4 (Nearly every day). This questionnaire has shown good reliability with a Cronbach's  $\alpha$  of 0.89 (Kroenke et al., 2001). An adapted PHQ-9 will also be used to measure past episodes of depression. The method of aggregation will consist in adding up the values of each item. In this study, the standard diagnostic cutoff score of PHQ-9  $\geq 10$  (He et al., 2020) will be used to create groups based on present and past episodes of depression. This questionnaire will be completed online at pre-intervention to classify participants according to their symptom levels.

*Generalised Anxiety Disorder-7* (Spitzer et al., 2006) is a 7-item self-report questionnaire to assess any present episodes of anxiety according to the DSM-IV diagnostic criteria. Each item is rated on a four-point scale from 0 (Not at all) and 3 (Nearly every day), with the final score being between 0-21 (calculated by adding up the values of each item). An adapted version of this questionnaire was also used to measure past episodes of anxiety. The cutoff score used in this study to consider present or past episodes of anxiety was GAD-7  $\geq 10$ , following the severity scale: minimal (0-4), mild (5-9), moderate (10-14), and serious (14-20). This questionnaire will be completed online at pre-intervention to classify participants according to their symptom levels.

### **Other measures**

*Pemberton Happiness Index.* The PHI (Hervas & Vazquez, 2013) is an 11-item self-report questionnaire measuring general, eudaimonic, hedonic, and social well-being. All the items will be summed up to reach a general well-being measure. It has been shown to have very good reliability ( $\alpha = .92$ ). This procedure will be completed by participants at both pre- and post-intervention evaluations.

*Dysfunctional Attitudes Scale.* The DAS (Weissman & Beck, 1978) is a scale of 40 sentences reflecting dysfunctional cognitive schemas. Participants have to rate each sentence from 0 (not applicable to me) to 3 (highly applicable to me). The sum of the scores is considered to be an index of stable dysfunctional attitudes (i.e., a measure of cognitive structures). Inverse items will be rescaled so that higher scores reflect higher levels of dysfunctional attitudes. The DAS is a predictor of major depression (Rude et al., 2010) and it has shown to have good reliability  $\alpha = .70$  (Sanz & Vázquez, 1993). This procedure will be completed by participants at both pre- and post-intervention evaluations.

*Ruminative Responses Scale.* The RRS (Nolen-Hoeksema & Morrow, 1991) is composed of two subscales measuring rumination cognitive style. For the present study, only the 5-item brooding subscale will be used to measure the tendency to ruminate about negative events by adding up all the items. The scale has shown good reliability ( $\alpha = .93$ ) (Hervás Torres, 2008). This procedure will be completed by participants at both pre- and post-intervention evaluations. *The scale for mood assessment-EVEA* (Sanz, 2001) is a measure of current mood that participants take immediately before and immediately after each of the sessions of the program. It is included to reflect some possible reactions to the cognitive training procedure. Participants have to rate, from 0 to 10, their current level of anger, happiness, anxiety, depression, and boredom. Scores

of each subscale (4 items each) are summed up providing an index of emotional change during the session.

*Credibility and expectancy questionnaire.* The CEQ (Deville & Borkovec, 2000) is a 6-item measure used to assess the expectancy and rationale credibility of participants regarding the online program they are offered before they start it. It consists of two subscales that measure credibility based on cognition (*what you think*) and treatment expectancy based on affect (*what you feel*). Both subscales have shown to have good internal consistency ( $\alpha = .86$  for credibility,  $\alpha = .90$  for expectancy).

*The Working Alliance Inventory for Internet interventions (WAI-I)* (Gómez Penedo et al., 2019) is a self-report measure to assess alliance in internet interventions. In this study, only the 8-item subscale of task and goal agreement with the program was used to measure the level of concordance of the program with participants' interests. This measure was used at the end of the program to know if participants were satisfied with the result. An example of an item is 'Through the online program I have become clearer about the things I need to do to help improve my situation'. Cronbach's  $\alpha$  for this subscale has been found to be good ( $\alpha = .84$ ) (Gómez Penedo et al., 2019).

*The Stressful Events Questionnaire (SE)* (Hernangomez, 2012) is a self-report scale to measure stressful situations that happen to participants between the second assessment and the follow-up (2 weeks and 3 months). The scale includes positive and negative ratings of high-impact events as well as daily events related to different contexts (social, emotional, academic/occupational, and 'other').

## **Procedure**

Figure 4 shows the schedule of enrolment, intervention and assessment following the recommendations for clinical trials (Chan et al., 2013). The main investigator will create a random sequence to assign participants to either the experimental or control group. After the volunteers contact the main researcher for initial information about the study, they will receive a phone call from the researcher to explain the procedure of the study and the outline of the intervention program. Participants will be given all the ethical considerations regarding their participation and will be allowed to ask any further questions. After they verbally consent to continue, they will be assigned a participation code, randomly generated to ensure anonymity. Then, participants will complete two different assessments. First, they will receive the questionnaires for the first assessment (i.e. PHQ-9, GAD-7, AST-D-II, DASS21, DAS, RRS, PHI, and CEQ), together with the information sheet providing details of the program. Questionnaires will be completed online, using the Qualtrics platform, to which participants will be invited via a personalized link sent to their mailbox. Second, the day after participants complete these questionnaires at home, they will attend the first session in the lab. At that moment, they will be given the consent form (explaining their right to freely withdraw from the study at any moment) and will be asked to sign it if they agree to continue. Then, the main investigator will explain in detail the rationale of the intervention 'Relearning how to think' and will answer any questions from the participants. If they finally agree to participate, they will be asked to sign the consent form and complete some demographic information. Then, the three experimental tasks (MCAT, computerised beads task, and recall task) will be administered.

TIME POINT	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
	<i>-t<sub>1</sub></i>	0 (Pre)	10 days	Post	Follow-up (2w)	Follow-up (3m)
<b>ENROLMENT:</b>						
Informed consent	X					
Allocation	X					
<b>INTERVENTIONS:</b>						
<i>Online program for the experimental group</i>			↔			
<i>Waiting time for the control group</i>			↔			
<b>ASSESSMENTS:</b>						
<i>Ambiguous Scenarios Test for Depression-II (AST-D-II)</i>		X		X	X	X
<i>Depression, Anxiety and Stress Scale-21 (DASS-21)</i>		X		X	X	X
<i>Pemberton Happiness Index (PHI)</i>		X		X	X	X
<i>Mouse-based (gaze) Contingent Attention Task (MCAT)</i>		X		X		
<i>Scrambled Sentence Task-Memory (SST-M)</i>		X		X		
<i>Computerised beads task</i>		X		X		
<i>Dysfunctional Attitudes Scale (DAS)</i>		X		X		
<i>Ruminative Responses Scale (RRS)</i>		X		X		
<i>Patient Health Questionnaire-9 (PHQ-9)</i>		X				

<i>Generalised Anxiety Disorder-7 (GAD-7)</i>		X				
<i>The scale for mood assessment-EVEA</i>			X			
<i>Credibility and expectancy questionnaire</i>		X				
<i>The Working Alliance Inventory for Internet interventions (WAI-I)</i>				X		
<i>Stressful Events Questionnaire</i>					X	X

Figure 4. Schedule of enrolment, interventions and assessments.

After completion of the three lab tasks, participants in the experimental group will receive in their mailboxes the link to complete the online program from home. They will need to log in to an online platform created for this study and will be invited to create their own account and password to access the materials. Information will be stored solely using the participant's code number and only the main researchers will have access to the data. These data will be recorded in the database of the platform and will be used by the researchers to monitor if participants in the experimental group complete all four online sessions before the post-intervention evaluation. When participants first access the platform, they will find only the first session available. Access to the next session will be granted only 24 hours after completing the previous one. This intermission between sessions aims to enhance participants' processing of the contents of each session as well as to avoid cognitive overload and boredom.

After finishing the 4-session training program, participants in the experimental group will be notified again, after approximately 10 days, for a second assessment session. The control group will be allowed to complete the intervention right after the second assessment. To improve adherence, both groups will receive a reminder for the

second assessment session the day before. Finally, participants will be sent the follow-up questionnaires (AST-D-II, DASS21, PHI, SE) twice (in the next 2 weeks and 3 months). To increase adherence during the follow-ups, participants will be sent up to a maximum of three reminders to complete questionnaires. Both groups will have the opportunity to complete a 'feedback question' to give their opinion about the intervention. This question will be included in the post-assessment for the experimental group and at the follow-ups for the control group.

The procedure has been approved by the university ethics committee (Ref. 2018/19-017) and has been registered (ClinicalTrials.gov NCT03987477). Moreover, it follows the recommendations for a clinical trial protocol (Chan et al., 2013).

### **Analytic plan**

Demographic data and pre-treatment measures will be analysed to test for group differences with analysis of variance and chi-squared test for nominal variables.

Complete case analyses will be conducted for those participants who complete all 4 online sessions and attend pre- and post-assessment evaluation sessions. A series of 2 (group: experimental, control) x 3 (symptom group: never, present, past) x 2 (time: pre-training, post-training) analyses of variance will be performed to evaluate the change between groups. The symptom group will be created based on present and past symptoms of depression and/or anxiety to explore their influence on the results. Intention-to-treat (ITT) analyses will be conducted with all participants, regardless of session or outcome measure completion. ITT mixed models (restricted maximum likelihood (REML) estimation) will be used to account for missing data (Salim et al., 2008). Binary logistic regression will be used to evaluate the assumption that data is Missing at Random (MAR). Exploratory mediation analyses will be conducted to study

the interplay between the different cognitive bias scores given the change of the intervention. Finally, follow-up assessments will be included in a series of analyses of variance to evaluate group differences in time. All analyses will be performed in SPSS Statistics 20 with an  $\alpha$  level of 0.05.

### **Discussion**

The current study will test the efficacy of a brief online intervention to target emotional negative cognitive biases. Although traditional CBM interventions are designed to change this type of dysfunctional processing in an automatic way (Cristea et al., 2015), the rationale of ‘Relearning how to think’ is to increase participants’ awareness of their own thought processes and guide them to change these processes, in a more effortful way, by following a clinically-oriented working frame.

The study uses a transdiagnostic conceptualisation of the role of cognitive biases in psychopathology. Given the high comorbidity between anxiety and mood disorders (Kessler et al., 2005), having intervention tools that can tap both problems could be clinically useful. Some of the video scenarios designed for the program were based on examples proposed by previous transdiagnostic approaches (Barlow, Farchione, Sauer-Zavala, et al., 2017) and the content is suitable for different common psychopathologies in which cognitive biases may play a role.

The study also addresses some of the questions that remain unanswered regarding CBM efficacy. It combines subjective (e.g. AST-D) along with objective measures (e.g. JTC measure, MCT) to assess cognitive biases. The present study aimed to complement both self-report and behavioural measures to avoid potential biases of respondents. Mental imagery is also used following the proposal that it may enhance CBM-I performance (MacLeod et al., 2009). Holmes, et al. (Holmes et al., 2009) found

that mental imagery of emotional content has a beneficial impact on cognitive change. ‘Relearning how to think’ includes imagery training to potentiate vividness of the scenarios and promote interpretation change.

Furthermore, it explores innovatively whether changes in interpretation biases may be associated with concomitant changes in attention and memory. There is very scarce basic research on the interrelation between different types of biases in emotional disorders (Everaert et al., 2014) and this study will offer a unique opportunity to explore whether a specific intervention designed to change the interpretation of ambiguous scenarios may also affect other domains of information processing.

Finally, there is an increasing interest in the use of online interventions and many researchers wonder if this format is also beneficial for individuals with clinical problems. The extant evidence suggests that psychological treatments delivered online can be as effective as face-to-face therapies (Cuijpers et al., 2007; Holmes et al., 2018) and seem to overcome some of the limitations traditional therapies present (Kazdin & Blase, 2011). For example, online sessions can be taken by the individual at any time, there is no need to wait to schedule dates, stigma is reduced and individuals increase their self-efficacy (Andersson, 2016). Specifically, CBM interventions seem to be highly suitable for the online format due to its flexibility in application, or the minimal requirement of supervision, in comparison to traditional therapies (Yiend et al., 2014). CBM could even be used in a self-management way so that it could be applied to patients waiting for treatment or presenting vulnerability factors (Schartau et al., 2009). In sum, we expect that this study will offer new responses to some of the challenges CBM procedures face to make them more feasible, efficient, and more capable of

providing answers to some theoretical issues related to the complex relations between emotion, cognition, and clinical psychology.

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## SUPPLEMENTARY MATERIALS

### **‘Relearning how to think’: A brief online intervention to modify biased interpretations in emotional disorders. Study protocol for a randomised controlled trial**

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## CONSENTIMIENTO INFORMADO DE LOS PARTICIPANTES

**CÓDIGO DEL PARTICIPANTE:** .....

**Yo (Nombre y apellidos)**.....

- He leído la hoja de información que se me ha entregado.
- He podido hacer preguntas sobre el estudio.
- He recibido suficiente información sobre el estudio.
- He hablado con \_\_\_\_\_
- Comprendo que mi participación es voluntaria.
- Comprendo que puedo retirarme:
  - Cuando quiera
  - Sin tener que dar explicaciones
  - Sin repercusiones de ningún tipo
- Toda la información relativa a los datos de los participantes incluidos en el estudio será estrictamente confidencial conforme con la Ley Orgánica de Protección de Datos (Reglamento (UE) 2016/679 General de Protección de datos). Un código alfanumérico de identificación será asignado para cada participante en toda la documentación con el fin de asegurar el mantenimiento del anonimato de los pacientes.
- Comprendo, que puedo si así lo solicito, obtener información sobre los resultados del estudio.
- Presto libremente mi conformidad para participar en este estudio.
- Autorizo a ser contactado para un posible seguimiento del estudio.

Firma del participante:

Fecha : .....

### **PERMISO PARA LA REVISIÓN LOS DATOS / CONFIDENCIALIDAD.**

Los investigadores son responsables del tratamiento de datos y se comprometen a cumplir con la normativa de protección de datos en vigor. Los datos recogidos para el estudio estarán identificados mediante un código, de manera que no se incluya información que pueda identificar a cada participante.

Toda la información que se registrará será estrictamente confidencial, conforme con la Ley Orgánica de Protección de Datos. Los resultados del estudio siempre se presentarán de forma global y nunca, bajo ningún concepto, de forma individualizada, con objeto de garantizar los derechos que le asisten en cuanto a la confidencialidad de los datos personales.

De acuerdo con el nuevo Reglamento General de Protección de Datos (Reglamento UE 2016/679 General de Protección de Datos), los datos personales que se requieren son los necesarios para cubrir los objetivos de este estudio. En ninguno de los informes del estudio aparecerá el nombre de los participantes y su identidad no será revelada a persona alguna salvo para cumplir con los fines del estudio, y en el caso de urgencia médica o requerimiento legal. Cualquier información de carácter personal que pueda ser identificable será conservada y procesada por medios informáticos en condiciones de seguridad por los investigadores del estudio. El acceso a dicha información será restringido y se realizará siempre bajo condiciones de confidencialidad. Los resultados del estudio serán comunicados, sin ninguna revelación de la identidad de los participantes, a la comunidad científica.

De acuerdo con la ley vigente, además de los derechos que se presentan en el consentimiento informado (acceso, modificación, oposición y cancelación de datos) ahora también se puede limitar el tratamiento de datos que sean incorrectos, solicitar una copia o que se trasladen a un tercero (portabilidad) los datos que se facilitan para el estudio. Para ejercitar sus derechos, los participantes podrán dirigirse al investigador principal del estudio. Los datos no se pueden eliminar aunque dejen de participar en el estudio para garantizar la validez de la investigación y cumplir con los deberes legales. Así mismo los participantes son informados de su derecho a dirigirse a la Agencia de Protección de Datos si no quedaran satisfechos.

#### **SISTEMA DE ALMACENAMIENTO Y CONTROL DE ACCESO A LA INFORMACIÓN**

Los datos serán almacenados con fines de investigación en una base de datos que custodiarán los investigadores del estudio ya que es el único que tendrá la correspondencia entre el código del paciente y sus datos identificativos. El participante tendrá derecho a acceder a estos datos siempre que lo solicite.



#### **CONSENT FORM**

**PARTICIPANT CODE:** .....

**I (name and surname)**.....

- I have read the information sheet that has been given to me.
- I have been able to ask questions about the study.
- I have received enough information about the study.

- I have spoken with \_\_\_\_\_
- I understand that my participation is voluntary.
- I understand that I can withdraw:
  - Whenever I want
  - Without explanations
  - With no repercussions of any kind
- All information related to the data of the participants included in the study will be strictly confidential under the Organic Law on Data Protection (Regulation (EU) 2016/679 General on Data Protection). An alphanumeric identification code will be assigned to each participant in all documentation to ensure the maintenance of anonymity.
- I understand that if I request it, I can obtain information about the results of the study.
- I freely give my consent to participate in this study.
- I authorize to be contacted for a possible follow-up of the study.

Participant signature:

Date: .....

#### **PERMISSION TO REVIEW THE DATA / CONFIDENTIALITY.**

Researchers are responsible for data processing and undertake to comply with current data protection regulations. The data collected for the study will be identified by a code, so that information that could identify each participant is not included.

All the information that will be registered will be strictly confidential, following the Organic Law on Data Protection. The results of the study will always be presented globally and never, under any circumstances, individually, to guarantee the rights regarding the confidentiality of personal data.

Under the new General Data Protection Regulation (EU Regulation 2016/679 General Data Protection), the personal data required in the study are only those necessary to meet the objectives of this study. The names of the participants will not appear in any of the study reports and their identity will not be revealed to anyone except to fulfill the purposes of the study and in the case of a medical emergency or legal requirement. Any personal information that may be identifiable will be kept and processed by computerized means under secure conditions by the study researchers. Access to such information will be restricted and will always be done under conditions of confidentiality. The results of the study will be communicated, without any disclosure of the identity of the participants, to the scientific community.

Under current law, in addition to the rights that are presented in the informed consent (access, modification, opposition, and cancellation of data), now it is also possible to limit the processing of incorrect data, request a copy, or that are transferred to a third party (portability). To exercise their rights, participants may contact the main investigator of the study. The data cannot be deleted even if they stop participating in the study to guarantee the validity of the research and to comply with legal duties. Likewise, participants are informed of their right to contact the Data Protection Agency if they are not satisfied.

**INFORMATION ACCESS CONTROL AND STORAGE SYSTEM**

The data will be stored for research purposes in a database that will be kept by the study researchers since it is the only one that will have the correspondence between the participants' code and their identifying data. Participants will have the right to access this data whenever requested.

### **Study 3. The efficacy of CBM-IClin: A brief online transdiagnostic intervention to modify emotional interpretation biases**

#### **The efficacy of CBM-IClin: A brief online transdiagnostic intervention to modify emotional interpretation biases**

Inés Nieto<sup>1</sup>

Carmelo Vazquez<sup>1</sup>

#### **Abstract**

**Background:** Negative cognitive biases play a significant role in the development and maintenance of emotional disorders. This study aimed to create a new online Cognitive Bias Modification program for emotional interpretation biases based on standard clinical cognitive behavioural procedures (CBM-IClin). The goal of the CBM-IClin is to guide individuals to elicit alternative, non-biased interpretations in an elaborative and explicit manner. **Methods:** Volunteering students were randomly assigned to either the experimental group or a waiting-list group. All participants completed measures of interpretation bias and symptoms of depression, anxiety, and stress before and after the intervention, and at two follow-ups (2 weeks and 3 months after the intervention). **Results:** After the intervention, interpretations were significantly less negative in the experimental group than in the control group, regardless of symptom severity. No changes were found in depression, stress, or anxiety levels. **Conclusions:** This study presents a new tool to reduce negative interpretation biases in emotional disorders. The limitations of this study and recommendations for future research in the field are discussed.

Trial registry: This study was pre-registered in ClinicalTrials.gov (NCT03987477) and PsyArXiv.

