Where is the bias?

*Measuring and retraining cognitive biases in problem drinkers*

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CHAPTER 6

General discussion
Aims and main findings

The main aim of this thesis was to evaluate the effectiveness of web-based attentional bias, memory bias and approach bias modification as an add-on to a brief motivational intervention in reducing alcohol use in problem drinkers (Chapters 2 and 5). The validity of the pictorial stimuli that were used during the assessment and retraining of the cognitive biases was investigated in an independent study (Chapter 3). Furthermore, it was tested whether alcohol use in problem drinkers was associated with the interplay between cognitive biases, executive functions and motivation to change, as hypothesized by dual process models (Chapter 4).

The validity of the pictorial stimuli

Biases in the cognitive processing of alcohol related cues are thought to play a role in the maintenance of problem drinking and alcohol use disorders (AUDs, Bechara, 2005; Deutsch & Strack, 2006; Franken, 2003; Wiers et al., 2007). Although these cues are not restricted to one of the senses – it can be the sound of a beer tap, the smell of wine, the taste of the first sip of whiskey – visual stimuli are commonly used to study cognitive biases. Both alcohol related words and pictures have been used for the assessment of cognitive biases, but pictures are usually preferred in cognitive bias modification (CBM, with the exception of interpretation bias modification, see for example Salemink, Woud, Roos, Wiers, & Lindgren, 2019; Woud, Hutschemaekers, Rinck, & Becker, 2015). Despite the importance of these pictorial stimuli in measuring and retraining cognitive biases, little research has been done on the quality of the used alcohol and non-alcohol related pictures.

Chapter 3 describes a study on the validity of a large set of pictures of alcoholic and non-alcoholic beverages that was designed for the use in cognitive
bias assessment and modification. In line with the definition of test validity (Borsboom et al., 2004), stimulus validity was defined as a causal effect of variation in the alcohol relatedness of the stimuli (i.e. whether the picture showed an alcoholic or a non-alcoholic beverage) on variation in an alcohol related attribute (i.e. the cue induced urge to drink in heavy drinkers). Students completed a recognition task and a rating task for a subset of pictures of alcoholic and non-alcoholic drinks. The results showed that the pictures of alcoholic beverages, but not those of non-alcohol beverages, elicited a stronger urge to drink in relatively heavier than in lighter drinkers. Overall, the beverages were quickly recognized as alcoholic or not, but pictures in which a person was serving, opening or drinking a beverage were recognized more slowly than pictures of non-contextualized beverages. Participants’ urge to drink was not affected by whether or not the beverage was shown in a social context. These results support the potential suitability of this picture set in the assessment and retraining of cognitive biases and suggest that pictures of beverages only should be favored over pictures of beverages in a social context. It should be noted, however, that the social content in the latter category of pictures was kept simple in order to limit distraction from the drink and optimize recognition speed. As a tradeoff, these pictures do not mirror real-life social drinking scenes and may not be optimal to test if adding a social context to alcoholic drinks elicits higher levels of craving. Furthermore, this study only investigated stimulus validity based on the explicit urge to drink, and not on automatic attention, memory associations, or approach responses.

The interplay between cognitive biases, executive functions and motivation
According to dual process theories of addiction (Wiers et al., 2007), the extent to which cognitive biases influence alcohol use is determined by a combination
of executive functions and motivation. Prior studies generally confirmed the moderating role of executive functions (Grenard et al., 2008; Houben & Wiers, 2009; Peeters et al., 2012; Peeters et al., 2013; Pieters et al., 2012; Salemink & Wiers, 2014; Thush et al., 2008; van Hemel-Ruiter et al., 2011). However, these studies were mostly conducted in at risk adolescents and heavy drinking students, and it was not investigated whether this pattern also held for problem drinkers. Furthermore, few studies examined how the interplay between cognitive biases and executive functions is affected by motivation to restrain or change one’s alcohol use (Ostafin et al., 2008; Sharbanee et al., 2013; Tahaney et al., 2014), while dual process models posit that the effect of executive functions is dependent on motivation.