**Keywords:** cognition, cognitive bias, depression, anxiety, transdiagnostic

## Introduction

Mood and anxiety disorders are highly prevalent in the population (Kessler et al., 2005) and carry great social and economic costs (Collins et al., 2011; Whiteford et al., 2013). Cognitive theories are some of the most accepted frameworks to understand depression and anxiety. These theories suggest that specific cognitive dysfunctions, such as dysfunctional thinking or cognitive biases (Barlow, et al., 2017; Beck et al., 1985; Clark & Beck, 1988), play a role in the onset and maintenance of both conditions. However, the effective causal role of cognitive variables is not yet well known (Beevers, 2015). For instance, cognitive-behavioural methods are efficacious in reducing both depression and anxiety symptoms (Andrews et al., 2018; Cuijpers et al., 2016), but the precise role of cognitive factors in explaining therapeutic change is still under dispute (D. A. Richards et al., 2016). Furthermore, there is still a relatively high percentage of patients who do not benefit from evidence-based treatments (Cuijpers et al., 2018) and rates of chronicity and relapse are still high (van Dis et al., 2020). These factors expose the need to explore complementary interventions that reduce symptoms and prevent relapses.

One of the procedures that have been proposed to study the causal role of cognitive factors in psychopathology is the *Cognitive Bias Modification (CBM)* approach. It was created as an experimental procedure aimed at selectively modifying biased cognitive processes that have been proposed to have a causal role in emotional disorders (e.g., attention, memory, or interpretation) to then evaluate its impact on symptoms (Hertel & Mathews, 2011; Mathews & MacLeod, 2002). The mechanism used in this approach is the repetition of trials that guide individuals to pay attention to positive stimuli (e.g., MacLeod et al., 2002) or train them to provide positive resolutions to ambiguous scenarios (Blackwell & Holmes, 2010). Recent meta-analyses have shown the potential benefits of CBM in negative mood (Menne-Lothmann et al., 2014), anxiety, and

depression measures (Cristea et al., 2015), and even transdiagnostic factors such as rumination (Hertel et al., 2014). Also, while changes in symptoms are modest after CBM (Jones & Sharpe 2017), there is evidence that training focused on interpretation biases (CBM-I) offers better results than procedures focused on training selective attention (Blanco & Vazquez, 2018; Cristea et al., 2015). In fact, a recent meta-analysis has shown the superiority of CBM-I over Attention Bias Modification procedures in comorbid depression and anxiety (Fodor et al., 2020).

Although promising, information on the role of the different variables that may be affecting CBM results is still scarce. Specifically, it remains unclear how vulnerability factors, such as the level of symptom severity of participants, could be modulating the benefits of these procedures (Cristea et al., 2015; Jones & Sharpe, 2017). For example, history of symptoms is known to be one of the most robust predictors of depressive relapse (Wojnarowski et al., 2019), and there is evidence that interpretation biases persist following the remission of depression symptoms (Wenzlaff & Eisenberg, 2001). Also, the multi-process model of cognitive vulnerability to anxiety integrates different parts of information processing (i.e., orientation, engagement, disengagement, and avoidance of threat-relevant stimuli, and threat-biased interpretations) to explain how negative biases may constitute a risk factor for this disorder (Ouimet et al., 2009). Thus, it is plausible that interventions to correct negative cognitive biases could help prevent full-blown episodes of both depression and anxiety. In fact, some authors have referred to CBM procedures as a potential “vaccine” against some symptoms (Lang et al., 2009). Additionally, the format of CBM interventions, typically using hundreds of trials to try to automatize adaptive cognitive biases, has been questioned (e.g., Duque et al., 2015). This way of proceeding by repetition significantly departs from the type of elaborate, effortful cognitive mechanisms that clinical therapists have proposed as key to facilitating

individuals to arrive at adaptive alternative explanations (Greenberger & Padesky, 2015). The change in symptoms following the change in negative cognitive biases has been hypothesized to be promoted by controlled processes instead of automatic ones (Hertel & Mathews, 2011). Regardless of the processing stage, difficulties in cognitive control over emotional material are consistently found in both depression and anxiety (Mathews & MacLeod, 2005). Thus, clinical procedures whose goal is to make individuals aware of this type of unconscious, unintentional, and uncontrollable processing of negative information could help them understand and gain control over their thoughts and emotions (Teachman et al., 2012).

The main aim of this study was to design a brief online interpretation bias modification program (CBM-IClin) which joins together the purpose of traditional CBM-I training (e.g., Blackwell & Holmes, 2010) and the clinical procedures that are followed in cognitive-behavioral therapies (e.g., Leahy, 2017). Therefore, the CBM-IClin focuses on the explicit goal of incentivizing individuals to create their own adaptive interpretations of ambiguous stories. Moreover, the content of the intervention was designed to be transdiagnostic, that is, based on common cognitive biases found in both depression and anxiety, as stated in cognitive theories of emotional disorders (Clark & Beck, 1988). Given the consistent coexistence of anxiety and depression across studies (Kessler et al., 2005; Wittchen, 2002), and their shared genetic architecture (Thorp et al., 2021), transdiagnostic approaches may be beneficial both to increase the understanding of these disorders as well as the clinical efficacy of the interventions (Kalin, 2020). Thus, the effect of the CBM-IClin was studied on participants undergoing the program compared to those assigned to a waiting-list control group, following a comparative approach recommended for novel interventions (Gold et al., 2017). It was hypothesized that the proposed CBM-IClin would significantly change interpretations of ambiguous situations

towards less negative (i.e., more positive, or neutral) resolutions. Moreover, it was expected that the CBM-IClin could also improve symptoms of depression, anxiety, and stress<sup>3</sup>. Following a common strategy to study the role of vulnerability given a history of symptoms (e.g., Haeffel et al., 2005; Joormann & Gotlib, 2010), exploratory analyses were used dividing the sample into three groups: current subclinical symptoms, past but no current symptoms, and individuals with neither current nor past symptoms.

## **Materials and Methods**

### **Participants and recruitment**

Participants were volunteers recruited via social media associated with university student services and through announcements in classes and posters placed throughout the faculty. The intervention was announced as a free online program to ‘learn how to control the influence of thoughts in emotional reactions’. If interested, students could get course academic credits in exchange for their participation within an official faculty program framework. Participation criteria included being older than 18 years old and being interested in the aim of the program<sup>4</sup>. Exclusion criteria included lacking internet access and visual or auditory disabilities that could make participants unable to follow the online sessions. There were no restrictions regarding other concomitant treatments during the study. However, this information was recorded to evaluate its possible interference with the CBM-IClin. (18 participants were under treatment at the time of the study<sup>5</sup>, see Table 1).

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<sup>3</sup> Given the relative lack of data for the maintenance of these changes in the long term (Hallion & Ruscio, 2011), the protocol of the study included the evaluation changes two weeks and three months after the post-intervention. However, a mistake with the design did not allow the completion of this aim (see further explanation in the Procedure section).

<sup>4</sup> Participants were not selected based on high symptoms of depression and anxiety given the link between participation and course credit (all students needed to have the same opportunities to gain these credits for equity reasons). This could imply the finding of floor-effects and it is discussed as a limitation.

<sup>5</sup> The inclusion of concomitant treatment as a covariate in the main analyses did not change the results.



Table 1. *Descriptive statistics and differences at baseline between groups*

	Baseline Experimental		Baseline Control		χ <sup>2</sup>		p		Post-intervention Experimental		Post-intervention Control		2-week follow-up Experimental		2-week follow-up Control		3-month follow-up Experimental		3-month follow-up Control	
	N	%	N	%			M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
					t	p														
Gender (female)	55	45.5	48	39.7	2.47	.12														
Concomitant treatment	12	10.1	6	5	2.24	.14														
Age	21.66	4.23	21.47	2.45	0.30	.77	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PHQ-9	7.52	4.91	7.13	4.18	0.46	.65	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PHQ-9 past	11.14	8.04	9.82	7.99	0.90	.37	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GAD-7	7.35	4.35	7.77	5.14	-0.48	.63	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GAD-7 past	5.90	7.09	5.17	7.17	0.56	.58	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CEQ <sup>1</sup>	0.52	4.71	-0.56	4.92	1.19	.24	-	-	-	-	-	-	-	-	-	-	-	-	-	-
WAI-I <sup>2</sup>	-	-	-	-	-	-	3.74	0.53	-	-	-	-	-	-	-	-	-	-	-	-
ASTD-D-II	12.67	20.60	12.72	17.26	-0.20	.99	26.98	17.62	17.0	18.71	16.09	18.69	16.14	16.52	28.29	18.36	22.55	18.44		
DASS21-D	4.95	5.01	3.70	3.87	1.52	.13	4.13	4.10	4.48	4.45	4.13	4.73	3.56	3.50	3.88	4.10	4.10	4.78		
DASS21-S	7.40	4.35	7.78	5.22	-0.44	.66	7.11	3.89	8.28	4.90	7.09	4.36	7.37	4.97	6.76	4.26	6.45	4.17		
DASS21-A	4.41	3.69	4.56	3.92	-0.19	.85	3.70	3.97	4.40	4.21	3.80	3.44	3.61	3.71	3.56	3.10	3.52	2.99		

NOTE: Higher scores in the AST-D-II reflect lower negative interpretation bias. N= number of participants, M= mean, SD= standard deviation. **Variables measured only at baseline:** PHQ-9 = Patient Health Questionnaire-9; GAD-7= Generalized Anxiety Disorder-7; CEQ = Credibility Expectancy Questionnaire. **Variables measured at baseline and post-intervention: Cognitive bias measures:** AST-D-II = Ambiguous Scenarios Test for Depression; **Symptoms measures:** DASS21-D = Depression, Anxiety and Stress Scale-21-Depression subscale; DASS21-S = Depression, Anxiety and Stress Scale-21-Stress subscale; DASS21-A = Depression, Anxiety and Stress Scale-21-Anxiety subscale. **Variables measured only at post-intervention:** WAI-I = Working Alliance Inventory for Internet interventions.

<sup>1</sup> These scores correspond to the standardized scores in the complete questionnaire.

<sup>2</sup> This score corresponds to the 18 participants who had completed at least one session of the online program and who completed the questionnaire

The sample size was calculated based on the estimated effect size of the change in interpretation bias before and after a CBM intervention ( $d = .43$ ) (Menne-Lothmann et al., 2014). Following G\*Power calculations, the minimum sample size ( $\alpha$  set at 0.05, power at 0.95) to find a difference in a repeated-measures multivariate analysis of variance (ANOVA) with one within-subjects factor (two-time points) and one between-subjects factor (two groups), was 73 participants. Twenty percent more participants were recruited due to expected attrition (Crutzen et al., 2015).

The final sample consisted of 121 participants<sup>6</sup>, with 103 women (85%) and a mean age of 21.56 (18-49). CONSORT 2010 Flow Diagram is shown in Figure 1. The study was approved by the University Ethics Committee (Ref. 2018/2019-017), and all participants provided informed consent before participation. Anonymity was ensured by codifying participants' names with numbers.

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<sup>6</sup> The mismatch between the sample size obtained in the power analysis and the final sample size was due to the link between participation and course credit: all those students who were interested had to complete the study for equity reasons.

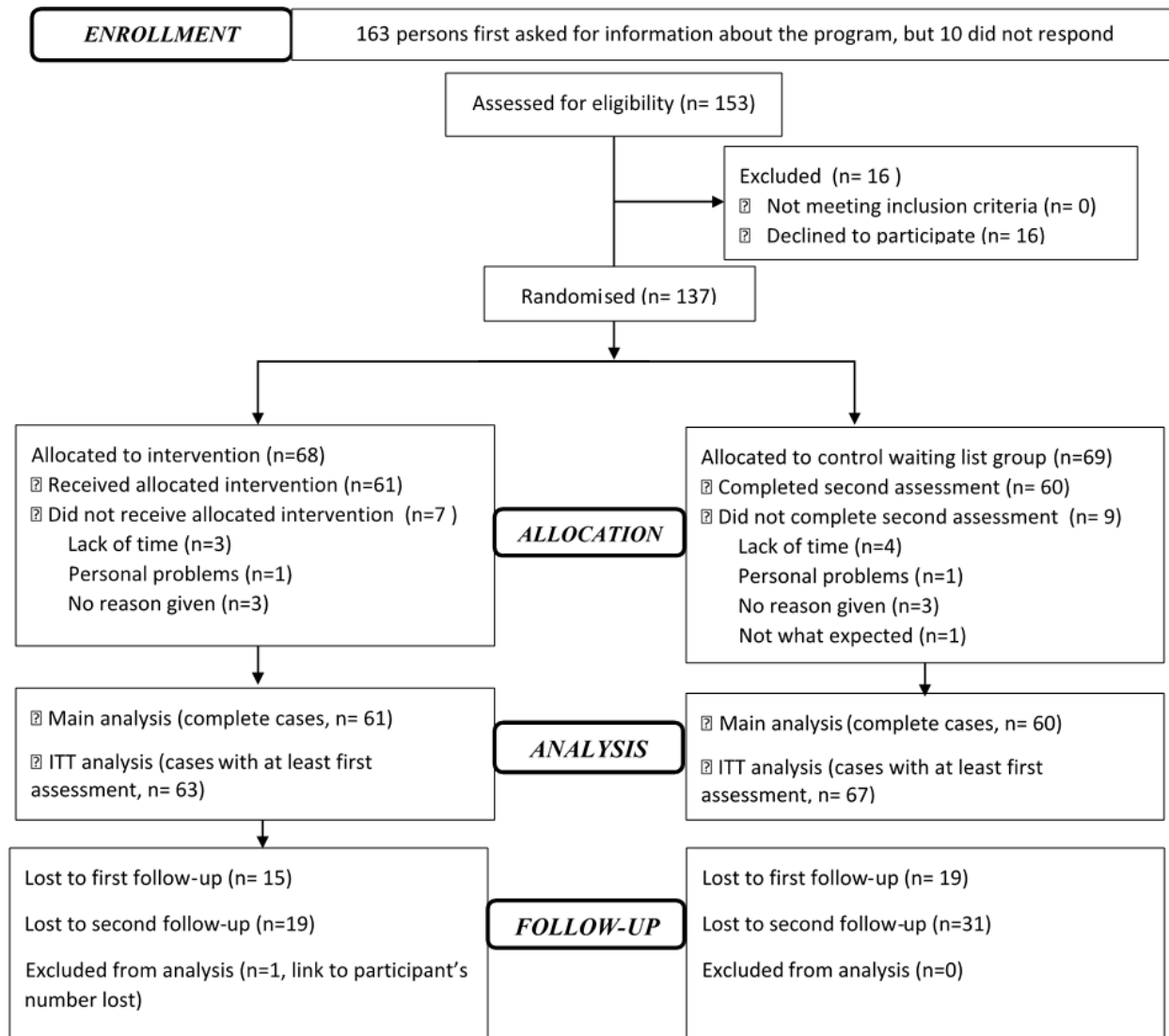


Figure 1. CONSORT flow diagram

### The CBM- $I_{\text{Clin}}$ program


The CBM- $I_{\text{Clin}}$  is a brief online program designed to modify negative emotional interpretation biases. While original CBM studies (e.g. Mathews & Mackintosh, 2000) were designed to train participants to change cognitive interpretation biases automatically, the current intervention aimed to teach participants the meaning and consequences of emotional cognitive biases and how to modify them by using thought training techniques proven to be successful in the clinical field (Vittengl et al., 2007).

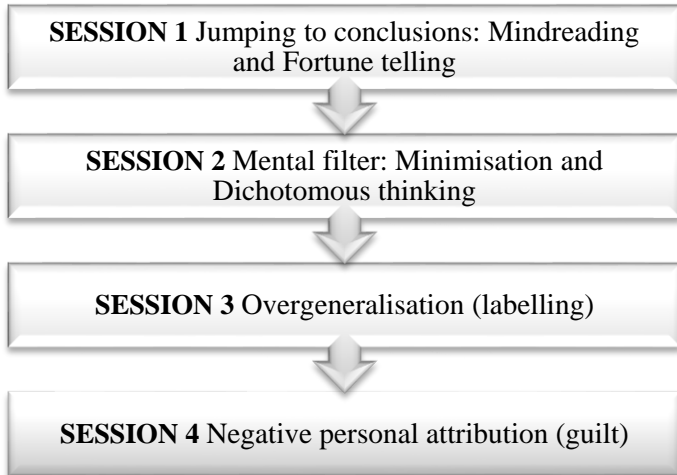
The program was composed of four audio-visual sessions with psychoeducational content, open-answer questions, and cognitive exercises to be completed by users. Different cognitive biases, such as dichotomous thinking or overgeneralization, were targeted in each session following classical descriptions of cognitive-behavioural interventions (Burns & Beck, 1999; Beck, 1976)-see Figure 2. The organization of the contents was based on the Cognitive Error Rating Scales (CERS; Drapeau et al., 2010), a manual created for therapists to evaluate cognitive errors during clinical sessions, and the CBM-errors (Lester et al., 2011), a clinical strategy to promote more benign interpretations following Beck's theory (Lee et al., 2015).

Each session of CBM-IClin consisted of four parts (see Figure 2). Parts 1 and 2 were focused on psychoeducation about the cognitive aspects of emotional disorders. First, each type of cognitive bias was described and explained with one example in video format. Some of these videos were specifically created for this intervention. Based on clinical vignettes described elsewhere (Barlow et al., 2017), professional actors represented examples of each cognitive bias in daily life scenes. The video started with an ambiguous situation (e.g., for mindreading, a woman appeared experiencing physical sensations at her workplace, such as sweating and hyperventilation, and hiding in the bathroom). Then, participants were asked to answer an open-ended question about possible interpretations of the scene. This exercise aimed to involve participants in the session actively and to facilitate personal and effortful alternative endings of the story. After answering the question, participants pressed a button to continue watching the scene, which ended with a standard biased interpretation of the situation (e.g., the woman explains that she always tries to hide those physical sensations because 'others may think she is crazy') and was followed by an explanation of why that interpretation was negatively biased (e.g., the woman's co-workers have always been nice to her and there

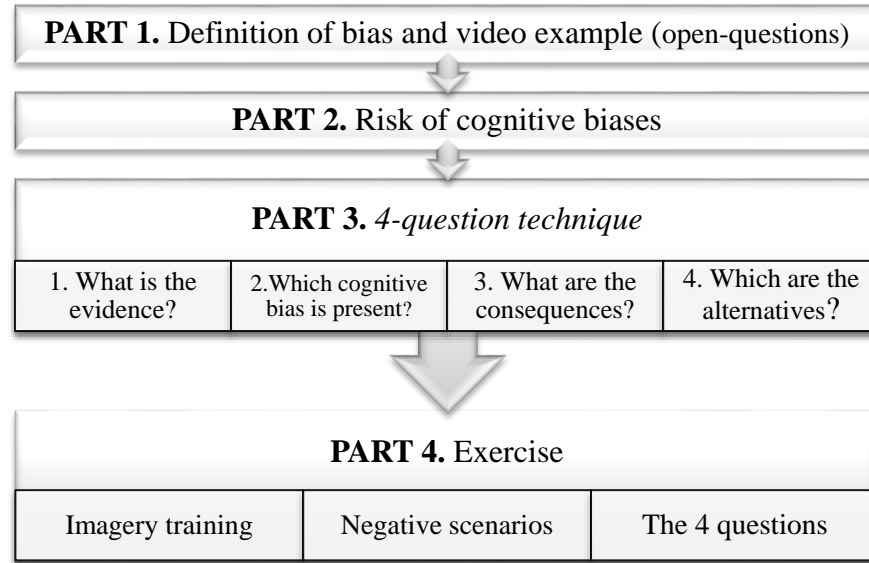
is no evidence that they would react negatively). In the second part, users were provided with information about potential risks of using biased negative interpretations (e.g., an example of mindreading may be a person thinking ‘My colleague doesn’t like me’ → which may lead this person to act in consequence: ‘I won’t say hi to my colleague’ → evoking a situation that did not exist in the first place: the colleague does not try to speak to this person anymore). Part 3 introduced strategies to avoid biased interpretations based on the widely used “4-question technique” ( Beck et al., 1985). This technique involves 4 steps to re-evaluate the negative interpretation of a given situation: 1) finding evidence for the negative thoughts, 2) detecting potential cognitive biases, 3) identifying negative consequences in holding those biases, and 4) creating alternative adaptive ways of thinking. Finally, during part 4, to facilitate the creation of adaptive alternative explanations, participants had to apply this strategy in an exercise adapted from Holmes et al.'s (2009) imagery training. At the beginning of the exercise, participants received instructions explaining how to imagine themselves vividly in the situations that were presented next. Then, participants were asked to close their eyes and listen to a recording of a negative scenario narrated by a female voice while a black screen was presented. These scenarios (adapted from Holmes et al.'s (2009) imagery training) consisted of a series of negative interpretations of daily life situations (e.g., *Your partner travels to work by car and normally arrives home promptly every day. Today you notice that he/she is over an hour late. Your first thought is that there must have been a car crash*) followed by a beep sound signalling participants to open their eyes and answer the exercise questions (see Table 2). The exercise started with a 10-point VAS scale to assess sadness, happiness, anxiety, and anger (Cowen & Keltner, 2017; Trampe, Quoidbach, & Taquet, 2015) and was followed by applying the 4-question technique to each scenario. After the 4<sup>th</sup> question (i.e., creating alternative ways of thinking), participants were asked to

evaluate the degree to which they believed the new interpretation, which is essential to promote a change. Participants were also asked to rate how the alternative view would make them feel by choosing one out of four emotional states (sadness, happiness, anxiety, and anger).