As described in Chapter 4, the baseline data of the web-based study on CBM were used to test the hypothesized three-way interaction between cognitive biases (i.e. valence and approach associations), executive functions (working memory and response inhibition), and motivation to change in problem drinkers. It was expected that the interaction between cognitive biases and executive functions would be stronger in individuals with relatively stronger motivation than in individuals with weaker motivation. The results were largely inconsistent with this prediction: the expected three-way interaction was only found between valence associations, working memory, and motivation to change. As expected, working memory capacity moderated the relationship between valence associations and drinking in individuals with strong motivation, but not in those with relatively weak motivation. However, this pattern was not found for approach associations or response inhibition. Possible explanations for these unexpected results are the low reliability of the measure of response inhibition, and the fact that both motivation to change
and alcohol use were relatively high in this sample. Alternatively, it could mean that the factors that play a role in the early stages of (heavy) alcohol use differ from those that determine alcohol use in individuals who demonstrate problematic alcohol use.

**The effectiveness of web-based CBM in problem drinkers**

Retraining cognitive biases in individuals with AUDs was found to add to the effects of in-patient treatment in preventing or delaying relapse (Eberl et al., 2013; Manning et al., 2016; Rinck et al., 2018; Schoenmakers et al., 2010; Wiers et al., 2011). Based on the promising findings of prior research, the current study set out to investigate whether web-based CBM could reduce alcohol use in problem drinkers outside the addiction clinic. Further goals were to compare the relative effectiveness of different CBM procedures, and to examine whether combining these procedures could augment the effects.

Chapters 2 and 5 describe the design and results of an RCT on web-based attentional bias (intervention/placebo), memory bias (intervention/placebo), and approach bias (intervention/placebo) retraining in a 2x2x2 factorial design. Problem drinkers \((N = 427)\) were randomly assigned to one of eight CBM conditions. Participants first completed a personalized feedback intervention (*DrinkingLess*, Riper et al., 2008; Riper et al., 2009), aimed at increasing motivation to change, after which they received 12 sessions of CBM over six weeks. Cognitive biases were assessed at pre- and post-test and alcohol use was additionally measured three and six months later. The results showed that none of the (combinations of) CBM interventions led to a larger reduction in alcohol use compared to the placebo conditions. Furthermore, CBM did not appear to affect cognitive biases, but this finding should be interpreted with caution given the insufficient reliability of some of
the bias measures. These finding suggest that web-based CBM does not add to the effects of a brief motivational intervention in helping problem drinkers to decrease their alcohol use. This conclusion is consistent with other studies on CBM outside the addiction clinic, which have been conducted in parallel with this study. CBM does not appear to be effective in reducing problem drinking, neither as a stand-alone intervention (Clerkin et al., 2016; Wiers et al., 2015), nor combined with a brief motivational intervention (Cox et al., 2015; Jones, A. et al., in press, and our RCT described in Chapter 5).

**Implications for future research**

*What stimuli are suitable for the assessment and modification of cognitive biases?*

Studying the role of cognitive biases in problem drinking requires alcohol related stimuli that can trigger these biases, and that are easy to distinguish from non-alcohol related stimuli. In our study on the validity of the newly created set of pictures of alcoholic and non-alcoholic drinks, the results confirmed that the pictures met the latter requirement: participants quickly and accurately identified the drinks as alcoholic or not (see Chapter 3). Relatively heavy drinkers experienced a stronger urge to drink in response to pictures of alcoholic drinks than light drinkers, but this study not assess if the alcohol relatedness of the pictures produced variation in the strength of cognitive biases. However, in the RCT on CBM (see Chapter 5), problematic drinkers did not demonstrate baseline biases in the processing of alcohol related pictures: none of the pictorial cognitive bias measures revealed group-level biases towards (or away from) alcoholic drinks. While we did not explicitly test if the stimuli improved the reliability of the measures of cognitive biases and the effectiveness of the CBM procedures, it is safe to conclude that the
stimuli were not sufficient to achieve these goals. These findings raise the question of what stimulus characteristics make stimuli suitable for studying cognitive biases in problem drinking.

One of the stimulus characteristics that may affect the measurement and retraining of cognitive biases is their complexity (Ataya et al., 2012). Pictures that are more complex are likely to introduce more noise in the RT data, and therefore reduce the reliability of assessment tasks. In an attempt to minimize the complexity of our pictures and optimize the speedy recognition of the alcohol relatedness of the pictures, we inadvertently compromised on the similarities to real-life drinking scenes, including social content (see Groefsema, Engels, & Luijten, 2016 for a discussion of how social content may impact reactivity to alcohol related cues). It is possible that this reduced the validity of the pictures, in the sense that they may have been less capable of triggering cognitive biases, and thereby reduced the effectiveness of the CBM procedures. Since minimizing measurement error in RTs appears more important in the assessment than in the modification of cognitive biases, it may be advisable for future research to use stimuli that match real-life drinking scenes for CBM procedures, and use less complex stimuli for assessment purposes.

Another stimulus feature that may impact the measurement and modification cognitive biases is the degree of familiarity of the drinks (Groefsema et al., 2016). Given our aim to closely match the pictures of alcoholic and non-alcoholic drinks in terms of color and other irrelevant

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1 We did not ask participants in the CBM study to evaluate the stimuli, other than to indicate their craving in response to pictures of three alcoholic and three non-alcoholic drinks. Across time points, participants indicated a relatively stronger urge to drink in response to the non-alcoholic compared to alcoholic drinks (see Chapter 5, Tables 4-6).
features, we decided against personalizing the stimuli. Instead, we aimed to optimize the relevance of the stimuli and generalization of the training effects by including a wide range of beverage types and brands. Furthermore, stimulus personalization was deemed less relevant in problem drinkers compared to social drinkers. However, at least in social drinkers, personalized stimuli have been shown to enhance the reliability of assessing attentional bias (Christiansen, Mansfield, Duckworth, Field, & Jones, 2015) and it could also be that CBM is more effective when using personalized stimuli. Indirect support for the latter suggestion comes from a study which used personalized words in attentional bias modification and found a reduction in alcohol use in heavy drinking students (McGeary, Meadows, Amir, & Gibb, 2014).

To summarize, while the use of personalized stimuli reflecting real-life drinking scenes may reduce the reliability of cognitive bias measures, it may enhance their validity and the effectiveness of CBM. It is important to note that the reliability of bias measures is also influenced by other task characteristics, such as the use of difference scores (Hedge et al., 2018), the number of trials (Ataya et al., 2012), the order of the stimulus categories (e.g. the blocked or unblocked presentation of the words in the alcohol Stroop task), and the use of eye-tracking during the assessment of attentional bias (Christiansen et al., 2015).

Why do we need more reliable measures of cognitive biases?

Theoretically, an important advantage of CBM is that it has clear working mechanisms, which can inform us about the cognitive factors that play a role in the maintenance of problem drinking and AUDs. For example, attentional bias modification should reduce attentional bias for alcohol related cues, which is in
turn expected to reduce alcohol use. However, the insufficient reliability of many measures of cognitive bias means that it is often unclear if CBM has resulted in bias change. This hinders progress in the field of CBM in several ways.

First, the interpretation of the effect of CBM on addictive behavior is hampered if we cannot reliably assess whether a change in cognitive bias has taken place. When CBM reduces symptoms, it is informative to a) evaluate whether this effect can be attributed to a change in the targeted bias; b) investigate to what extent the effects generalize to untrained measures of the same bias; and c) explore potential mediators of the effects of bias change on behavior (e.g. whether a reduction in attentional bias affects behavior via a change in valence associations, as suggested by Field and colleagues (2016)). When CBM does not affect behavior, it is relevant to establish whether the CBM procedure did not successfully change the cognitive bias, or whether the process of CBM did not result in behavioral change (Grafton et al., 2017; MacLeod & Clarke, 2015; Wiers et al., 2018). In the former case, CBM research should prioritize the development of better CBM procedures, which consistently change cognitive biases. In the latter case, the theorized causal role of cognitive biases in the maintenance of addiction should be reevaluated, and cognitive biases might not be a relevant target for intervention. All of these questions can only be adequately answered if we have reliable measures of cognitive biases.