 RELEARNING HOW TO THINK



A)



B)

C)

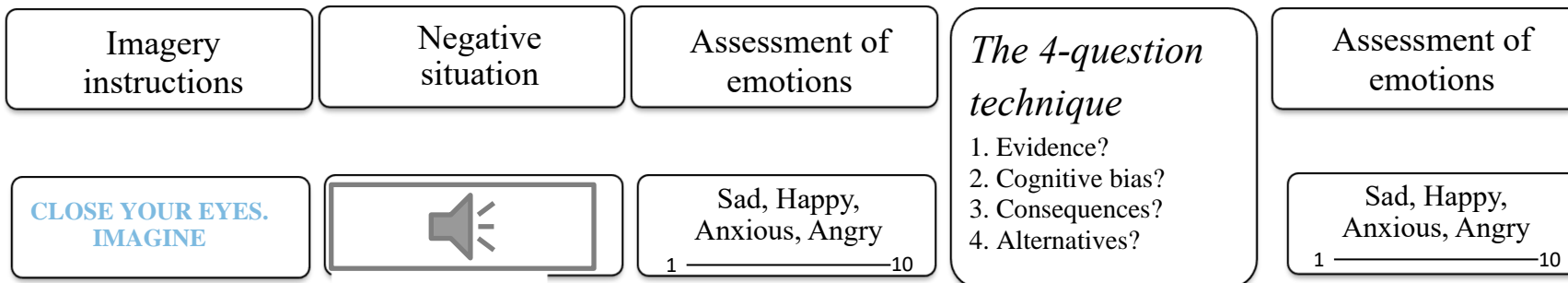


Figure 2. Structure of the online intervention: A) classification of the specific cognitive biases targeted in the four online sessions, B) structure of each session and C) practice exercise.

Table 2. Session exercise questions and format of the answers. These questions were completed after an adapted version of Holmes, Lang, and Shah's (2009) imagery training and the presentation in an audio format of a daily situation that was interpreted negatively.

	Question	Answer Format
	If you had that thought, how would you feel?	From 0 to 10: sad, happy, anxious, angry
“The 4-question technique”	1. What’s the evidence in the situation? Look for data that support the interpretation of the scenario. Some guiding questions that can help you assess this are: <i>Is the interpretation in that situation based on a fact or is it just a thought? What can I find in the situation that proves that the interpretation makes sense?</i>	Open answer
	2. To what degree would that be an error or bias of thought in that situation? Some guiding questions that can help you assess this are: <i>Am I interpreting from what happens in reality or am I going further? Am I trying to anticipate what will happen in the future? Am I underestimating my achievements or positive qualities? Am I generalizing this situation to any other time in my life? Am I blaming myself for no reason?</i>	To what degree would that be an error or bias of thought in that situation? From 0 to 10
	3. What could be the effect of this type of thinking? Look for consequences of interpreting the way it is done in the situation. Some guiding questions that can help you assess this are: <i>Do those negative thoughts help me or make me feel worse? What are the advantages and disadvantages of thinking that way?</i>	Open answer
	4. What alternative points of view are there? Look for positive or neutral, but also realistic, alternatives. Some guiding questions that can help you assess this are: <i>Am I considering my perspective as the only possible one?</i> If so, continue with: <ul style="list-style-type: none"> <li>• How would another person without negative bias react?</li> <li>• What would a person I love have told me if (s)he had found out that I was thinking like this?</li> <li>• Has something similar happened to me before that could help me now?</li> <li>• Would I think the same way in 5 years?</li> <li>• Could there be something positive in that situation that I would not be considering?</li> </ul>	Please write at least 3 alternatives. 1..... 2..... 3..... Choose the option that could be most beneficial to you (least harmful to you).
	To what degree would you believe the selected alternative in that situation?	From 0 to 10
	How would that alternative thought make you feel?	From 0 to 10: sad, happy, anxious, angry

## Measures

*Ambiguous Scenarios Test for Depression-II.* The AST-D-II (Rohrbacher & Reinecke, 2014) is a self-report measure of interpretation bias. It consists of 15 ambiguous scenarios where participants are asked to imagine these scenarios as vividly as possible and as if it is happening to them at that moment (e.g., *As you enter the room, the commission welcomes you and begins with the oral examination. After just a few minutes you know intuitively how the examination will go*). Then, they must rate each scene on a scale from -5 (very unpleasant) to 5 (very pleasant) to evaluate the degree to which their interpretation of ambiguity is positive or negative. The higher the rate, the more positive their interpretation is. For this study, the internal consistency of the scale was good ( $\alpha = .80$ ).

*Depression, Anxiety and Stress Scale-21.* The DASS-21 (Lovibond & Lovibond, 1995) is a 21-item self-report questionnaire measuring symptoms of depression, stress, and anxiety. Each of the three subscales contains 7 items and provides a different score for each construct. In this study, the internal reliability for each subscale was  $\alpha=.89$ ,  $\alpha=.82$ , and  $\alpha=.74$ , respectively.

*Patient Health Questionnaire-9.* The PHQ-9 (Spitzer et al., 1999) is a 9-item self-report questionnaire designed to assess episodes of depression based on DSM-IV diagnostic criteria. Each item is rated in frequency on a four-point scale from 1 (Not at all) to 4 (Nearly every day). The questionnaire showed good internal reliability in this study ( $\alpha = .82$ ). An adapted PHQ-9 was also used to measure past episodes of depression by asking participants to complete it if *'they have ever had a two-week period, or longer, (excluding the previous two weeks) where they: felt sad, depressed or empty, or lost interest for most of the things in life*. In this study, the standard diagnostic cut-off score of PHQ-9  $\geq 10$  (He et al., 2020) was used for present and past episodes of depression.

*Generalized Anxiety Disorder-7* (GAD-7, Spitzer et al., 2006) is a 7-item self-report questionnaire designed to assess episodes of anxiety according to the DSM-IV diagnostic criteria. Each item is rated on a four-point scale from 0 (Not at all) to 3 (Nearly every day), with the final score being between 0-21. The internal reliability of the scale for this study was  $\alpha = .89$ . An adapted version of this questionnaire was also used to measure past episodes of anxiety by asking participants to complete it if ‘*they have ever had a six-month period, or longer where they: felt nervous, anxious, or agitated, or they were unable to control their worry*’. The cut-off score used in this study to consider present or past episodes of anxiety was  $GAD-7 \geq 10$ , following the severity scale: minimal (0-4), mild (5-9), moderate (10-14), and serious (14-20) (Spitzer et al., 2006).

*Credibility and expectancy questionnaire*. The CEQ (Deville & Borkovec, 2000) is a 6-item measure used to assess participants’ expectancy and rationale credibility of an intervention. It consists of two subscales that measure credibility based on cognition (*what you think*) and treatment expectancy based on affect (*what you feel*). The items were adapted to fit the online program of this study. The internal reliability of the scale was  $\alpha = .64$ .

*The Working Alliance Inventory for Internet interventions (WAI-I)* (Gómez Penedo et al., 2019) is a self-report measure designed to assess alliance in internet interventions. In this study, only the 8-item subscale of Task and Goal agreement with the program was used to measure the level of concordance of the program with participants’ interests. This measure was presented to the experimental group post-intervention to know if participants were satisfied with the result. An example of one of the items is ‘Throughout the online program, I have become clearer about the things I need to do to help improve my situation. Cronbach’s  $\alpha$  for this subscale was good ( $\alpha = .83$ ).

**Procedure**

Following Gold et al.'s (2017) recommendations for new interventions, participants were randomly assigned to the experimental condition (cognitive bias intervention) or the waiting-list control running an Excel macro. Then, participants had to complete two steps in the assessment. First, they received via email an information file about the CBM-IClin, and the link to complete pre-treatment questionnaires (PHQ-9, GAD-7, AST-D-II, DASS21, and CEQ) using Qualtrics. Second, the day after they had completed these questionnaires, participants attended the first lab session. The rationale of the intervention was explained to them and they signed the consent form and answered some demographic questions. They were also instructed on how to access the four online sessions of CBM-IClin. They had to access an online platform designed for this study and create their account and password. In the first access, only the first session was available. A 24-hour lag between sessions was established to promote participants' assimilation of the sessions and avoid cognitive overload and boredom. Completion of each session was recorded, and information was coded with the participant's code number, only being accessible to the main researchers.

At the end of the pre-intervention assessment session, participants in the experimental condition received the link to start the online program via email. All participants were evaluated again approximately 10 days later for the second assessment (AST-D-II, DASS21, and WAI-I). All the participants in the experimental condition (N=61) completed the four online sessions between assessments. Participants in the control condition (N=60) were only given access to the intervention after the second assessment, i.e., 10 days after the first evaluation. They were invited to voluntarily complete the online program at any time after that point.

All participants were contacted twice after the second assessment to complete the follow-up questionnaires (AST-D-II, DASS21). First after two weeks and then after three months. Out of the 60 participants in the control condition, 23 had completed at least one session two weeks after the second evaluation (first follow-up) had taken place and 7 more had completed at least one session three months after the second evaluation (second follow-up) <sup>7</sup>.

### **Data analysis plan**

Baseline differences between conditions were evaluated with analyses of variance for quantitative variables and  $\chi^2$  tests for nominal variables. A series of 2 (Time: pre-intervention, post-intervention) 2 (Condition: experimental, control) repeated measures ANOVAs were conducted to test the effect of the intervention. Then a series of 2 (Time: pre-intervention, post-intervention) x 2 (Condition: experimental, control) x 3 (Symptom group: never, past or currently symptomatic) repeated measures ANOVAs were conducted to explore the effect dependent on symptom stage. The symptom groups were formed based on baseline scores on the PHQ-9 and the GAD-7 measures (present and past), being the correlation between depression and anxiety scores high ( $r=.76$ ). The group distribution can be found in Table 3. The never-symptomatic group included those participants who had never suffered symptoms of depression or anxiety, the past-symptomatic group included those participants with past symptoms of depression, anxiety, or both (PHQ-9-past  $\geq 10$  and/or GAD-7-past  $\geq 10$ ), and the currently-symptomatic group included those participants who showed PHQ-9  $\geq 10$  and/or GAD-7 scores  $\geq 10$  in the present (regardless of the history of depression or anxiety symptoms).

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<sup>7</sup> Maintenance of changes in time was studied with a series of 2 (Group: experimental, control) x 4 (Time: pre-intervention, post-intervention, 2-weeks follow-up, 3-months follow-up) ANOVAs. However, the results of these analyses are only reported in Table 4, given that, for ethical reasons, the control group started to receive the treatment before the follow-ups (see the *Procedure* section). Given the time overlap, it was not possible to consider the waiting list group as a control group in the last two assessments.

Bonferroni-adjustment comparisons were computed for post-hoc analyses of mean differences.

Table 3. Means and standard deviations of baseline symptoms per group

Groups	% total	N		Current		Past	
		Exp.	Ctrl.	PHQ-9	GAD-7	PHQ-9	GAD-7
Never symptomatic <sup>a</sup>	31.1	17	20	4.43 (2.19)	4.08 (2.31)	3.08 (3.65)	0.24 (1.48)
Past symptomatic <sup>a</sup>	31.1	19	18	5.35 (2.53)	5.29 (2.57)	14.41 (5.69)	7.84 (7.29)
Currently symptomatic <sup>b</sup>	37.8	23	22	11.36 (4.44)	12.20 (3.78)	13.31 (8.20)	7.98 (7.49)

<sup>a</sup> Depression and/or anxiety symptoms

<sup>b</sup> Includes participants with or without a history of depression and/or anxiety

The main analyses were complete-case analyses (i.e., including those participants who attended both pre- and post-assessment evaluation sessions). However, results were also explored by using the more conservative intention-to-treat (ITT) approach. ITT analyses included all participants, regardless of whether they had completed all assessment or online sessions. First, data were found to be missing completely at random according to Little's MCAR test ( $\chi^2 = 316.85$ ,  $df = 321$ ,  $p = .56$ ), meaning that the probability of losing these values was not related to the values in the data set (Rubin, 1976). Then, following Newman's (2014) recommendations, missing data were estimated using the iterative expectation-maximization (EM) method.

Sensitivity analyses were also computed with the correction of outliers. First, extreme values were detected using the interquartile range (IQR) rule. This rule consists of multiplying the IQR by 1.5, adding this value to the third quartile, and then subtracting it from the first quartile (Tukey, 1977). It is considered that values outside these cutoffs are outliers, which were only detected in AST-D-II (1.65% of observations), DASS-21 depression subscale (1.65% of observations), and DASS-21 anxiety subscale (1.65% of

observations). Then, the winsorise function of the library ‘statar’ in R was applied to correct these values.

Results for both ITT analyses and analyses without outliers are only reported if different from the main analyses. SPSS Statistics 20 was used to conduct the main analyses with an  $\alpha$  level of 0.05, and R software was used to conduct the detection and correction of outliers.

## **Results**

### **Group characteristics**

There were no demographic or baseline differences between conditions (see Table 1).

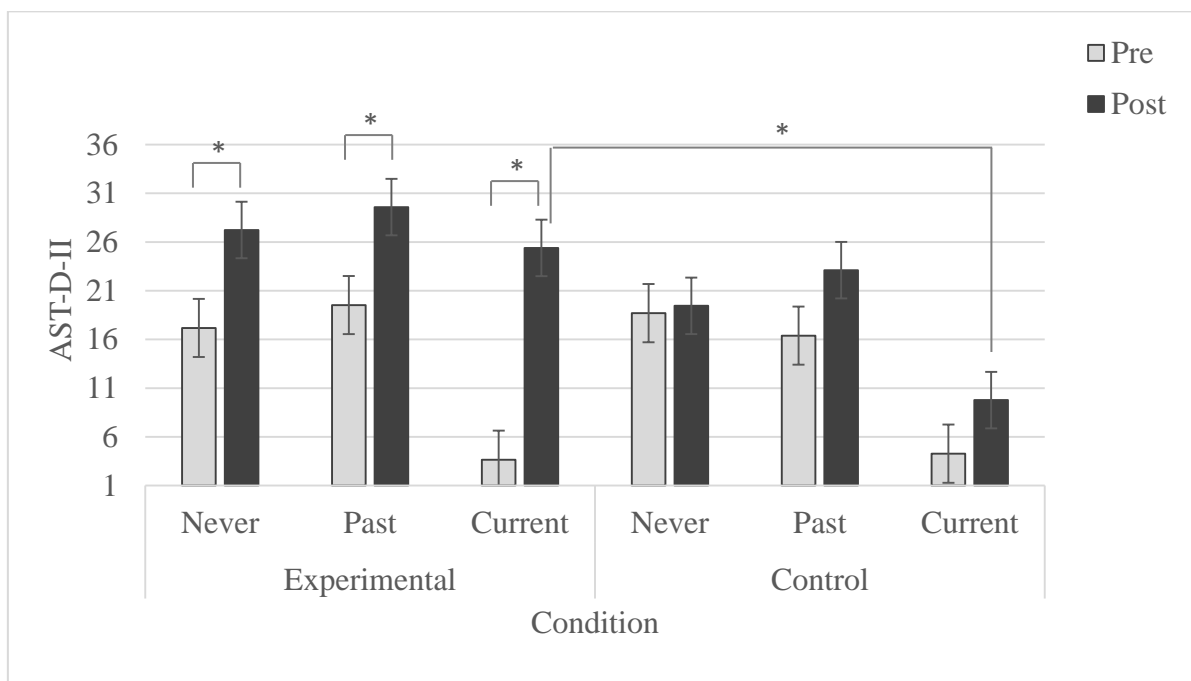
### **Effects of the intervention**

#### a) Change in interpretation bias (AST-D-II)

A 2 (Time: pre-intervention vs. post-intervention) x 2 (Condition: experimental vs. control) repeated measures ANOVA for interpretation biases showed that there was a significant main effect of Time ( $F(1,117)= 47.65, p < .001, \eta^2=0.29$ ) given that AST-D-II scores were significantly lower at baseline than at post-intervention ( $F(1,117)=47.65, p < .001$ ). Moreover, there was not a significant main effect of Condition ( $F(1,117)=2.66, p=.11, \eta^2 =0.02$ ), but there was a significant Time x Condition interaction ( $F(1,117)=14.24, p < .001, \eta^2 =0.11$ ). Post-hoc Bonferroni analyses revealed that, although participants in both conditions were not significantly different at baseline ( $t(118)= -0.56, p=.99$ ), the experimental condition showed significantly more positive interpretations than the control condition at post-intervention ( $t(118)=10.271, p=.003$ ; see Table 1).

The results for the 2 (Time) x 2 (Condition) x 3 (Symptom group) repeated measures ANOVA can be found in Figure 3. Results revealed significant main effects of Time ( $F(1, 113)=46.7, p < .001, \eta^2= 0.29$ ), and Symptom group ( $F(2, 113)= 5.86, p=.004, \eta^2= 0.09$ ) on the AST-D-II, showing that negative interpretation bias was significantly

higher at baseline than at post-intervention and was also higher for the current symptomatic group than for the never-symptomatic or past-symptomatic groups. The main effect of Condition was not significant ( $F(1, 113)=2.85, p=.09, \eta^2=0.03$ ), but the Time x Condition interaction was again significant ( $F(1, 113)=12.96, p<.001, \eta^2=0.10$ ) in the same direction as above. The Time x Symptom group interaction was also significant ( $F(2, 113)=3.30, p=.04, \eta^2=0.06$ ). Bonferroni post-hoc analyses showed that participants with current symptoms had significantly lower positive interpretation scores than the never ( $t(114)=-13.98, p=.002$ ) or past-symptomatic ( $t(114)=-13.995, p=.002$ ) groups at baseline, but these differences became non-significant at post-intervention (never:  $t(114)=-5.76, p=.47$ ; past:  $t(114)=-8.76, p=.09$ ). Neither the interaction between Condition and Symptom group ( $F(2, 113)=0.18, p=.83, \eta^2=0.00$ ) nor the triple interaction ( $F(2, 113)=2.03, p=.14, \eta^2=0.04$ ) effects were significant.



*Figure 3.* Change in interpretation bias scores by Condition and Symptom Group. Higher scores in the AST-D-II indicate more positive interpretations.

b) Changes in depression, stress, and anxiety symptoms (DASS-21)

Regarding the DASS-21, a 2x2 repeated measures ANOVA for depression symptoms showed no significant main effects of Time ( $F(1,116)=0.20, p=.89, \eta^2=0.00$ ) or Condition ( $F(1,116)=0.33, p=.57, \eta^2=0.003$ ). However, there was a significant Time x Condition interaction ( $F(1,116)=6.04, p=.02, \eta^2=0.05$ ). Post-hoc tests did not show significant differences either at baseline ( $t(116)=1.25, p=.13$ ) or post-intervention ( $t(116)=-0.41, p=.60$ ) between groups. The interaction was explained by the non-significant reduction in depression symptoms in the experimental condition ( $t(117)=0.88, p=.07$ ) and the non-significant increase in depression symptoms in the control condition ( $t(117)=-0.78, p=.10$ ). No significant main or interaction effects were found for stress (Time:  $F(1,116)=0.06, p=.81, \eta^2=0.00$ ; Condition:  $F(1,116)=1.09, p=.30, \eta^2=0.01$ ; Time x Condition:  $F(1,116)=1.05, p=.31, \eta^2=0.01$ ) or anxiety symptoms (Time:  $F(1,116)=1.66, p=.20, \eta^2=0.04$ ; Condition:  $F(1,116)=0.35, p=.56, \eta^2=0.003$ ; Time x Condition:  $F(1,116)=0.65, p=.42, \eta^2=0.01$ ).

The 2x3x2 ANOVA for the three DASS-21 subscales revealed a significant main effect of Symptom group ( $F(2,112)=26.54, p<.001, \eta^2=0.32$ ) for depression scores. Participants who were currently depressed showed significantly higher symptoms than those in the never- or past- symptomatic groups. Neither the main effects of Time ( $F(1,112)=0.01, p=.91, \eta^2=0.00$ ) or Condition ( $F(1,112)=0.17, p=.68, \eta^2=0.00$ ) were significant for depression scores. However, there was a significant interaction effect between Time and Condition ( $F(1,112)=5.70, p=.02, \eta^2=0.05$ ) in the same direction as above. The interaction between Time and Symptom group was also significant ( $F(2,112)=6.36, p=.002, \eta^2=0.10$ ) and post-hoc analyses revealed that the current symptomatic group had a significant reduction of depression symptoms between assessments ( $t(113)=1.52, p=.005$ ), while the never-symptomatic ( $t(113)=-1.09, p=.06$ )

and past-symptomatic ( $t(113)=-0.54, p=.35$ ) groups did not significantly change between the two assessments. The interaction between Condition and Symptoms group ( $F(2,112)=1.67, p=.19, \eta^2=0.03$ ) and the triple interaction ( $F(2,112)=1.35, p=.26, \eta^2=0.02$ ) effects were not significant for depression symptoms.

For stress and anxiety symptoms a significant main effect of Symptom groups showed that currently symptomatic participants had higher levels of stress ( $F(2,112)=36.29, p<.001, \eta^2=0.39$ ) and anxiety ( $F(2,112)=20.43, p<.001, \eta^2=0.27$ ) than never or past-symptomatic groups. No other main effects were significant either for stress (Time:  $F(1,112)=0.27, p=.61, \eta^2=0.00$ ; Condition:  $F(1,112)=1.90, p=.17, \eta^2=0.02$ ) or anxiety (Time:  $F(1,112)=1.71, p=.19, \eta^2=0.02$ ; Condition:  $F(1,112)=0.49, p=.48, \eta^2=0.00$ ) symptoms. For stress symptoms, there was a significant interaction between Time and Symptom group ( $F(2,112)=6.03, p=0.003, \eta^2=0.10$ ), where never-symptomatic ( $t(113)=-1.45, p=.04$ ) and the past-symptomatic ( $t(113)=-0.74, p=.28$ ) participants increased their stress levels between assessments while the current symptomatic group showed a significant reduction ( $t(113)=1.59, p=.01$ ). However, neither the Time x Condition ( $F(1,112)=0.94, p=.34, \eta^2=0.01$ ), the Condition x Symptom group ( $F(2,112)=1.92, p=.15, \eta^2=0.03$ ) or the triple interaction ( $F(2,112)=0.04, p=.96, \eta^2=0.00$ ) reached significance. For the anxiety subscale, there were no significant interaction effects (Time x Condition:  $F(1,112)=0.52, p=.48, \eta^2=0.00$ ; Time x Symptom group:  $F(2,112)=0.73, p=.49, \eta^2=0.01$ ; Condition x Symptom group:  $F(2,112)=0.83, p=.44, \eta^2=0.02$ ; Time x Condition x Symptom group:  $F(2,112)=0.98, p=.38, \eta^2=0.02$ ).

Table 4. *Results for the ANOVA 4 (Time: pre-intervention, post-intervention, 2-week follow-up, 3-month follow up) x 2 (Condition: experimental, control)*

Interpretation bias		F	p-value	$\eta^2$
AST-D-II	Time	14.79	<.001	0.20
	Condition	1.81	.18	0.029
	Time x Condition	3.41	.02	0.05
Symptoms (DASS-21)				

Depression	Time	0.79	.47	0.01
	Condition	0.02	.89	0.00
	Time x Condition	0.20	.84	0.00
Stress	Time	1.69	.17	0.03
	Condition	1.36	.25	0.02
	Time x Condition	0.39	.76	0.01
Anxiety	Time	0.72	.51	0.01
	Condition	0.85	.36	0.01
	Time x Condition	0.52	.62	0.01

### Discussion

The main aim of this study was the design and development of a new CBM-I intervention, guided by standard clinical cognitive-behavioural procedures, to test its efficacy in reducing negative interpretation bias and improving symptoms of depression, stress, and anxiety. Results showed that the program CBM-I<sub>Clin</sub> was effective at reducing self-reported negative interpretation bias. Specifically, the intervention condition showed a significant increment of positive interpretations after the intervention, which was true regardless of symptom stage (see Figure 3). None of the symptom groups on the waiting list significantly changed interpretation bias scores between assessments. This result suggests that the intervention is helpful not only for individuals with current symptoms of distress but also for those who had past emotional difficulties and not in the present. Previous meta-analyses have shown that the efficacy of CBM procedures is not affected by participants' severity of symptoms (Cristea et al., 2015). However, we should also consider that in the present study, the only symptom group that showed a significant difference between the experimental and the control conditions after the intervention was the one with current symptoms (see Figure 3). Although the level of personal agreement of the experimental condition with the tasks and goals of the program (WAI-I) was comparable to previous studies for online interventions (Gómez-Penedo et al., 2019), future research should explore whether this type of program is truly beneficial for healthy

and vulnerable samples. The translation of these initial results to the clinical field could provide information about the usefulness of our intervention as a therapeutic as well as a prevention tool. This is highly relevant, given the elevated percentages of relapse that characterize emotional disorders (Monroe & Harkness, 2011). Also, previous studies have already used CBM programs taking a preventive approach in adolescence ( de Voogd et al., 2018), which could help reduce the high levels of emotional disorders in the population.

Regarding symptoms, it is not possible to conclude that the program **was** effective to reduce depression, stress, or anxiety levels. These results are in line with previous CBM studies (e.g., LeMoult et al., 2017) and the current controversy regarding the clinical utility of these interventions ( Cristea et al., 2015; Hallion & Ruscio, 2011). A recent meta-analysis on CBM interventions concludes that these programs have consistent but minor effects on symptoms of depression and anxiety (Fodor et al., 2020). A possible explanation is that only individuals with specific characteristics may find benefits from these types of programs. For example, Price et al. (2016), in their meta-analysis, showed that the mediation role of change in attention bias to change symptoms was only significant in those participants for whom the attention bias modification program had been particularly effective. Cuijpers et al., (2018) explored the role of specific characteristics of patients in the efficacy of other psychological therapies for depression and found that being a primary care patient, a woman, an older adult, or having comorbidity with medical disorders could increase efficacy. Also, a recent study created a Personalised Advantage Index (PAI) to discover the optimal treatment for each patient based on moderators that could explain the differences in the efficacy of cognitive-behavioural therapy (CBT) and a positive psychology group intervention for depression (IPPT-D) (Lopez-Gomez et al., 2019). The authors showed that those patients with higher

levels of negative cognitions (increased automatic negative thoughts and depressed cognitions) did not benefit as much from CBT techniques as they did from IPPT-D. Something similar may apply to CBM interventions given the links found between the individual's cognitive control and emotion regulation abilities. It has been shown that threat-related interpretation bias trainings may be more effective for individuals with high, but not low, cognitive control abilities (Salemink & Wiers, 2012). Thus, it could be feasible that, in the future, these types of analyses could help find personalised recommendations for CBM interventions. Although some of these moderators (e.g., age, sex, or type of sample) have been addressed in CBM (e.g., Cristea et al., 2015; Menne-Lothmann et al., 2014), results are mixed and future research could help understand the contribution of these variables (e.g., baseline levels of cognitive biases or symptoms).

It is also possible that CBM procedures help change psychopathological symptoms but that these are not reflected in the most often used measures in research studies. Recently, it has been pointed out that depression is characterized by a high heterogeneity of symptoms and that the instruments used to measure it are artificially restricted to several symptoms limiting the validity of results (Fried, 2017). Also, the effects of the intervention may be best detected when individuals meet stressors that might potentially trigger cognitive biases. Cognitive theories of depression present cognitive biases as vulnerability factors that could have a negative effect only under stress, instead of being constantly activated (Ingram & Siegel, 2009). Following this idea, CBM programs may show their benefits only when participants encounter a stressor that triggers those biases. In fact, a review of meta-analyses of CBM concludes that Attention Bias Modification is more effective as a stress buffer than it is at reducing symptomatology (Jones & Sharpe, 2017). Also, some authors already refer to CBM

interventions as ‘cognitive vaccines’ to prevent, rather than treat psychopathological symptoms (Browning et al., 2012; Holmes et al., 2009).

### **Strengths and limitations**

The first limitation of this study is that participants were unselected, and symptomatology reached serious levels only in some cases (11 participants with baseline PHQ-9 $\geq$ 14; 14 participants with baseline GAD-7  $\geq$ 14). The use of clinical samples is necessary to evaluate the extent to which CBM interventions can help in the recovery of patients and shed light on the controversy of the clinical utility of these interventions. Second, the present design was not fully crossed since randomization was made based on intervention but it was not stratified by clinical grouping. This can make it more difficult to interpret the results from the exploratory analyses. Also, the instrument used to measure interpretation bias (the Ambiguous Scenarios Test for Depression) was developed based on depression-relevant items, which could have been a limitation to reflect changes in more anxiety-related bias. However, there is a high overlap between the cognitive distortions found in depression and anxiety and it is well-known the high comorbidity that characterizes both disorders (Kessler et al., 2005). Future studies could benefit from the use of both direct and indirect measures to evaluate cognitive change, which has been recommended to evaluate potential differences when measuring self-reported and non-conscious or automatic processing (Everaert et al., 2017; MacLeod et al., 2009). The inclusion of both modalities of measures could improve our understanding of how processing biases operate. Another limitation is that participants in the control group were offered the intervention after the second evaluation, making the comparison of groups in the follow-up assessments difficult to interpret. Finally, the adapted versions of PHQ-9 and GAD-7 to measure past symptoms have not been validated.

The present study also has several strengths. The first one is the innovative nature of the CBM-I<sub>clin</sub>, which aims to change cognitive biases using the conceptual framework

of traditional CBM training while being rooted in evidence-based practices used in psychotherapy. This new approach may open new roads to overcome some of the limitations already pointed out in CBM (Koster & Bernstein, 2015; Lee et al., 2015). While most of earlier CBM procedures are based on the idea that repetitive exposure to positive stimuli can lead to automatically change the type of processing later in daily life (Schartau et al., 2009), some disorders like depression seem to be more affected by elaborative mechanisms (Duque, et al., 2015) and cognitive control deficits that go beyond automatic processes (Villalobos et al., 2021). Also, this new intervention was carefully built by adapting clinical materials of already validated intervention programs (Barlow et al., 2017) and including mental imagery training. Previous reviews and meta-analyses have found that imagery instructions boost the effectiveness of CBM-I procedures (Jones & Sharpe, 2017; Menne-Lothmann et al., 2014; Duque et al., 2015), given the close relationship between imagery and emotions (Holmes & Mathews, 2005). Despite its innovations, CBM-IClin preserves some of the advantages of the original CBM procedures. The online format makes it highly accessible and cost-effective (Kazdin & Blase, 2011), and its short-duration (4 sessions) could prevent lack of adherence or attrition, while also matching or even enlarging the duration of cognitive modules used in cognitive-behavioural therapy manualized programs (e.g., Barlow et al., 2017; Lewinsohn et al., 1985). Thus, the CBM-IClin may be a promising tool to reduce cognitive biases, although its effects on symptoms still need to be further studied.

Some recommendations for future studies include the use of a longitudinal design, which is needed to shed light on the causal role of cognitive biases (Everaert et al., 2017). Moreover, the measurement of other cognitive or psychological variables that could be affected by a change in interpretation bias should be explored. For example, it has been found that depressed and anxious individuals show negative cognitive biases at other

processing levels (attention and memory) and some authors already state the need to know how they interact with each other (Everaert & Koster, 2020). Also, the study of cognitive bias with other factors associated with emotional disorders, such as dysfunctional emotion regulation (Yoon & Rottenberg, 2020), cognitive control deficits, or repetitive styles of thinking (Villalobos et al., 2021) would be highly beneficial. Finally, the inclusion of well-being measures when modifying interpretation bias could give information, not only about the reduction of negative outcomes, but also the increment in positive ones.

In sum, this program may help modify negative interpretation bias in emotional disorders. For the first time, a CBM-I program has been designed to promote elaborative, effortful cognitive mechanisms, as proposed by cognitive theories. In addition, there is some indication that the CBM-I<sub>clin</sub> could be effective to improve negative interpretation biases both in participants with current subclinical emotional symptoms and in at-risk participants with a history of symptoms. **However, the efficacy of the program to change symptoms was not supported in the present study.** Although preliminary, the present work widens the potential value of CBM interventions for prevention and therapy.

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**Declaration of interests:** None.

**Ethics approval and consent to participate**

This project was approved by the School of Psychology Ethics Committee on June 17, 2019 (Ref. 2018/2019-017). All participants provided informed consent before starting the first study session. To ensure anonymity, their names were coded with numbers.

**Registry:** This study was pre-registered in ClinicalTrials.gov (NCT03987477) and PsyArXiv

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**Study 4. Disentangling the mediating role of modifying interpretation bias on emotional distress using a novel cognitive bias modification program**

The fourth study of the dissertation focused on evaluating the mediating role of the change in interpretation bias, after the use of the CBM-IClin, on the change of other related variables. It was found that the change negative interpretation biases, given the program, had a direct effect on the change in negative memory bias, an indirect effect on the change in depression symptoms via the change in interpretation bias, and both direct and indirect effects on the change in self-reported dysfunctional attitudes.

The results are presented in the article Nieto, I., & Vazquez, C. (2021).

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**Disentangling the mediating role of modifying interpretation bias on emotional distress  
using a novel cognitive bias modification program**

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**Abstract**

**Background:** Negative interpretation bias is a potential risk factor for emotional disorders. In this study, we tested a clinically inspired 4-session online Cognitive Bias Modification-Interpretation (CBM-IClin) program to modify negative interpretation biases. **Methods:** We randomized one hundred and twenty-one volunteer young adults (Mean age=21.6 years, SD= 3.5; 85% women) with varying levels of emotional distress to either an experimental or waitlist control group. Mediation analyses were used to disentangle the associations between the intervention, changes in interpretation biases (assessed by both a self-report and an experimental task), and changes in measures of cognitive vulnerability and symptoms of depression and anxiety. **Results:** The results showed that the CBM-IClin could change negative interpretation biases. Also, it had a direct effect on the change in negative memory bias, an indirect effect on the change in depression symptoms via the change in interpretation bias, and both direct and indirect effects on the change in self-reported dysfunctional attitudes. **Limitations:** The study included a non-clinical sample of participants and it did not control for some potential confounding factors (e.g., attentional disorders). Furthermore, participants' engagement during the sessions at home was not supervised. **Conclusions:** The CBM-IClin is a potential tool to prevent and intervene in emotional disorders in young adults and could complement other traditional CBM procedures or clinical interventions.

**Keywords:** cognition, bias, depression, anxiety, prevention

### **Introduction**

Classical cognitive models of emotional disorders (Beck, 1967; Clark & Beck, 1988) consider that negative biases could be vulnerability elements that trigger the full development of symptoms. The association between depression, and anxiety and negative modes of processing information has been supported by meta-analytic evidence (Everaert et al., 2017; Nieto, Robles, et al., 2020). The role of these biases as vulnerability factors has been shown in empirical studies where at-risk participants (e.g. children of depressed parents) present with higher levels of negative interpretation, attention, and memory biases than those at low risk (Platt et al., 2017; Sfarlea et al., 2020).

Although there are several treatments available for depression and anxiety, they are not universally effective, and relapse rates remain high upon recovery (Cuijpers et al., 2018, 2020). A specific therapeutic and preventive target to improve treatment outcomes could be the direct modification of cognitive biases. Along that line, Cognitive Bias Modification (CBM) programs were developed to promote adaptive changes in cognitive biases through the repetition of trials containing positive or neutral information. The key idea behind these procedures is that the automatic processing of information can be changed (Fodor et al., 2020). Meta-analytic studies have shown that CBM has small to moderate efficacy in changing cognitive biases and symptoms (Cristea et al., 2015), making them suitable candidates to enhance the results found in other therapies. For example, attention bias modification may benefit youth who do not respond to cognitive-behavioural therapy (Pettit et al., 2020), and interpretation bias training has shown positive effects on adolescents' interpretation processes and mood (Lothmann et al., 2011). Given the theoretical basis of the relationship between

emotional disorders and cognitive biases, it is necessary to use statistical procedures that aim to approach causality and a mediated relationship can be considered an intrinsically causal relationship ( Hayes, 2018). By using this approach, previous CBM studies have shown the mediational effect of change in cognitive biases (e.g., attention bias in Heeren et al., 2012) over selected outcomes (i.e., change in physiological reactivity). While pre-treatment levels of cognitive biases may moderate treatment effectiveness, change in cognitive bias is usually hypothesized to mediate this relationship (e.g. Kuckertz et al., 2014). Yet, little is known about the mediators and moderators of change (Jones & Sharpe, 2017) and methodological and design recommendations to test mediator variables are not followed consistently, making it difficult to derive clear conclusions (Lemmens et al., 2016).

Given the need to enhance intervention procedures for depression and anxiety and the potential causal role of negative cognitive bias, it seems necessary to develop novel procedures to change biases not only in contexts of full-blown emotional disorders but also in prevention programs. Until now, only a few CBM procedures have used a preventive approach. The COgnitive bias modification to Prevent dEpression (COPE) trial (Basanovic et al., 2019) was a year-long randomized controlled trial of an online CBM program for participants reporting mild-to-moderate symptoms of depression at baseline. The authors did not find a reduction in the incidence of clinical symptoms of depression which could be explained by the lack of significant changes in attention and interpretation biases, given that CBM procedures are designed to reduce negative cognitive biases as a mechanism to improve symptoms (Clarke et al., 2014). In fact, research has shown that changes in interpretation biases mediate the changes in anxiety symptoms (Salemink, van den Hout, et al., 2010). Another approach to prevention has been used at discharge for patients who may need booster sessions to

avoid relapse (Beard et al., 2021). The authors developed a smartphone app for people with acute mental health symptoms of different diagnoses that aimed to treat negative biases in interpretation processes of ambiguous information. Although preliminary, the results showed that both interpretation bias and emotional symptoms could be improved by this type of intervention.

We designed the present study, first, to provide a new intervention, based on clinical cognitive models (Beck, 1967; Clark & Beck, 1988), to change the negative interpretation biases that typically accompany depression and anxiety. The program ‘Relearning how to think’ was created as a clinically inspired Cognitive Bias Modification-Interpretation (CBM-IClin) program aiming to target elaborative processing of information [see a full description in Nieto & Vazquez, 2021]. Given the high comorbidity rates between depression and anxiety (Kalin, 2020), the CBM-IClin has the added value of a transdiagnostic perspective by including contents relevant for both disorders. The program was applied to university students, a population that, given all the challenges associated with the academic pressures and changes in lifestyles, are particularly vulnerable to developing emotional disorders (Eisenberg et al., 2009). Therefore, the impact of the CBM-IClin program was evaluated in young adults compared to a waitlist control group, following the procedures recommended for novel interventions (Gold et al., 2017). Our main hypothesis was that the CBM-IClin program would significantly reduce levels of negative interpretation biases (as measured with both self-report and experimental task), from baseline to post-intervention, in the experimental group, whereas the control group would show no significant changes.

Second, given the theoretical and empirical link between cognitive bias and emotional disorders, mediation models were used to explore the potential causal role of negative interpretation bias on symptoms of depression, stress, and anxiety, as well as

levels of dysfunctional attitudes, and well-being. We expected that the effect of the online program (i.e., the change in negative interpretation bias) would mediate the change in these variables. Finally, we expected that the change in negative interpretation bias, given by the intervention, would mediate the change in other outcome variables. These outcome variables include negative attention and memory biases, and rumination and were selected based on previous evidence of the interaction between processing biases, emotional disorders, and emotion regulation (Everaert, Grahek, et al., 2017; Sanchez-Lopez et al., 2017; Sanchez-Lopez, Everaert, et al., 2019).

## **Method**

### **Participants and recruitment**

The sample was 121 volunteer young adults ( $M_{\text{age}} = 21.6$  years,  $SD = 3.5$ ; 85% women). Participants were recruited by offering them a free online program, which was publicly announced as a procedure to ‘learn how to control the influence of thoughts on emotional reactions.’ Exclusion criteria were visual and/or auditory disabilities that could make participants unable to follow the online program, and lack of Internet access at home. Participants were given the opportunity to obtain course academic credits in exchange for their participation as framed within an official university program.