Second, the most direct way to test for what subgroups CBM is most likely to be effective is provided by moderated mediation analyses (e.g. Eberl et al., 2013; Rinck et al., 2018) and as such, dependent on reliable bias measures. For example, to examine whether abstinence is required for CBM to be
effective, one could examine whether individuals who strive toward abstinence show a greater decrease in cognitive biases in response to CBM than individuals who aim to reduce their alcohol use, and whether this difference in turn produces variations in craving. Determining for whom CBM is effective (through moderation analysis) is especially relevant since this could explain the inconsistent results of CBM, a topic to which we will return later.

Third, reliable bias measures are necessary to be able to falsify theories on the role of cognitive biases. Using measures with inadequate reliability invariably results in alternative explanations for unexpected results. For example, in our RCT on CBM (see Chapter 5), we found that CBM did not decrease problem drinking beyond non-specific effects. Since we also found few indications that CBM resulted in reductions in the targeted biases, our results did not disprove the theory that reducing cognitive biases would lead to reductions in alcohol use. However, given the lack of reliability of most of our bias measures, we can also not be sure that the CBM procedures did not change the cognitive biases. Of course, the necessity of reliable measures is not restricted to cognitive biases. In our examination of the baseline data of the CBM study (see Chapter 4), we found the expected interaction between cognitive biases, executive functions and motivation for only one of the four examined three-way interactions. Since one of our measures of executive functions had poor reliability, it is unclear whether these results call for an adaptation of dual process theories in problem drinkers, or whether they can be attributed at least in part to inadequate measures.

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2 It is noteworthy that the only measures on which we found trends for reductions in cognitive biases as a result of CBM were among the bias measures with relatively higher reliability (i.e. the Approach Avoidance Task, and the valence version of the brief Implicit Association Task).
In summary, reliable measures of cognitive biases are needed to interpret the effects of CBM on addictive behavior, to examine how and for whom CBM works, and to allow for the falsification of the theories on cognitive biases in addiction. In addition to developing and employing reliable measures of cognitive biases, future research would do well in reporting the reliability of the measures in the analytical sample, so that this can be taken into account when interpreting the results. It should be noted that validity could also be a concern for some cognitive bias measures. For example, relatively lower RTs for addition related words in the alcohol Stroop task could result from either positive or negative evaluations of alcohol (Field, M. et al., 2016).

Under what conditions is CBM effective?

The lack of specific CBM effects on problem drinking (Clerkin et al., 2016; Cox et al., 2015; Jones, A. et al., in press; Wiers et al., 2015, and our RCT described in Chapter 5) contrasts with the effects of CBM on relapse in in-patients with AUDs (Eberl et al., 2013; Manning et al., 2016; Rinck et al., 2018; Schoenmakers et al., 2010; Wiers et al., 2011). This discrepancy, which was confirmed in a recent meta-analysis (Boffo et al., in press), raises the question under what conditions CBM is most likely to be effective. Methodological differences between the studies that did and did not find CBM to be effective may shed light on the factors that moderate the effect of CBM on addictive behavior.

One possibility is that CBM is only effective in individuals with more severe levels of addiction, since the studies that found positive effects were all conducted in in-patients with AUDs, as opposed to problem drinkers. However, this explanation seems implausible, because the participants in the studies that were conducted outside the addiction clinic were heavy drinkers, who were motivated to change their alcohol use. Even the studies in which participants
were formally diagnosed with (Clerkin et al., 2016), or showed high risk of an AUD (see Chapter 5) did not find CBM to be effective in reducing alcohol use. It is therefore unlikely that the ineffectiveness of CBM in problem drinkers can be explained by a lack of room for (or motivation for) improvement.