Following G\*Power calculations, the minimum sample size ( $\alpha$  set at 0.05, power at 0.95) to find a difference in interpretation bias before and after a CBM intervention (Repeated Measures ANOVA), and based on an effect size of  $d = .43$  (Menne-Lothmann et al., 2014), was 73 participants. Based on expected attrition found in similar studies (e.g., Crutzen et al., 2015), we planned to recruit twenty percent more participants. CONSORT 2010 Flow Diagram is shown in Figure 1. The study was approved by the university school of psychology Ethics Committee (Ref. 2018/2019-017) and all participants provided informed consent before participation. To ensure anonymity, we coded their names with numbers.

### **The ‘Relearning how to think’ program**

The CBM-IClin program aimed to reduce negative interpretation biases associated with emotional disorders, based on classical descriptions (Beck, 1976; Burns & Beck, 1999), such as dichotomous thinking, or overgeneralization. The program comprises four sessions combining psychoeducation, video examples, open-ended questions, and cognitive restructuring training exercises aiming to enhance elaborative processing of information [see a full description in Nieto & Vazquez, 2021]. The rationale behind this program was that teaching participants the meaning and consequences of negative cognitive biases could increase the awareness of their cognitive processes and, then, help them change possible maladaptive biases by training conscious processing with techniques similar to those used in the clinical field (Vittengl et al., 2007). Figure 2 shows the organization of each session of the program.

### **Measures**

- a) Current and past episodes of depression and anxiety

*Patient Health Questionnaire-9.* The PHQ-9 (Spitzer et al., 1999) is a 9-item self-report questionnaire to assess episodes of depression based on DSM-IV (American Psychiatric Association, 1994) diagnostic criteria. The questionnaire showed good internal reliability in our sample ( $\alpha = .82$ ). An adapted PHQ-9 was also used to measure past episodes of depression by asking participants to complete it if ‘they ever had a 2-week period, or longer, (different from the previous two weeks) when they: felt sad, depressed or empty, or lost interest for most of the things in life.’ Both versions were used to assess participants’ pre-intervention depression levels. The internal reliability observed in our sample for this adaptation was  $\alpha = .85$ .

*Generalized Anxiety Disorder-7.* The GAD-7 (Spitzer et al., 2006) is a 7-item self-report questionnaire that assesses episodes of anxiety according to the DSM-IV (APA, 1994) diagnostic criteria. The internal reliability of the scale in our sample was  $\alpha$

= .89. An adapted version of this questionnaire was also used to measure past episodes of anxiety by asking participants to complete it if ‘they ever had a six-month period, or longer, when they: felt nervous, anxious, or agitated, or could not control their worry.’ Both versions were used to assess participants’ pre-intervention anxiety levels. The internal reliability found in our sample for this adaptation was  $\alpha = .66$ .

b) Credibility and quality of the intervention

*Credibility and Expectancy Questionnaire.* The CEQ (Deville & Borkovec, 2000) is a 6-item measure used to assess participants’ expectancy and rationale credibility of an intervention. The items were completed by participants at baseline and the internal reliability of the scale in our sample was  $\alpha = .64$ .

*The Working Alliance Inventory for Internet interventions.* The WAI-I (Gómez Penedo et al., 2019) is a self-report measure of the alliance in internet interventions. In this study, only the 8-item subscale of ‘task and goal agreement with the program’ was used to measure the level of concordance of the program with participants’ interests. We assessed this variable only in the experimental group after the intervention. Cronbach’s  $\alpha$  in our sample for this subscale was good ( $\alpha = .83$ ).

c) Self-report cognitive bias measures

*Ambiguous Scenarios Test for Depression-II.* The AST-D-II (Rohrbacher & Reinecke, 2014) is a self-report measure of interpretation bias that was used both at pre- and post-intervention. It comprises 15 ambiguous scenarios which must be rated on a scale from -5 (Very unpleasant) to 5 (Very pleasant), with higher scores indicating more positive interpretations. Participants were asked to imagine each scenario as vividly as possible and happening to them (e.g. *As you enter the room, the commission welcomes you and begins with the oral examination. After just a few minutes, you know intuitively*

*how the examination will go.*). For the current study, the internal consistency of the scale was good ( $\alpha = .80$ ).

#### d) Experimental cognitive bias tasks

*Attentional and interpretation bias task.* The Mouse-based (gaze) Contingent Attention Task (MCAT; ( Sanchez-Lopez, De Raedt, et al., 2019) was used both at pre- and post-intervention to measure interpretation bias (MCAT<sub>Int</sub>) while monitoring attention towards emotional stimuli (MCAT<sub>Att</sub>). At the beginning of the task, participants were instructed to click a fixation cross on the left side of the computer screen to facilitate natural left-to-right standard reading patterns. Then, the *reading screen* was presented with an emotional scrambled sentence (e.g., “am winner born loser a I”) consisting of 6 words, all hidden with a blank mask. Participants had to move the mouse cursor over each mask to read the word hidden so that the time spent reading each word (duration in milliseconds) was recorded. When the mouse was pointed to the next blank space, an extra word was revealed while the previous one was hidden again. Participants were instructed to mentally form a grammatically correct sentence using only five words with a time limit of 14 seconds per sentence. Then, the *answer screen* was presented with the six words unmasked for participants to click, in 7 seconds, the words in the sentence's order they had mentally formed. The task consisted of 4 practice trials and 20 actual trials divided in two blocks of 10. Participants were given the possibility to rest for some minutes between blocks. At the beginning of the task, participants were asked to memorize a 6-digit number (presented on the screen for 5 seconds) and keep that number in mind during the entire task to maximize the appearance of biases by increasing the cognitive load. We calculated two ratios in this procedure. First, we calculated the number of correctly unscrambled negative sentences divided by the total number of correctly unscrambled positive and negative sentences as

an index of automatic negative interpretation bias. Second, we calculated time spent (in ms) reading negative words on the *reading screen* divided by the total time spent (ms) reading positive and negative words as the index of overall negative attentional bias. In both cases, higher scores represented more negative cognitive biases. The split-half reliability was 0.95 for the index of overall negative attentional bias, and 0.87 for the index of automatic negative interpretation bias.

*Memory Bias Task (MBT).* As a measure of memory bias, participants were given 5 minutes to freely remember the sentences they had constructed during the MCAT procedure (both at pre- and post-intervention). We coded memories as positive or negative based on the valence of the recalled items. To avoid the inclusion of false memories, memories that did not match the content of the original task items were not coded. The ratio between negative sentences and the total number of emotional sentences recalled was used as an index of negative memory bias.

#### e) Outcome measures

*Depression, Anxiety and Stress Scale-21.* The DASS-21 (Lovibond & Lovibond, 1995) is a 21-item self-report questionnaire used to measure symptoms of depression, stress, and anxiety both at pre- and post-intervention. Each of the three subscales contains 7 items and provides a different score for each construct. In the current study, the internal reliability for each subscale was  $\alpha=.89$ ,  $\alpha=.82$ , and  $\alpha=.74$ , respectively.

*Dysfunctional Attitudes Scale.* The DAS (Weissman & Beck, 1978) is an instrument of 40 sentences reflecting dysfunctional cognitive schemas mainly related to themes of dependency (e.g., ‘If others dislike you, you cannot be happy’), self-control (e.g., ‘Taking even a small risk is foolish because the loss is likely to be a disaster’), or achievement (e.g., ‘I should be upset if I make a mistake’), which are common in

depression and anxiety (Kush, 2004). It was administered to participants both at pre- and post-intervention. In our sample, the scale showed good internal reliability ( $\alpha = .79$ ).

*Ruminative Responses Scale.* The RRS (Nolen-Hoeksema & Morrow, 1991) includes two subscales measuring a ruminative cognitive style. In the current study, we used only the 5-item brooding subscale both at pre- and post-intervention. The internal reliability for the scale was  $\alpha = .72$  in our sample.

*Pemberton Happiness Index.* The PHI (Hervas & Vazquez, 2013) is an 11-item self-report questionnaire measuring general, eudemonic, hedonic, and social well-being. It was administered to participants both at pre- and post-intervention. It showed good reliability in the present study ( $\alpha = .82$ ).

## **Procedure**

First, we randomly assigned participants to the experimental group (CBM-IClin) or the waiting list control group, using an Excel macro. Then, the day before their first visit to the lab, we sent participants, via e-mail, a brief information document about the program ‘Relearning how to think’ together with a Qualtrics link to fill out the baseline questionnaires (i.e., PHQ-9, GAD-7, CEQ, AST-D-II, DASS-21, DAS, RRS, PHI). During their first visit, we explained to participants the rationale of the intervention and then signed the consent form and completed the experimental tasks measuring cognitive biases (MCAT and MBT). At the end of the first visit, the experimental group received the link via email to start the CBM-IClin. We re-invited participants in both groups for a second assessment approximately 10 days later. Further descriptions of the procedure are detailed in the Supplementary file.

This study was pre-registered in PsyArXiv (DOI: 10.31234/osf.io/auh6) and ClinicalTrials.gov (NCT03987477).

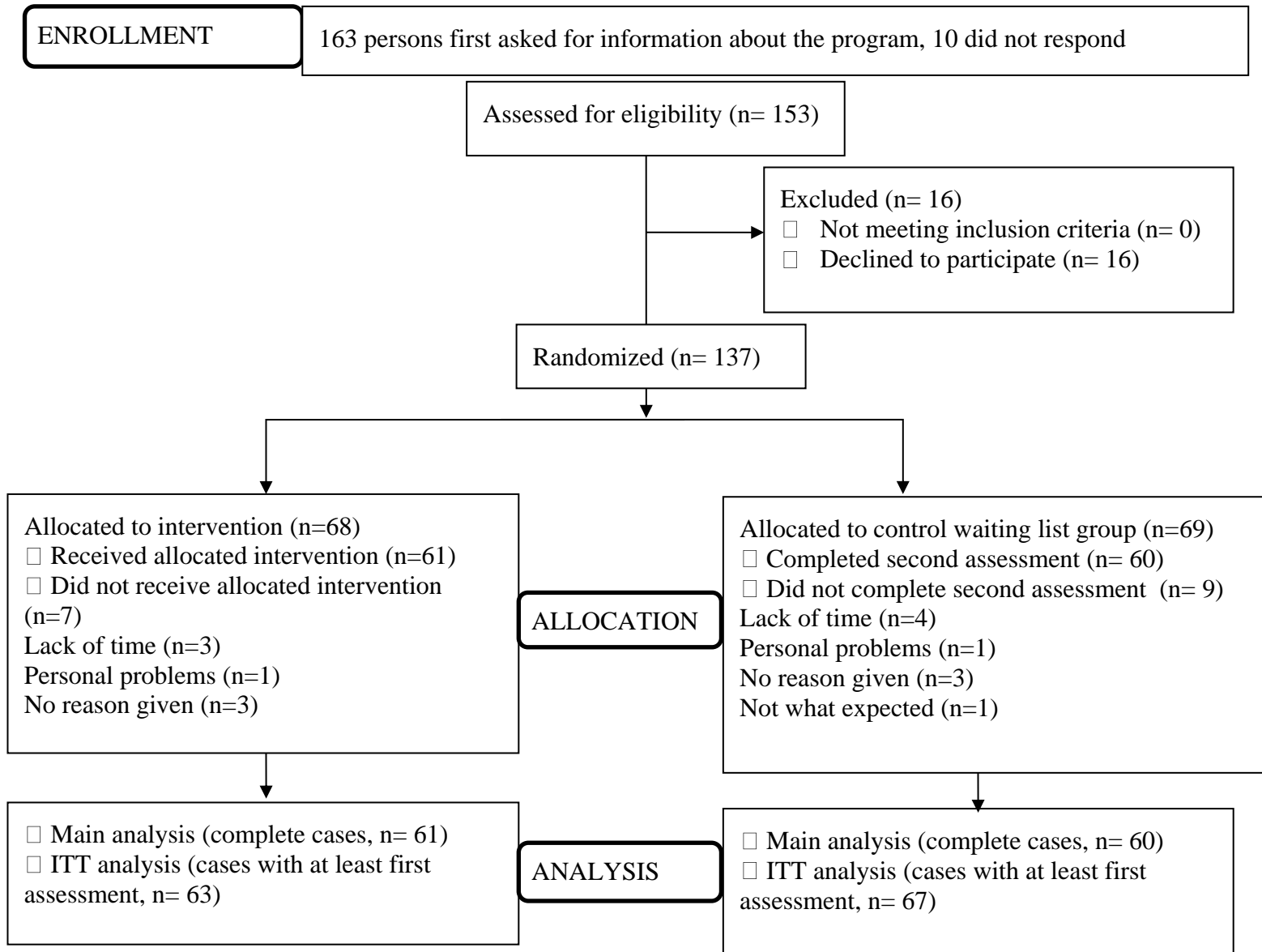
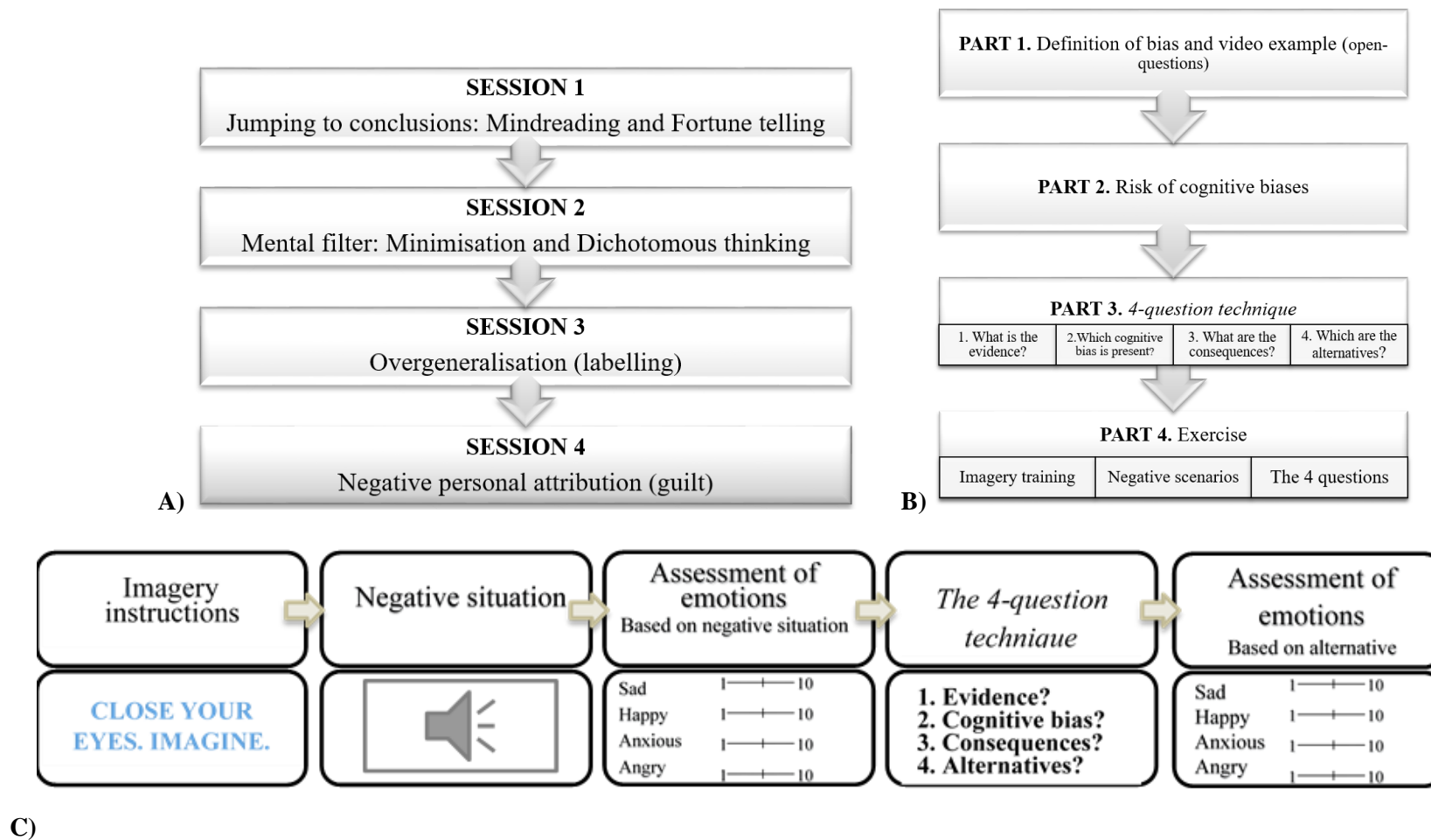


Figure 1. CONSORT 2010 Flow Diagram



*Figure 2.* Structure of the online intervention: A) classification of the specific cognitive biases targeted in the four online sessions based on cognitive models (Burns & Beck, 1999; Beck, 1976), the Cognitive Error Rating Scales (CERS; Drapeau, Perry, Dunkley, & Blake, 2010), and the CBM-errors (Lester et al., 2011) B) the four parts in which each session was divided: psychoeducation with definitions and examples of each type of cognitive bias with open-questions to increase participants' engagement, psychoeducation about the negative effects of these negative automatic interpretations, explanation of the 4-question technique, and exercise, practice exercise in which participants apply the 4-question technique to 5 negative scenarios in audio format. This technique involves four steps to re-evaluate the negative interpretation of a given situation: 1) finding evidence for negative thoughts, 2) detecting potential cognitive biases, 3) identifying negative consequences of holding those biases, and 4) creating alternative adaptive ways of thinking.

**Data analysis**

First, baseline group differences were analysed with ANOVAs for continuous variables and chi-square tests for nominal variables. Also, we conducted a series of 2 (Group: experimental vs. control) x 2 (Time: pre-intervention vs. post-intervention) repeated measures ANOVAs<sup>8</sup> to test significant pre-post intervention differences.

Following Preacher and Hayes's procedure (2004), simple mediation models were used to determine the degree to which a change in interpretation bias, given the intervention, explained the change in cognitive and symptom variables (see Outcome measures). Figure 3 illustrates the effects tested in the mediation models and further details can be found in the Supplementary Materials file.

Main analyses were complete-case analyses, i.e. including those participants who completed both pre- and post-intervention measures. Sensitivity analyses were computed from two different approaches: intention-to-treat analyses (using the iterative expectation-maximization method; Newman, 2014) and correcting for outliers (further details are provided in the Supplementary file). We only report the results of both sensitivity analyses when there is a significant deviation from the main analyses.

SPSS Statistics 20 was used to conduct ANOVAs,  $\chi^2$  tests, and ITT analyses. R 4.0.2 was used to finding and correct for outliers and to calculate split-half reliabilities. The PROCESS SPSS macro was used to test the mediation models (Hayes, 2018).

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<sup>8</sup> ANOVA assumptions were tested with Q-Q plots and boxplots for normality, Levene's test for homoscedasticity, and Box's M test for equality of covariance matrices. Although data met the two latter assumptions, normality plots revealed extreme values in some of the variables. Therefore, sensitivity analyses without outliers were conducted. Details can be found in the Supplementary File.

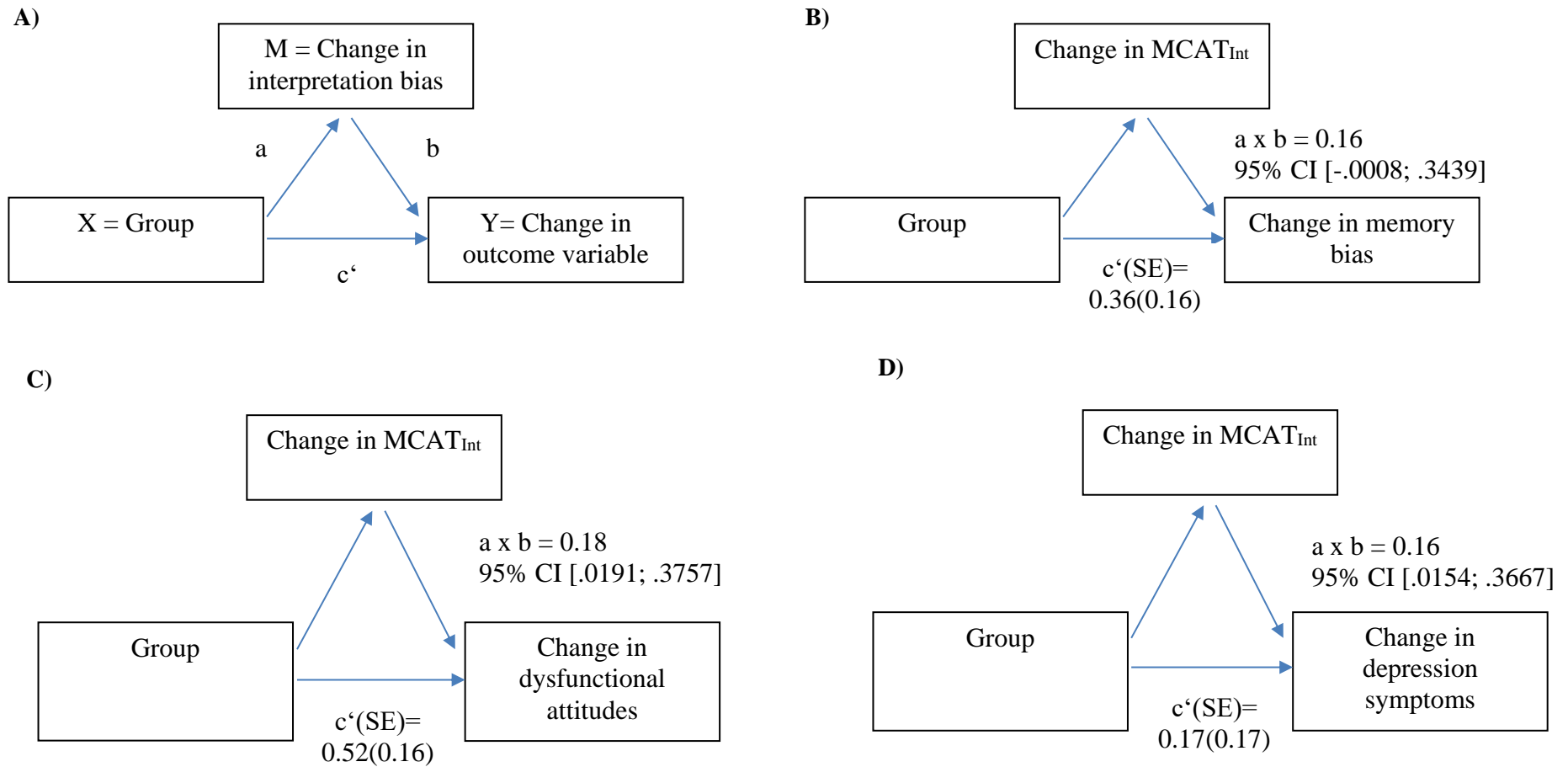


Figure 3. A) Generic mediation model design: 'c' represents the direct effect of X (Group) on Y (change in outcome variables) after controlling for M (change in interpretation bias), and  $a \times b$  represents the indirect effect of X (Group) on Y (change in outcome variables) through M (change in interpretation bias) B) Results of the mediation analysis with memory bias as the outcome variable C) Results of the mediation analysis with dysfunctional attitudes as the outcome variable D) Results of the mediation analysis with depression symptoms as the outcome variable.

### **Results**

Demographic and baseline differences between groups are shown in Table 1. 24.4% of the sample showed current symptoms of depression (PHQ-9  $\geq$  10; He et al., 2020), 32.2% showed current symptoms of anxiety (GAD-7  $\geq$ 10; Spitzer et al., 2006) and 31.1% reported past symptoms of depression and/or anxiety (past PHQ-9  $\geq$  10, past GAD-7  $\geq$ 10). More details about the distribution of participants based on present and past symptoms of depression and anxiety can be found in the Supplementary materials file. Regarding task and goal agreement with the program (WAI-I), participants in the experimental group showed an elevated level at post-intervention, comparable to previous studies for online interventions (Gómez Penedo et al., 2019).

Table 1. *Descriptive statistics, differences at baseline between groups and results at post-intervention*

	Baseline				Post-intervention					
	Experimental		Control		Experimental		Control			
	N	%	N	%	$\chi^2$	p-value	N	%	N	%
Gender (female)	55	45.5	48	39.7	2.47	.12	55	45.5	48	39.7
	M	SD	M	SD	t	p-value	M	SD	M	SD
Age	21.66	4.23	21.47	2.45	0.30	.77	21.66	4.23	21.47	2.45
PHQ-9	7.52	4.91	7.13	4.18	0.46	.65				
PHQ-9 past	11.14	8.04	9.82	7.99	0.90	.37				
GAD-7	7.35	4.35	7.77	5.14	-0.48	.63				
GAD-7 past	5.90	7.09	5.17	7.17	0.56	.58				
AST-D-II	12.66	20.60	12.72	17.26	-0.06	.99	27.27	17.84	17	18.71
MCAT <sub>Att</sub>	0.50	0.02	0.50	0.02	0.00	.87	0.49	0.03	0.50	0.03
MCAT <sub>Int</sub>	0.33	0.19	0.32	0.19	0.01	.69	0.26	0.17	0.29	0.19
MBT	0.38	0.25	0.31	0.23	0.08	.09	0.26	0.19	0.32	0.23
DASS21D	4.95	5.01	3.70	3.87	1.25	.13	4.07	4.10	4.48	4.45
DASS21S	7.40	4.35	7.78	5.22	-0.39	.66	7.09	3.97	8.28	4.90
DASS21A	4.41	3.69	4.56	3.92	-0.14	.85	3.76	4.04	4.40	4.21
DAS	125.93	34.84	120.12	28.90	5.81	.33	112.59	31.25	125.48	32.82
RRS	13.16	3.38	12.75	3.61	0.41	.53	12.53	3.30	12.70	3.56
PHI	71.62	15.75	74.65	12.75	-3.03	.27	76.52	12.53	74.85	12.15
CEQ	0.52	4.71	-0.56	4.92	1.19	.24				
WAI-I	-	-	-	-	-	-	3.74	0.53	-	-

NOTE: Higher scores in the AST-D-II reflect lower negative interpretation bias, while higher MCAT<sub>Int</sub> scores represent higher negative interpretation bias. N= number of participants, M= mean, SD= standard deviation. **Variables measured only at baseline:** PHQ-9 = Patient Health Questionnaire-9; GAD-7= Generalized Anxiety Disorder-7; CEQ = Credibility Expectancy Questionnaire. **Variables measured at baseline and post-intervention: Cognitive bias measures:** AST-D-II = Ambiguous Scenarios Test for Depression; MCAT<sub>Att</sub> = Mouse-based Contingent Attention Task-Attention bias index; MCAT<sub>Int</sub> = Mouse-based Contingent Attention Task - Interpretation bias index; MBT = Memory Bias Task. **Outcome measures:** DASS21D = Depression, Anxiety and Stress Scale-21-Depression subscale; DASS21S = Depression, Anxiety and Stress Scale-21-Stress subscale; DASS21A = Depression, Anxiety and Stress Scale-21-Anxiety subscale, DAS = Dysfunctional Attitudes Scale; RRS = Ruminative Responses Scale-brooding subscale; PHI = Pemberton Happiness Index. **Variables measured only at post-intervention:** WAI-I = Working Alliance Inventory for Internet interventions.

### Changes from pre- to post-intervention

#### a) Cognitive biases

A 2 (Group: experimental vs. control) x 2 (Time: pre- intervention vs. post-intervention) repeated measures ANOVA for interpretation biases showed that there was a significant main effect of Time, either when assessed with self-report (AST-D-II:  $F(1,117)= 47.65, p < .001, \eta^2=0.29$ ) or with the experimental task (MCAT<sub>Int</sub>:  $F(1, 117)= 14.15, p < .001, \eta^2 =0.11$ ). Post-hoc analyses showed that positive interpretation bias was significantly lower at baseline than at post- intervention (AST-D-II  $F(1,117)=47.65, p < .001$ ) and negative interpretation bias was significantly higher at baseline than at post- intervention (MCAT<sub>Int</sub>:  $F(1,117)= 14.15, p < .001$ ). There was no significant main effect of Group for any measure (AST-D-II:  $F(1,117)=2.66, p=.11, \eta^2 =0.02$ ); MCAT<sub>Int</sub>:  $F(1,117)=0.08, p=.78, \eta^2 =0.001$ ). However, there was a significant Time x Group interaction for self-reported interpretation bias (AST-D-II:  $F(1,117)=14.24, p < .001, \eta^2 =0.11$ ). Post-hoc Bonferroni analyses revealed that, although both groups were not significantly different at baseline ( $t(118)= -0.56, p=.99$ ), the experimental group showed significantly more positive interpretations than the control group at post-intervention ( $t(118)=10.271, p=.003$ ; see Table 1). This interaction did not reach significance when interpretation bias was measured with the experimental task (MCAT<sub>Int</sub>:  $F(1,117)=3.73, p=.056, \eta^2 =0.03$ )<sup>9</sup>.

A 2 (Group: experimental vs. control) x 2 (Time: pre-intervention vs. post-intervention) repeated measures ANOVA for attention bias (i.e. MCAT<sub>Att</sub>) showed no significant main effects of Time ( $F(1,117)=0.01, p=.92, \eta^2 =0.00$ ), Group ( $F(1,117)=1.70, p=.20, \eta^2 =0.01$ ), or interaction ( $F(1,117)=0.11, p=.74, \eta^2 =0.001$ ).

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<sup>9</sup> The interaction between Time and Group became significant in sensitivity analyses without outliers (MCAT<sub>Int</sub>:  $F(1,117)=4.65, p=.03, \eta^2 =0.04$ ) and in ITT analyses (MCAT<sub>Int</sub>:  $F(1,117)=5.71, p=.02, \eta^2 =0.04$ ).

For the memory bias task (MBT), there was no significant effect of Group ( $F(1,119)=0.02, p=.89, \eta^2=0.00$ ), but there was a significant effect of Time ( $F(1,119)=7.07, p=.009, \eta^2=0.06$ ). This was qualified by a significant Time x Group interaction ( $F(1,119) = 11.50, p = .001, \eta^2=0.09$ ). Post-hoc analyses with Bonferroni correction showed that the experimental group ( $t(120)=0.13, p<.001$ ), but not the control group ( $t(120)= -0.02, p=.61$ ), significantly reduced the negative memory bias between the two assessments (see Table 1).

b) Outcome variables

Regarding the DASS-21, a 2x2 repeated measures ANOVA for depression symptoms showed no significant main effects of Time ( $F(1,116)= 0.20, p=.89, \eta^2=0.00$ ) or Group ( $F(1,116)=0.33, p=.57, \eta^2=0.003$ ). However, there was a significant Time x Group interaction ( $F(1,116)=6.04, p = .02, \eta^2=0.05$ ). Post-hoc tests showed changes in the expected direction. In the experimental group, depressive symptoms decreased between assessments ( $t(117)=0.88, p=.07$ ), while the control group exhibited an increase on them ( $t(117)=-0.78, p=.10$ ), although none of these effects were significant. No significant main or interaction effects were found for stress (Time:  $F(1,116)=0.06, p=.81, \eta^2=0.00$ ; Group:  $F(1,116)=1.09, p=.30, \eta^2=0.01$ ; Time x Group:  $F(1,116)=1.05, p=.31, \eta^2=0.01$ ) or anxiety symptoms (Time:  $F(1,116)=1.66, p=.20, \eta^2=0.04$ ; Group:  $F(1,116)=0.35, p=.56, \eta^2=0.003$ ; Time x Group:  $F(1,116)=0.65, p=.42, \eta^2=0.01$ ).

The 2x2 repeated measures ANOVA for dysfunctional attitudes (DAS) showed no significant main effects (Time:  $F(1,116)=3.40, p=.07, \eta^2=0.03$ ; Group:  $F(1,116)=0.42, p=.52, \eta^2=0.004$ ), but there was a significant Time x Group interaction ( $F(1,116)=18.72, p<.001, \eta^2=0.14$ ). Bonferroni corrected post-hoc analyses revealed that the experimental group significantly reduced dysfunctional attitudes ( $t(117)=13.35, p<.001$ ), while the control group showed no change ( $t(117)=-5.37, p=.08$ ). No

significant main or interaction effects were found for rumination (Time:  $F(1,116)=2.17$ ,  $p=.14$ ,  $\eta^2=0.02$ ; Group:  $F(1,116)=0.04$ ,  $p=.84$ ,  $\eta^2=0.00$ ; Time x Group:  $F(1,116)=1.57$ ,  $p=.21$ ,  $\eta^2=0.01$ ), or well-being (Time:  $F(1,110)=2.11$ ,  $p=.15$ ,  $\eta^2=0.02$ ; Group:  $F(1,110)=0.14$ ,  $p=.71$ ,  $\eta^2=0$ ; Time x Group:  $F(1,110)=1.79$ ,  $p=.18$ ,  $\eta^2=0.02$ ) measures.

### Mediation effect of interpretation bias change given the intervention

Following the repeated measures ANOVA results, three simple mediation models were tested. Figure 3 illustrates these models and the results can be found in Table 2. Change scores refer to the residualized change scores obtained in the linear regression of pre-intervention on post-intervention (further details can be found in the Supplementary Materials file).

Table 2. Results of the mediation models

Model	X	M	Y	Total effect			Direct effect		Indirect effect	
				R <sup>2</sup>	c (SE)	t (p)	c'	t (p)	a x b	95% CI
1	Gr	MCAT <sub>Int</sub> change	MBT change	0.07	0.52 (0.18)	2.92 (.004)	0.36 (0.16)	2.23 (.03)	0.16	[-.0008, .3439]
		AST-D-II change		0.07	0.51 (0.18)	2.86 (.005)	0.48 (0.19)	2.52 (.01)	0.03	[-.1298, .2136]
2	Gr	MCAT <sub>Int</sub> change	DASSD change	0.03	0.34 (0.18)	1.84 (.07)	0.17 (0.17)	1.01 (.32)	0.16	[.0154, .3667]
		AST-D-II change		0.03	0.35 (0.18)	1.94 (.05)	0.24 (0.19)	1.24 (.22)	0.11	[-.0482, .3016]
3	Gr	MCAT <sub>Int</sub> change	DAS change	0.13	0.71 (0.17)	4.07 (<.001)	0.52 (0.16)	3.38 (.001)	0.18	[.0191, .3757]
		AST-D-II change		0.13	0.72 (0.17)	4.22 (<.001)	0.37 (0.16)	2.29 (.02)	0.35	[.1528, .6120]

X= independent variable, M= mediator variable, Y= dependent variable, Gr= Group; MCAT<sub>Int</sub> = Interpretation bias scores in the Mouse-based Contingent Attention Task; AST-D-II = Interpretation bias scores in the Ambiguous Scenarios Test for Depression; MBT = Memory Bias Task, DASSD= Depression, Anxiety and Stress Scale-21-Depression subscale; DAS= Dysfunctional Attitudes Scale.

#### Model 1. Mediation effect of the CBM-*I*<sub>Clin</sub> on the change in memory bias

Model 1 tested the effect of the CBM- $I_{Clin}$  on the change in memory bias, with the change in interpretation bias as a mediator variable. We computed separate models for each measure of interpretation bias (AST-D-II and  $MCAT_{Int}$ ).

Results showed that the intervention had significant total (AST-D-II coefficient=0.51,  $t=2.86$ ,  $p=.005$ ;  $MCAT_{Int}$  coefficient= 0.52,  $t=2.92$ ,  $p=.004$ ) and direct (AST-D-II coefficient =0.48,  $t=2.52$ ,  $p=.01$ ;  $MCAT_{Int}$  coefficient= 0.36,  $t=2.23$ ,  $p=.03$ ) effects on the change in memory bias (i.e., the intervention affected the change in negative memory bias even after controlling for change in negative interpretation bias). A non-significant indirect effect was found for this model, suggesting that the change in interpretation bias did not mediate the association between group and change in memory bias. The same pattern of results was found when interpretation bias was self-reported (AST-D-II indirect effect = 0.03 [-0.1298; 0.2136]) or measured with the  $MCAT_{Int}$ <sup>10</sup> (Figure 3).

*Model 2. Mediation effect of the CBM- $I_{Clin}$  on the change in depression symptoms*

Mediation model 2 tested the total, direct, and indirect (via a change in interpretation bias) effects of the intervention on the change in depression symptoms. Results showed that the program did not have significant total (AST-D-II coefficient=0.35,  $t=1.94$ ,  $p=.05$ ;  $MCAT_{Int}$  coefficient= 0.34,  $t=1.84$ ,  $p=.07$ ) or direct (AST-D-II coefficient=0.24,  $t=1.24$ ,  $p=.22$ ;  $MCAT_{Int}$  coefficient= 0.17,  $t=1.01$ ,  $p=.31$ ) effects on the change in depression symptoms (i.e., the intervention did not have an effect on the change in depression symptoms when controlling for the change in

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<sup>10</sup> This indirect effect for this model when interpretation bias was measured with the  $MCAT_{Int}$  became significant in intention-to-treat analyses ( $a \times b = 0.18$ , 95%CI [ 0.0198; 0.3543]) and when data were analysed without outliers ( $a \times b = 0.16$ , 95%CI [ 0.0185; 0.03120]).

negative interpretation bias). However, there was a significant indirect effect through the change in negative interpretation bias, suggesting that the association between group and change in depression symptoms was mediated by the change in negative interpretation bias. This effect was found when interpretation bias was measured with the experimental task (MCAT<sub>Int</sub>) (see Figure 3), but not when self-reported in the questionnaire (AST-D-II indirect effect = 0.11 [-0.0482; 0.3016]).

*Model 3: Mediation effect of the CBM-IClin on the change in dysfunctional attitudes*

The final model tested the effects of the intervention on the change in dysfunctional attitudes. Results showed that the intervention had a significant total (AST-D-II coefficient=0.72,  $t=4.22$ ,  $p<.001$ ; MCAT<sub>Int</sub> coefficient= 0.71,  $t=1.07$ ,  $p<.001$ ) effect on changes in dysfunctional attitudes. Also, the intervention had significant direct and indirect effects on the change in dysfunctional attitudes). Thus, the intervention both directly and indirectly affected dysfunctional attitudes (i.e. when controlling for changes in interpretation bias, but also via the change in interpretation bias). Importantly, these effects appeared both when interpretation bias was measured with the MCAT<sub>Int</sub> (see Figure 3) and when assessed through self-report (AST-D-II direct effect=0.37,  $t=2.29$ ,  $p=.02$ ; indirect effect = 0.35 [0.1528; 0.6120]).

### **Discussion**

The present study investigated the effects and operating mechanisms of a novel transdiagnostic online CBM program on young adults with varying levels of emotional distress. The program was based on standard clinical cognitive-behavioral procedures and aimed to reduce negative interpretation biases. We found that the experimental group showed significantly higher levels of positive interpretations after the intervention, compared to the control group. This effect, however, appeared when interpretation bias was assessed with a self-report questionnaire, but not when we used an experimental task (MCAT<sub>Int</sub>). Several explanations can be offered to account for this

discrepancy. For example, a previous review suggested that subclinical populations may not be an optimal sample to detect CBM changes when using these types of tasks, but it may also be the case that the content of the intervention is more closely related to some measures (e.g. AST-D-II), but not others (e.g. MCAT<sub>Int</sub>) (Hirsch et al., 2016). Also, some studies in the field differentiate between the increase of positive interpretations and the decrease of negative ones (e.g. Beard and Amir, 2008). Given that the AST-D-II measures the *pleasantness* of ambiguous scenarios, while the experimental task index focuses on the construction of negative sentences, it is possible that the discrepancy in results may reveal that the CBM-IC<sub>lin</sub> is well-suited to increase positive interpretations, but not to decrease negative ones. It is important that new clinical approaches consider separately both types of outcomes given that emotional disorders are characterized not only by high negative cognitions and distress, but also by a diminished tendency towards positivity (Dunn, 2012; Vazquez, 2017).

Discrepant results when using different instruments to measure cognitive biases are not a new phenomenon (Kappenman et al., 2015; Sfarlea et al., 2020), and could also reflect a difference in the underlying constructs that they are measuring. It has been shown that even low departures from perfect convergent validity between proxies can lead to different research results and conclusions (Carlson & Herdman, 2012). A recent study of the convergence between different measures of interpretation bias, more specifically, interpretation bias questionnaire (Wisco & Nolen-Hoeksema, 2010), scrambled sentences test (Richard M. Wenzlaff & Bates, 1998), homograph interpretation task (Grey & Mathews, 2000), and word-sentence association paradigm (Hindash & Amir, 2012), concluded that these measures may be tapping on different subcomponents of interpretation, which might explain the inconsistent findings in CBM-I research (O'Connor et al., 2021). Furthermore, some authors have proposed

that the use of an experimental task with time constraints and a cognitive load to measure interpretation bias, such as the one used in this study, may help to capture automatic instead of elaborative processes (Everaert, Podina, et al., 2017). If this is so, it suggests that the change in interpretation bias may have been produced at a conscious rather than implicit level. In spite of these alternative explanations, we must remind that sensitivity analyses showed a significant interaction between Time and Group also when interpretation bias was measured with the MCAT<sub>Int</sub>. Therefore, it is still possible that the intervention had a real effect in reducing negative interpretation bias but, given the presence of extreme values, the results did not reach significance.