A related possibility is that CBM is only effective in individuals with AUDs because they have stronger cognitive biases than problem drinkers. Based on dual process theories of addiction, CBM is expected to be most effective in individuals with strong cognitive biases (Wiers et al., 2007). However, the difference between CBM’s effectiveness in problem drinkers and in-patients is unlikely to have been caused by between-group variation in the strength of cognitive biases. For example, previous studies did not find a consistent relation between the strength of attentional bias and addiction severity (Field, M. et al., 2016). Similarly, in our study in problem drinkers (see Chapter 4), alcohol use prior to the CBM intervention was not related to alcohol approach associations, and only weakly related to positive valence associations. Furthermore, while one study found that the effect of approach bias modification was moderated by the strength of approach bias at baseline (Eberl et al., 2013), this finding was not replicated in a recent study (Rinck et al., 2018). We did not yet analyze potential moderators and mediators of the effectiveness of CBM in the RCT described in Chapter 5, but we found no evidence that the non-specific decrease in alcohol use was related to the degree of change in the cognitive biases (see Appendix 3, Table 2). Taken together, these findings make it unlikely that interpersonal differences in the strength of cognitive biases can account for the inconsistent results of CBM studies. This does not mean, however, that intrapersonal variation in the strength of cognitive biases could not moderate the effectiveness of CBM. For example, an ecological momentary
assessment study in heroin dependent in-patients found that attentional bias increased shortly before relapse (Marhe, Waters, van de Wetering, & Franken, 2013). It would be interesting to examine whether inviting participants to complete a CBM session when they show a momentary increase in attentional bias could prevent relapse.

A factor that appears more likely to influence CBM’s effectiveness is whether it is implemented to prevent relapse in individuals who are currently abstinent, or to reduce alcohol use in problem drinkers. Given the proposed bi-directional relationship between cognitive biases and alcohol use (Wiers et al., 2007), it is possible that continued alcohol use during CBM counters the effects of CBM on cognitive biases. In line with this explanation, none of the studies in which to goal was to reduce alcohol use found that the CBM procedures decreased cognitive biases (Clerkin et al., 2016; Jones, A. et al., 2016, and our RCT described in Chapter 5), while most studies in abstinent samples showed at least some indications of bias change (Eberl et al., 2013; Rinck et al., 2018; Schoenmakers et al., 2010; Wiers et al., 2011; but note that Manning et al., 2016 did not find evidence of a change in approach bias). Moreover, the effects of CBM on addictive behavior generally coincided with whether or not the targeted cognitive bias had successfully been manipulated (except for the study by Manning et al., 2016, in which approach bias modification did not lead to a change in bias, while it did decrease the relapse rate). To examine the necessity of abstinence, future research could investigate the effects of CBM in problem

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3 Note that other studies in which participants aimed to reduce their alcohol use either did not analyze change in the targeted biases due to suboptimal bias measures (Wiers et al., 2015), or only did so implicitly, by assessing bias change during the CBM intervention, but without a post-test to examine if CBM produced a change in cognitive bias relative to the control condition (Cox et al., 2015).
drinkers who aim to quit drinking (see Elfeddali et al., 2016 for an example of CBM in smokers who make a quit-attempt). If abstinence would prove to be a prerequisite for CBM to be effective, this would of course limit its application potential, since the large majority of problem drinkers seeking web-based help aims for restrained use and not abstinence. For example, 78% of the participants in our web-based RCT aimed to reduce rather than abstain, and in the study of Riper and colleagues (2008) this was 93%.

The lack of effectiveness of CBM outside the addiction clinic might also be related to the sometimes less controlled research setting of these studies, which varies from completely web-based (Wiers et al., 2015, and our RCT, see Chapter 5), via online training and laboratory based assessment (Jones, A. et al., in press), to both laboratory based training and assessment (Clerkin et al., 2016; Cox et al., 2015). Ensuring participants’ undivided attention to the task at hand seems most important for measuring (reductions in) cognitive biases, since this requires detecting small differences in reaction times (RTs) for alcohol related compared to neutral stimuli, based on a limited number of trials. However, none of the studies in problem drinkers in which at least the assessment was completed in the laboratory demonstrated lasting CBM effects on cognitive biases or alcohol use. For training purposes, momentary distractions should be compensated by having to repeat incorrect trials, and by the large number of completed trials over multiple sessions. It therefore appears implausible that the web-based training setting of some studies could account for the null results of CBM in problem drinkers.