The second aim of this study was to explore the change in other key cognitive and symptom variables upon undergoing the intervention. While there was no significant change in negative attention bias, anxiety, stress symptoms, brooding, or well-being, the CBM-IClin significantly changed negative memory biases, depression symptoms, and dysfunctional attitudes. Mediation models showed that the change in negative interpretation bias did not mediate the effect of the intervention on negative memory biases. This could be surprising given the evidence that attention, interpretation, and memory biases interact with each other (Everaert & Koster, 2020; Mogg & Bradley, 2018). The combined cognitive bias hypothesis (CCBH) (Hirsch et al., 2006) states that cognitive biases influence each other, and this interactive effect is stronger than if the biases were working in isolation. However, it is possible that the program directly improved negative memory biases given that it was designed to increase awareness of one's own cognitive processes (i.e. participants in the experimental group might have selectively remembered the positive stimuli among all that were presented). Experimental literature has shown that memory bias does not only depend on the codification of a memory from a prior negative interpretation, but also

depends on the degree to which individuals imagine themselves as actors in those scenarios ( Hertel & Brozovich, 2010). It is possible that the CBM-IClin helped participants not only to create more positive interpretations, but also to imagine themselves less in the negative ones. Finally, research on the interaction between interpretation and memory processes suggest that CBM-I could create a new ‘frame of mind’ that promotes the retrieval of information that is congruent with that frame (Salemink & Hertel, 2010), which could explain the direct effect of the CBM-IClin on memory. The asymmetrical effect of CBM procedures on different types of emotional processing (attention, interpretation, memory) has previously been found in a sample of young adults (Bowler et al., 2017). Clarifying these potential pathways between different cognitive biases could be important to increase the efficacy of interventions. For instance, future research could study whether extant CBM interventions aimed at modifying memory biases (e.g., Barry et al., 2019) might facilitate subsequent changes in attention or interpretation biases.

The change in depression symptoms because of the intervention cannot be interpreted unequivocally. ANOVA results showed no significant changes in depression symptoms in any group. Yet, mediation models showed that, while the intervention did not have a significant total or direct effect on change in depression symptoms, there was a significant indirect effect of the intervention through a change in negative interpretation bias. We only found this effect when interpretation bias was assessed using the experimental task (MCAT<sub>Int</sub>), and not when assessed through self-report (AST-D-II). Interestingly, although the most recent meta-analysis on the field of CBM concludes that these programs moderately improve depression and anxiety symptoms, there is high variability between studies (Fodor et al., 2020). For example, a previous study about CBM-I in social anxiety found that changes in positive interpretations, but

not in threat interpretations, mediated the effect of group on social anxiety symptoms (Beard & Amir, 2008). Although sources of variability are still unknown, it could be possible that part of it stems from the type of instruments used to measure symptoms and cognitive biases. For example, two meta-analyses on attention bias training in anxiety reached different conclusions regarding the efficacy of the intervention in the reduction of symptoms when examining the effect with different measures (Linetzky et al., 2015; Price, Wallace, Kuckertz, Amir, Graur, & Cummings, 2016). As Fried (2017) recently pointed out, the standard instruments used to assess problems like depression poorly reflect the wide variety of symptoms that characterize the disorders, which limits the validity of research results. Similarly, regarding cognitive biases, a recent meta-analysis has also found that there is a high variety of self-report instruments and unfortunately, many of them have limited evidence to support their psychometric robustness (Nieto et al., 2020).

Dysfunctional attitudes significantly changed after the CBM-IClin, which was explained by both a direct effect of the intervention and an indirect effect through a change in interpretation bias. We found these effects both when interpretation biases were self-reported and when measured with an experimental task. The direct effect of the program is consistent with the fact that its content was based on the negative cognitive biases proposed in the classical cognitive models of emotional disorders (Beck and Clark, 1997), which directly link negative processing of information with dysfunctional attitudes. Moreover, dysfunctional attitudes were measured by the DAS (Weissman & Beck, 1978), i.e. an instrument that assesses maladaptive cognitions such as concerns with evaluation or negative causal attributions that are present both in depression and anxiety (Dyck, 1992). Although dysfunctional attitudes are theoretically conceived as rather permanent cognitive schemas, empirical evidence has shown that

they are susceptible to change (Haefffel et al., 2005). For instance, research has found that patients who respond to cognitive therapy do not show increased levels of dysfunctional attitudes (cognitive reactivity) after a sad mood induction procedure (Jarrett et al., 2012), which might reflect the acquisition of therapeutic techniques aimed at evaluating, challenging, and modifying dysfunctional thoughts, similar to the ones used in the ‘Relearning how to think’ program. The clinical implications are relevant, given the potential role of negative cognitive schemas as vulnerability factors (Beck and Clark, 1997). However, this role needs further investigation given that meta-analytic conclusions on the role of dysfunctional cognitions in maintaining or exacerbating depressive symptoms are mixed (Cristea et al., 2015; Wojnarowski et al., 2019).

Finally, the lack of change in symptoms of anxiety and stress after the intervention could have several explanations. A previous meta-analysis investigating CBM for attention and interpretation bias found that the change in anxiety and depression symptoms after training only appeared when participants were assessed in response to a stressful task (Hallion & Ruscio, 2011). Congruent with the diathesis-stress model, this finding suggests that CBM efficacy is better evaluated when cognitive biases are more likely to appear in the face of a stressor. Moreover, although cognitive-behavioral therapy moderately reduces anxiety symptoms (van Dis et al., 2020), it is possible that the specific focus of the CBM<sub>Clin</sub>, designed to enhance elaborative information processing, benefits the improvement of depression symptoms, but it cannot tackle some automatic mechanisms (e.g., biases in orienting responses) which are more related to anxiety disorders (B. Teachman et al., 2012). The same argument could explain the lack of changes found in negative attention biases. While research has consistently found that depression is characterized by interpretation biases, anxiety is more associated with attention biases than other types of biases ( Mathews & MacLeod,

2005). Yet, the literature about attention bias training to improve anxiety symptoms has led to mixed conclusions (Linetzky et al., 2015; Price et al., 2016), which has questioned some conceptual foundations of this training (McNally, 2019; Mogg & Bradley, 2018). The lack of changes in attention biases can also be explained from previous studies supporting the idea that attention bias impacts psychological functioning through its relationship with other elaborative processes (e.g., Marchetti et al., 2018; Sanchez et al., 2015). Therefore, possible effects on attention biases may underlay the changes in interpretation and memory processing.

Secondary hypotheses were not met. The CBM-IClin did not affect rumination or well-being, although these results must be considered with caution as the internal consistency of the rumination and well-being scales (i.e., RRS, PHI) were low to moderate (Nunnally, 1978) in our sample. Regarding rumination, repetitive negative thinking has been related to cognitive biases in general (Villalobos et al., 2021) and negative interpretation bias in particular (Hirsch et al., 2016). Moreover, previous studies have found that the change in interpretation bias after CBM mediates the change in worry and rumination processes (Hayes et al., 2010; Hertel et al., 2014). However, the evidence on the possibility of changing rumination through CBM has yielded mixed results. Whereas some studies have shown positive results (Sanchez-Lopez, Everaert, et al., 2019), others have failed to do it so (Hirsch et al., 2020). Future studies would benefit from identifying the active components of different interventions that make them effective for specific symptoms or modes of processing (like ruminative thinking) which will facilitate the administration of more personalized interventions (Lopez-Gomez et al., 2019).

Regarding well-being, it was expected that the creation of more positive interpretations would lead to higher levels of well-being. Previous studies have shown

that negative interpretations are connected to lower levels of well-being (Blanco et al., n.d.) and that CBM-I can increase positive mood (Holmes et al., 2006). However, there were no significant results in this direction. Nevertheless, the assessment of well-being by means of the PHI was perhaps not an optimal choice. In the context of a CBM intervention, a focus on positive emotions, which are more sensitive to circumstances than overall assessments of well-being, might have been the best assessment option. Yet, future CBM studies are encouraged to include measures of emotion regulation and well-being in their research given the evidence of the interconnection between these variables (Gross et al., 2019).

It is possible that the results of CBM interventions would be better with longer treatments blended with evidence-based treatments. Several studies suggest that the modification of negative interpretation processes could have an augmentation effect in CBT results (Beard et al., 2019; Teachman et al., 2010). If these results are confirmed, CBM programs could be an additional tool to respond to the serious consequences associated with emotional disorders in terms of disability, chronicity, and relapse (Lorimer et al., 2020; Wojnarowski et al., 2019; World Health Organization, 2017).

### **Strengths and Limitations**

We must address some limitations of the current study. First, the recruitment procedure implied the inclusion of participants who were interested in a program to ‘learn how to control the influence of thoughts on emotional reactions’ (see *Participants and recruitment*). This selection of participants could have biased the results given that it is a sample potentially more willing to change. Also, our study did not specifically select individuals with significant cognitive biases or with high levels of symptoms. Interpretation bias trainings could be more beneficial for those adolescents and young adults who show greater levels of negative cognitions before undergoing the intervention (de Voogd et al., 2018; Micco et al., 2014). Some CBM studies have shown

that higher levels of negative processing increase the clinical response to these trainings (Amir et al., 2011). However, the meta-analytic literature shows no clear evidence regarding the moderating role of symptom severity (clinical, subclinical, and healthy samples) in the benefits of CBM interventions (Jones and Sharpe, 2017). While the use of non-clinical samples is still a common practice in CBM studies (e.g. Meţel et al., 2019; Beard and Amir, 2008), future research must determine the characteristics of participants that could benefit the most from these interventions.

Second, the ability to disengage from negative materials, which is a key component of attention in emotional disorders (Sanchez et al., 2013), was not assessed in this study. Future research should include tasks that allow exploration of the differences between these diverse attention bias indices (e.g., orienting towards, maintaining attention or delayed disengagement, and orienting away) (Mogg & Bradley, 2018). These types of measures are relevant as there is already evidence that psychological interventions can significantly improve engagement and disengagement attentional processes in depressed individuals (Vazquez et al., 2018).

Third, some design and methodological limitations should be noted. The recruitment procedure did not involve the exclusion of some potential confounding variables, such as drug use or attentional disorders. Given the dependence of the assessment and intervention on memory and reading abilities, more stringent inclusion and exclusion criteria should be used in future CBM studies to better discern the effect of these intervention procedures. Also, it has been argued that the analysis of moderation effects using residualized change scores models can lead to biased estimates of the true mediated effect given that the pre-test and post-test mediator and dependent variable scores are reduced to a single score (M and Y, respectively) (Valente & MacKinnon, 2017). Given these different approaches,

future studies are encouraged to take them into consideration (see Valente and MacKinnon, 2017).

Fourth, an enriching approximation for future cognitive bias research would be to incorporate other cognitive processes such as the lack of positive biases (Gruber et al., 2020; Colette R. Hirsch & Mathews, 2000; Matt, Vazquez, et al., 1992), emotion regulation strategies, or cognitive control processes (LeMoult & Gotlib, 2019; Mogg & Bradley, 2018) with long-term follow-ups to reveal changes in underlying processes (Everaert & Koster, 2020). If CBM procedures aim to be clinically used, it is important to determine whether post-treatment effects are transient improvements of cognitive patterns or whether they may lead to long-term changes in information processing and emotional symptoms.

Finally, given that the CBM-IClin was administered individually at home, it is difficult to know the level of participant engagement when completing the sessions. Adherence to treatment in unguided web-based interventions for depression is lower than guided web-based interventions given that feelings of accountability may be reduced when there is no contact with a therapist or supervisor (Mohr et al., 2011; Richards & Richardson, 2012). Future online CBM interventions should include monitoring mechanisms to guarantee the level of engagement of participants while completing the sessions. This seems necessary as this could be an obstacle to the scalability of this type of internet-based intervention (McNally, 2019).

The present study has several strengths. First, the program ‘Relearning how to think’ was designed to improve the traditional approaches to change cognitive biases, in line with previous recommendations (Koster & Bernstein, 2015; Pe et al., 2015). For example, our training program includes mental imagery, which is beneficial for

cognitive change given the close relationship between imagery and emotions (Emily Holmes & Mathews, 2005; Jones & Sharpe, 2017). Also, the CBM<sub>Clin</sub> was created based on materials (e.g., clinical vignettes) already used and validated in previous interventions (Barlow, Farchione, Bullis, et al., 2017). The program included materials with specific contents related to depression or anxiety, rather than negative topics in general, which is relevant to activate cognitive biases (Armstrong & Olatunji, 2012). Yet, given our results, it could be possible that the focus of the program on elaborative processing makes it more suitable for disorders like depression, which are better characterized by deficits in elaborative mechanisms (Duque et al., 2015). Second, the use of both self-report and experimental tasks to measure cognitive biases has been encouraged to know whether direct and indirect measures reflect the same cognitive processes and whether negative cognitive biases operate both at explicit or implicit levels in emotional disorders (Everaert, Podina, et al., 2017; Hirsch et al., 2016). Also, the use of measures that differentiate from the intervention content is important to discern real changes in interpretation from participants' learning on how to answer to a specific format. This is important, given previous evidence that changes in interpretation on a training task did not generalize to a different task (Salemink et al., 2007). Finally, the online format of the procedure benefits from high accessibility and the cost-effectiveness that comes with internet-based interventions (Kazdin & Blase, 2011).

In sum, this study provides a promising program to change negative interpretation biases. To our knowledge, this is the first CBM procedure that is not designed to change automatic information processing through repetition, but aimed at increasing participants' construction of alternative adaptive interpretations of ambiguous scenarios. Our approach may accommodate more naturally to the clinical nature of evidence-based

cognitive-behavioral therapies for emotional disorders. This study also sheds light on the mechanisms of action that seem to be relevant in the proposed intervention to modify interpretation biases, which we believe are not only valuable for clinical purposes but also for the advancement of theory and research.

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## Supplementary materials

### Disentangling the mediating role of modifying interpretation bias on emotional distress using a novel cognitive bias modification program

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#### Procedure

To complete the four online sessions of the intervention program, participants received access to an online platform, specifically designed for this study. They were instructed to create an account and a password for themselves upon their first access, which was linked to their participant number. This information was accessible only to the main researchers. To promote assimilation of the materials and to avoid boredom and overload, participants could access the next training session only 24 hours after having completed the previous one. The only additional restriction was that the participants had to complete the four sessions within a 10-day period between the pre- and post-assessments. All participants in the experimental group (N=61) were required to complete the four online sessions prior to the second assessment (post-intervention). Participants in the control group (N=60) did not receive the link to the online program until after they had completed the second assessment session, being allowed to complete the program at any time after that point.

#### Data Analyses

Following Preacher and Hayes's procedure (2004), simple mediation models were used to determine the degree to which a change in interpretation bias, given the intervention, explained the change in cognitive and symptom variables (see *Outcome measures*). Figure 3 illustrates the effects tested in the mediation models: 'c' represents

the direct effect of X (Group) on Y (change in outcome variables) after controlling for M (change in interpretation bias), and  $a \times b$  represents the indirect effect of X on Y through M. After testing the significance of the total (effect of group on the outcome variable) and direct effects, 5000 samples bias-corrected bootstrapping procedure was used to determine the significance of the indirect effect (Preacher & Hayes, 2008). This significance is reached when the estimated 95% bootstrap confidence intervals do not contain 0. The mediator and dependent variables of these models were the residualized change scores computed as the result of the linear regression of pre-intervention on post-intervention (Collins, & Horn, 1991). This procedure has been previously used as a reliable method to control for the variability of baseline scores (Sanchez et al., 2016; Segal et al., 2006).

Main analyses were complete-case analyses, i.e. including those participants who attended both pre- and post-assessment evaluation sessions. However, sensitivity analyses were computed from two different perspectives: intention-to-treat analyses and correcting for outliers. First, intention-to-treat (ITT) analyses were computed including all participants, regardless of whether they had completed Time 1 and Time 2 assessments, using imputation techniques. Data were found to be missing completely at random according to Little's MCAR test ( $\chi^2 = 316.85$ ,  $df = 321$ ,  $p = .56$ ), implying that the probability of losing these values was not related to the values in the data set (Rubin, 1976). Then, following Newman's (2014) recommendations, missing data were estimated using the iterative expectation-maximization (EM) method. Second, data were also analyzed after correcting for outliers. The interquartile range (IQR) rule was used to detect and remove extreme values from the variables. This rule consists of multiplying the IQR by 1.5 and then adding this value to the third quartile while subtracting it from the first quartile (Tukey, 1977). It is considered that values outside

these cutoffs are outliers. Outliers were detected only in AST-D-II (1.65% of observations), DASS-21 Depression subscale (1.65% of observations), and DASS-21 Anxiety subscale (1.65% of observations).

## Results

Using standard diagnostic cut-off scores of PHQ-9  $\geq 10$  (He et al., 2020) and GAD-7  $\geq 10$  (Spitzer et al., 2006) the distribution of participants based both on present and past symptoms of depression and anxiety was as follows:

N (%)	Never anxious	Past- anxious	Currently anxious	Currently and past- anxious	TOTAL
Never depressed	37	4	5	1	47 (39.5%)
Past-depressed	18	15	4	6	43 (35.8%)
Currently depressed	2	0	3	2	7 (5.8%)
Currently and past- depressed	0	4	7	11	22 (18.5%)
<b>TOTAL</b>	<b>57 (47.5%)</b>	<b>23 (19.2%)</b>	<b>19 (16%)</b>	<b>20 (16.8%)</b>	<b>119 (100%)</b>

The distribution of these subcategories in the control and experimental groups can be found in the following table with the means and standard deviations of symptoms:

Groups	N %			Current		Past	
		Exp. Gr.	Ctrl. Gr.	PHQ-9	GAD-7	PHQ-9	GAD-7
Never symptomatic <sup>a</sup>	31.1%	17	20	4.43 (2.19)	4.08 (2.31)	3.08 (3.65)	0.24 (1.48)
Past symptomatic <sup>a</sup>	31.1%	19	18	5.35 (2.53)	5.29 (2.57)	14.41 (5.69)	7.84 (7.29)
Currently symptomatic <sup>b</sup>	37.8%	23	22	11.36 (4.44)	12.20 (3.78)	13.31 (8.20)	7.98 (7.49)

<sup>a</sup> Depression and/or anxiety symptoms

<sup>b</sup> Includes participants with or without a history of depression and/or anxiety

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## GENERAL DISCUSSION AND FINAL CONCLUSIONS

The present doctoral dissertation had three main purposes. First, it aimed to increase our knowledge on the interpretation processes that take place in emotional disorders. In the first study, it was found that those samples with high levels of depression symptoms show higher levels of self-reported catastrophizing and Beck's categories of interpretation bias than non-symptomatic samples. This result complements previous meta-analytic findings supporting the presence of a general negative interpretation bias in people with depression as measured mostly by experimental tasks (Everaert, Podina, et al., 2017). This addition to the literature of cognition in emotional disorders is highly relevant from a clinical perspective. First, in

clinical practice, patients are mostly evaluated with questionnaires. Second, Beck's cognitive model is one of the main building blocks of cognitive-behavioral therapy, which is the standard gold to treat emotional disorders. This meta-analysis supports the importance to make cognitive distortions a target in treatment.

It is important to note that levels of heterogeneity were high for both the large (catastrophizing) and medium (general interpretation bias) effect sizes. However, moderation analyses helped explain at least part of this variability. A common moderator of both effects was the instrument to measure depression symptoms. While both catastrophizing and general interpretation bias appeared to be significant when symptoms were measured by DSM criteria, neither of the effects were significant when using the CES-D. This moderation effect is coherent with the low overlap in the symptoms measured by the most common scales to measure depression (Fried, 2017). The present meta-analysis gives some clues about the specific aspects (items) of depression that may be more related to negative cognitive bias. This could be directly applied in the clinical practice to detect those patients who could benefit more from targeting the negative modes of processing information. Some other significant moderators were geographic location and percentage of women for catastrophizing results, and type of sample, and the instrument to measure bias for interpretation bias results. The moderation effects of geographic location, percentage of women, and instrument to measure bias should be taken with caution given that both disappeared in sensitivity analyses excluding outliers. Regarding the type of sample, the difference in general interpretation bias between depressed and healthy samples was only found when comparing clinical, but not subclinical, and non-symptomatic groups. This finding suggests that negative interpretation bias may only be present in clinical populations. However, it is not consistent with previous results showing that this type of processing

is present in clinical, subclinical, and remitted samples (Everaert, Podina, et al., 2017).

Thus, further replication is needed.

The second main aim of this dissertation was the design and evaluation of a novel interpretation bias modification program. Although there is some mixed evidence regarding the therapeutic value of CBM trainings, many authors support its potential and provide insight on how to improve them (Hertel & Mathews, 2011; Kuckertz & Amir, 2017). The ‘Relearning how to think’ program presented in this dissertation adds some of these components, such as the use of imagery to increase participants' involvement, and elaborative techniques coming from cognitive behavioral therapy. The results of the program were promising in the near-transfer effects given that there was a significant change in negative interpretation bias as measured by self-report. However, the interaction between time and condition was not significant when using an experimental task. This lack of consistency is not surprising given the low convergence between different measures of interpretation bias, specifically, between direct and indirect measures (O'Connor et al., 2021). While the AST-D-II may capture a more conscious and elaborate aspect of interpretations, the MCAT may capture a more implicit, pre-conscious part of the process given time constraints and the cognitive load of the task. The same pattern of results has been found in recent studies (Sfärlea et al., 2021) and previous meta-analytic findings (Everaert, Podina, et al., 2017). It is also possible that the AST-D-II, which measures the perceived ‘pleasantness’ of the scenario, captures the change in positive interpretation bias, while the MCAT reflects a change in negative interpretation bias. There is evidence that both processes may not belong to the same continuum, but represent different constructs (Steinman et al., 2020). Taken all these considerations together, the ‘Relearning how to think’ program could be specifically beneficial to make participants aware of their cognitive processes and then

potentiate a more positive way to elaborate information. Future studies should also consider, not only the nature of the measurement method, but the relevance of the computation method to calculate cognitive indices. Zvielli et al.'s (2016) found that quantifying attentional bias as an aggregated mean did not reveal differences between remitted depressed patients and a healthy control group, but using computational methods to calculate attentional bias *dynamics* from trial to trial did. Moreover, the authors found this procedure was more reliable than the traditional aggregated mean bias scores. This type of refinements in the study of cognition can help in the study of CBM efficacy. The 'Relearning how to think' program did not show efficacy to directly improve symptoms of depression, stress, or anxiety. This lack of efficacy point also to the necessity to identify if some individuals are more prone to benefit from these interventions and the working mechanisms through which these procedures work.

The third and final aim of this dissertation was, in fact, to uncover the underlying mechanisms of CBM. The mediation analyses in Study 4 showed that the intervention had direct and indirect effects on different variables. The program had an indirect effect on the change in depression symptoms via the change in interpretation bias. This result goes in line with meta-analytic evidence showing that CBM transfer-effects appear when there have been prior changes in the targeted bias (Grafton et al., 2017). Also, similar results have been found with recent ABM programs, where the change in attention bias mediated the change in depression symptoms (Beevers et al., 2021). There was also an indirect effect of the change in interpretation bias in the change in dysfunctional attitudes. This finding has relevant clinical implications, given that negative cognitive schemas are theorized to be risk factors that may precipitate the development of symptoms (see Figure 1) (Beck & Clark, 1997). However, this theorized process requires further investigation given mixed findings (Wojnarowski et

al., 2019). Also, the clinical implications are limited to the fact that the CBM-I program developed in this thesis was not effective to change anxiety and stress symptoms. The mediation analyses also revealed that the intervention did change memory bias, but not via the change in interpretation bias. Although memory change has not traditionally been the focus of CBM, there is evidence that it is subject to change (Nadel et al., 2012). Regarding this result, it is necessary to note the controversy of how to capture memory bias (LeMoult & Gotlib, 2019). It is possible that the measures of interpretation and memory bias used in the study reflect the encoding stage of information rather than later retrieval stages. If so, findings of the change in interpretation bias may overlap with the findings of the change in memory bias (Köhler et al., 2015). However, it is also possible that the intervention did manage to elicit a change in retrieval processes by promoting a new 'frame of mind' (Salemink, Hertel, et al., 2010). Also, the program encouraged participants to create alternative, less negative, interpretations of situations and imagined themselves immersed in the process of changing interpretations. Thus, the change in memory bias is consistent with the finding that memories do not only emerge from prior interpretations but also depend on the degree to which individuals imagine themselves as actors in those scenarios (Hertel & Brozovich, 2010). Given the impact that both positive and negative memories can have on emotion regulation (Gillihan et al., 2007; Nieto, Koster, et al., 2020) and the emotion regulation difficulties in emotional disorders (Joorman, 2019; Young et al., 2012) programs improving memory processes are also a promising tool. In fact, (autobiographical) memory has been discussed as a tool to improve adaptive behavior and prevent different psychopathological problems (Vanaken et al., 2021)

Finally, the program did not change levels of rumination or well-being.

Regarding the change in rumination, a CBM training more oriented to change executive

functioning could be beneficial for this purpose. There is evidence that CBM programs aimed to specifically improve cognitive control produce improvements in rumination levels in depressed and formerly depressed participants (Hoorelbeke & Koster, 2017; Siegle et al., 2007). Some authors even suggest that ABM trainings may directly serve as trainings to change emotion regulation ability (Van Bockstaele, Notebaert, MacLeod, et al., 2019). Although the 'Relearning how to think' program aimed to increase awareness of interpretation biases to be able to consciously change them with more adaptive alternatives, we do not know if cognitive control was altered. Also, CBM-I programs may be better suited to change specific emotion regulation strategies, such as reappraisal (Sanchez et al., 2016). Rumination has also been widely associated with reduced forgetting of negative material and it has been suggested that programs aimed to reduce overgeneralized memory bias could reduce levels of rumination (Joormann & Tran, 2009; LeMoult & Gotlib, 2019). Although the CBM-I<sub>Clin</sub> had a direct effect on memory bias, recall dynamics is composed of multiple phases, some of which could be more related and better able to affect rumination than others (van Vugt et al., 2012). In general, findings regarding the effect of CBM trainings in emotion regulation strategies are not consistent (Van Bockstaele, Notebaert, Salemink, et al., 2019), which makes it important for future studies in the area to include these type of measures to get more knowledge about the interaction between cognitive biases, emotion regulation and cognitive control. Regarding the change in well-being, there is not much CBM research studying its impact on this construct. Nevertheless, it seems important to include this measure given the evidence that cognitive biases may be predictors of well-being (Smith et al., 2018). A recent study found an association between well-being and a maintenance attentional bias towards positive information (Blanco & Vazquez, 2021). However, it is possible that, as suggested in the field of emotion regulation, well-being

is more related to the flexibility to select, based on the context, certain cognitive processes (e.g. specific emotion regulation strategies, or interpretation alternatives) than to the change towards positivity (Bonanno & Burton, 2013). Although the CBM-IClin emphasized the idea that there are not good or bad interpretations with sentences like *“Not always when a thought makes us feel bad it is necessarily distorted. The key is knowing how to differentiate them.”* or *“There are always different ways to see reality. Look for the one which is the least damaging but also credible for you.”*, future replications could include measures of cognitive flexibility to evaluate whether there is a change in this construct together with an increase in well-being. Cognition is no longer understood as a stable structure but as a group of changing functions that can be altered. This new perspective requires new research approaches focused on flexibility. For example, emotion regulation strategies are no longer divided in functional (good) and dysfunctional (bad) categories, but research suggest that psychopathology could be more related to lack of emotion regulation flexibility (e.g., Palacio-Gonzalez & O’Toole, 2022). Research in cognitive biases is also changing towards the dynamics of these processes by using new instruments that capture how people adjust their beliefs in the face of new information (e.g., Bias Against Disconfirmatory Evidence task, Everaert et al., 2018), measurement protocols requiring participants to complete cognitive bias tasks using ecological assessments (e.g., Blanco et al., 2021), and computation methods that deviate from aggregated scores and better capture the temporality of these processes (e.g. van Vugt et al., 2012; Zvielli et al., 2016).

### **Limitations and strengths**

Some limitations need to be acknowledged in the present dissertation. In Study 1, the use of Beck’s model as a conceptual framework limited the scope of the review leaving some cognitive biases related to depression outside (e.g. jumping to conclusions

(Wittorf et al., 2012). However, this decision was taken based on the influence of the model and as a way to decrease the variety of results. Second, the lack of empirical studies fulfilling the inclusion criteria limited the analyses to be performed. For example, depression groups could only be compared to healthy controls but not to other types of comparison groups (e.g., with some other pathologies). The specificity of these biases is a major proposition in cognitive models of depression (Beck & Perkins, 2001) and it would have been highly valuable to be able to establish these differences with other groups such as participants with anxiety. Also, individual categories of bias could not be analyzed separately except for the catastrophizing bias.

There were also limitations in the design and evaluation of the new CBM-I program (Studies 2-4). Regarding the design of the intervention, some authors have proposed that the online format of these types of interventions may decrease its potential for cognitive change due to a lower commitment and emotional involvement of participants (Carlbring et al., 2012; de Voogd et al., 2017). However, many internet-delivered interventions have been successful in changing cognitive biases (e.g. Hirsch et al., 2021). Moreover, this format is one of the attractiveness of the program, which together with its short duration and partially self-paced design makes it a good candidate to complement longer treatments. Also, the intervention was composed of 4 sessions to be completed over 10 days, with no limits on the timing of sessions except being 24 hours apart. One consequence of this design is that the mean duration of treatment, as well as the time between the last session and post-assessment, could vary between participants, adding some error variance to the results. As already mentioned, Study 3 was not a fully crossed design to evaluate change between symptom groups, and the waiting-list control group was given access before the follow-up evaluations. Thus, only change from pre- to post-intervention between the experimental and control

groups could be fully interpreted. Regarding the sample of these studies, it was an unselected sample composed of undergraduates with 85% female. These characteristics may make it difficult to generalize results to other types of populations. For example, some meta-analyses suggest that CBM programs could be more beneficial for people with high levels of cognitive bias or clinical symptoms (Hallion & Ruscio, 2011; Menne-Lothmann et al., 2014). However, some other reviews find no difference based on this distinction (Cristea et al., 2015; Jones & Sharpe, 2017). Finally, the instrument selected to measure self-reported interpretation bias (AST-D-II) was specifically designed to measure interpretation biases related to depressed mood, which may leave behind some specific aspects of interpretation biases in anxiety.

Despite these limitations, the present dissertation also has many strengths. First, it managed to distinguish between the constructs of cognitive bias and maladaptive cognitive schemas, and negative automatic thoughts. This is one of the reasons why the number of studies meta-analyzed in Study 1 was limited. However, while all of these components are proposed in Beck's model depression (see Figure 1), they may play different roles in the development of the disorder. Thus, it is worth making a clear distinction to fully understand the nature of depression (Ingram & Kendall, 1986). Second, the inclusion of an open-ended feedback question after the CBM-IClin gives some clues about how to improve this type of intervention. Previous studies on participants' experience with CBM report barriers such as lack of credibility or difficulty to concentrating (Beard et al., 2011; de Voogd et al., 2017). Some of the most common concerns (see Appendix A1) were the lack of identification with the scenarios, the need to personalized the content, and the repetitiveness of the training. This finding goes in line with previous studies showing that lack of personal identification with the scenarios of the training may decrease its efficacy (Standage et al., 2013). It may be

advisable for future studies to include only participants prone to benefit from these programs (e.g. those showing high levels of negative interpretation bias), and also try to make them more personalized to increase engagement. Some efforts have already been made with this purpose. For example, a new CBM paradigm for alcohol disorders integrates the consideration of personally relevant information within the training, while also taking a higher focus on elaborative (vs. associative/automatic) approach (Wiers et al., 2020). Some positive aspects of the training are the inclusion of imagery training and the active role that participants play in the generation of alternative interpretations. Prior studies have shown that both the ability to imagine the alternative scenarios and the involvement in its generation are factors that promote the change in cognitive biases (Holmes et al., 2006; Hoppitt et al., 2010). Another observation made by participants in the feedback question was the need to support online sessions with face-to-face meetings to deepen the content of the program. This feedback goes in line with recent findings on participants' engagement with CBM-I, which showed that human support and personalization were key to increasing involvement (Beard et al., 2021). Taken together, CBM trainings such as the 'Relearning how to think' program could be highly effective when used together with long-term therapies in more severe cases, or as boost-sessions to reduce relapses when treatment has finished.

For a final thought, it seems important for future research to adopt a wider view of psychological processes. As mentioned in the Introduction, there is evidence that cognitive biases do not work in isolation. They interact with each other, as proposed by the CCBH, but also together with other cognitive processes such as cognitive control and emotion regulation. All these connections seem to parallel a network similar to the ones shown in the brain. For a long time, it has been studied how neural connections underlie cognitive functions such as information processing, thoughts, or emotions

(Singer, 1999). However, it has been proposed that brain regions should not be studied in isolation given that it is its neural context, i.e. the pattern of neural interactions in those regions, which could help explain cognitive functions (McIntosh, 2000). Something similar has been recently proposed concerning psychological elements, a ‘psychonectome’, which would represent the pattern of interconnections between psychological constructs such as visuospatial memory, selective attention, or emotion regulation skills. The key point in these perspectives is that the focus of understanding is no longer an element (such as a specific brain region or a specific cognitive function), but the relationships between them. (Roca et al., 2019).

## **Conclusion**

The present dissertation sheds light on the robustness of some cognitive biases in depression and the best ways to explore them with meta-analytic evidence. Also, it provides a promising alternative strategy to treat interpretation bias in emotional disorders, **although the effects in symptoms were inconclusive and replication of results and further investigation of the program is needed.** Finally, it reveals some of the mechanisms of action that may be playing a role in the change of cognitive biases given an intervention. Altogether, these findings may not only be valuable for clinical purposes but also the advancement of theory and research in the field of cognition and emotional disorders.

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## APPENDIX 1: Open-ended feedback about the program

Table A1. *Feedback provided by university students about the CBM-IClin (n=53)*

Main theme	Comments on the open-ended feedback question about the program
Useful and liked the program	<ol style="list-style-type: none"> <li>1. I think it is very important for people to feel more understood and normalized regarding cognitive biases, I think it is a program that can be useful for many people.</li> <li>2. It is very good that all the sessions follow the same scheme because it becomes familiar and you don't feel so lost as you move forward.</li> <li>3. I have found it very interesting, both for me and to be able to help the people around me if things like that happen to them.</li> <li>4. It should be accessible to everyone because it really is very useful to learn to control thoughts better.</li> <li>5. I really liked the voice they used for the online program, made me feel relaxed and answered calmly. Bringing it into the realm of everyday life made it easier to understand.</li> <li>6. Overall, it's pretty good.</li> <li>7. I found it very entertaining.</li> <li>8. Very complete and very well done.</li> <li>9. It was very interesting to me. It has revealed another way of evaluating things and has given me tools that will be very useful in my day to day life and that will, undoubtedly, help me feel better when I face different situations that I initially can see as negative.</li> <li>10. Thank you very much for your help and work. It has helped me a lot to face the different situations that I face daily, improving my well-being. I really thank you and I wish you a happy future.</li> </ol>
Need to be personalized	<ol style="list-style-type: none"> <li>1. It was difficult for me to identify with some situations.</li> <li>2. Sometimes it was difficult for me to imagine the situations since, in almost none of them, I would have reacted as in the audio.</li> <li>3. More emphasize on how to handle flattery and guilt.</li> </ol>
Did not fill in the needs, not useful	<ol style="list-style-type: none"> <li>1. I think it is not very useful for people who know psychology. It is entertaining but basic for psychologists.</li> <li>2. I wish they gave more tools in addition to the DECA questions.</li> <li>3. I think it is a useful program for someone who does not study Psychology or who has never undergone any type of cognitive restructuring therapy since it explains very clearly why certain situations make us feel in a certain way. In the opposite cases, it becomes a bit repetitive and theoretical.</li> </ol>
Short, need more content	<ol style="list-style-type: none"> <li>1. I loved it but I would have included even more theory to learn more. It has been very interesting.</li> <li>2. I think I would add some more sessions, but otherwise great.</li> <li>3. More sessions to practice it better.</li> <li>4. More examples, more feedback on the answers themselves (we do not know if we answered the alternatives without any bias).</li> <li>5. I think it would be nice to offer more examples about the content of each session.</li> <li>6. Access the sessions or the information once it is completed.</li> <li>7. Summary of the videos once completed.</li> </ol>
Repetitive, long	<ol style="list-style-type: none"> <li>1. At the end, it gets a bit monotonous</li> <li>2. Sometimes the sessions were a bit repetitive, especially when explaining the acronym DECA.</li> <li>3. It may be good to include more variety of exercises in the online sessions</li> <li>4. Change the dynamics of each session.</li> <li>5. The sessions were very complete and dynamic. The theory was very well explained. I have found it to be a very good method. Although perhaps, at times, the exercises were too long.</li> </ol>

6. Maybe it should be more extensive. I think focusing on DECA and repeating it is very beneficial although sometimes boring because and repetitive. I would have liked to be able to extend it more in the time because, in my personal case, I had to complete sessions one day after another due to lack of time. I appreciate the review of the content of the previous session, although it should not be limited to only the previous one, but all others too.
  7. I think that repeating the three questions during all the sessions was tiresome, but it may also be necessary to strengthen the key concepts.
  8. I found it very interesting, but it was not necessary to explain from scratch how the acronym DECA worked every session, it made me lose interest.
  9. The 4 sessions are very similar, which made them tedious ... but in the end, the best way to learn is with repetition. It helped me feel better and adapt it to my daily life. I have noticed some change, being more aware of my thinking biases.
  
  10. It is a great job, but very repetitive, very long, especially too many evaluations. I would have liked questions for decatastrophizing "if that were true, what would be the worst that could happen?"; some emotional psychoeducation; more types of cognitive distortions ... Perhaps it should be applied to students in the first year, it is very limited and poor for master students. Something good is that there was music, examples, videos, so that it was not so boring
  11. Not repeating the DECA reminder so much.
  12. It was a very interesting program that everyone should know about, since it is a way of changing the way to see life. However, the final exercises were long, sometimes at the end of the exercise, I forgot what the situation was.
  13. I found the content of the program quite interesting, the only complaint is that the exercises were a bit repetitive at the end.
  14. Test or sessions a little shorter :)
  15. Shorter or more divided sessions.
  16. It's a bit repetitive.
  17. Doing always the same task becomes repetitive.
  18. A little repetitive
- Time complaints
1. More time to complete the program since sometimes it is difficult to combine everything in daily life. Finding a quiet space to concentrate to make the most of the program was more complicated than I thought.
  2. Allow more than 1 session in 24 hours.
  3. It is a very interesting program, it explains many things that I did not know. Time dedication was a little heavy. Less time divided into more days would be more bearable. But it is quite useful.
  4. Difficult for me to complete the sessions exactly each 24 hours because I could not complete them until night and the fatigue was greater. The sessions were quite monotonous but interesting. The video of the strategies was the same every time, which became repetitive. The similarity of activities increased fatigue and the mechanization of responses.
  5. I think the exercises were too long, and the 24-hour restriction was too strict. Maybe set the limit to one per day, but without taking into account the time
  6. Leave more time between the first face-to-face session and the second to do the online sessions
- Technical difficulties
1. The beep of the stories is quite unpleasant even if the sound is low. Improve the way to get in since I have had several problems.
  2. Sometimes it does not work quite well, since it needs a lot of RAM (computer), but in general, I liked the presentation, the tone of voice, the form ...
- Explanations difficult to follow
1. The data question of the strategy was ambiguous to me: I was not sure if I had to write the data that drove me to interpret that way (considering the audio) or the data that was in the situation. Then, sometimes I felt that I repeated myself when writing alternatives and the data.
  2. When they ask in different situations how you feel, they should clarify if 0 means a lot or a little and the same with 10 because I assumed that 0 was 'I do not feel that way at all' and 10 'I totally feel that way', but I don't know if it was ok.
  3. When explaining the consequences phase, you change the word to 'effect', the acronym may be better remembered if you keep saying consequences.