A more conceivable way in which the research setting could impact CBM’s effectiveness is through craving. It is likely that participants experience higher levels of craving when completing CBM at home, in the presence of
environmental stimuli that have become associated with alcohol use, than in an addiction clinic or laboratory (Houben & Wiers, 2008), where such cues are absent. There is little empirical knowledge about how craving impacts CBM’s effectiveness. In line with the positive effects of CBM in clinical settings, one study found indications that CBM was more effective when the urge to drink was low (Wiers et al., 2010). Theoretically, however, CBM seems most relevant when craving is high. This would also be consistent with the finding that in anxiety, fear activation appears to enhance CBM’s effectiveness (Kuckertz et al., 2014). In order to examine the potential moderating role of craving, future research could ask participants to rate their urge to drink before completing a CBM session, in order to examine whether craving affects the magnitude of the change in cognitive bias. Depending on the direction of the effect, experimental research could examine whether CBM is more effective in reducing cognitive biases and alcohol use when participants time their CBM session based on their current urge to drink.

A last possibility is that changing cognitive biases only affects behavior when other determinants of AUDs are concurrently addressed, as suggested by the finding that CBM only appears to be effective when it is implemented as an add-on to in-patient treatment (Boffo et al., in press). This raises the question of what elements of the extensive in-patient treatment programs could have contributed to CBM’s effectiveness. Enhancing motivation to change appears insufficient for CBM to be effective (Cox et al., 2015; Jones, A. et al., in press, and our RCT described in Chapter 5). It is currently examined whether CBM is effective when added to a more extensive outpatient treatment, including

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4 Note that in addiction, craving is expected to be higher at home than in a laboratory or addiction clinic, while in social anxiety, fear levels are likely to be lower at home compared to the laboratory.
components aimed at behavioral change (see Bratti-van der Werf et al., 2018 for a study protocol).

In conclusion, the factors that appear most fruitful to examine as potential moderators of CBM effectiveness are abstinence; momentary interpersonal changes in craving and cognitive biases; and the combination with a more extensive treatment. Furthermore it would be both theoretically and clinically relevant to investigate whether these factors are needed for CBM to produce a change in cognitive bias, or for the change in bias to cause behavioral change. For example, while abstinence might be a prerequisite to reduce cognitive biases, the combination with other interventions might be needed to reduce alcohol use or prevent relapse. Notwithstanding the relevance of examining the conditions under which CBM is most likely to be effective, our expectations of CBM’s clinical potential should be tempered. While a recent meta-analysis tentatively supports CBM’s effectiveness as an add-on to in-patient treatment, the added effect on relapse is small (Boffo et al., in press). In addition, there is no convincing evidence that the strength of cognitive biases during treatment predicts long-term relapse (Christiansen et al., 2015; Snelleman, Schoenmakers, & van de Mheen, 2015). These findings suggest that the causal role of cognitive biases in the maintenance of AUD’s is modest, and that CBM will not be effective as an independent intervention. This does not, however, negate CBM’s clinical potential. It is a low-cost intervention that requires minimal effort to complete, so even small reductions in relapse over and above extensive treatments are clinically meaningful and warrant further investigation on how we can optimize its effectiveness.
Strengths and limitations

Our RCT (Chapters 5) was the first to examine the individual and combined effects of different web-based CBM procedures in problem drinkers. The design had several strengths, including the 2x2x2 factorial design and the fact that we assessed change in the targeted cognitive biases both on the task that was used during CBM and on an untrained task. Furthermore, we described our hypotheses and design prior to analyzing the results (Chapter 2) and we validated the pictorial stimuli in an independent study (Chapter 4). This was also one of the first studies to examine the role of motivation to change in the interplay between cognitive biases and executive functions, and to do so in problem drinkers as opposed to at-risk populations (Chapter 3). However, our studies also have limitations that should be taken into account in the evaluation of the results.

One limitation is that roughly the same sample was used in the evaluation the effectiveness of CBM (Chapter 5) as in the examination of association between alcohol use and the interaction between cognitive biases, executive functions and motivation to change (Chapter 3). Since there was little evidence that baseline variations in alcohol use were related to the strength of automatic associations, this would theoretically also diminish the relevance of retraining cognitive biases in this sample. However, CBM can be effective even when the majority of participants show no cognitive bias prior to the intervention (e.g. Wiers et al., 2011). Furthermore, while our measures of automatic associations showed adequate reliability, the reliability of the attentional bias measures was too low to confidently determine whether participants showed an attentional bias at baseline. Therefore, it is uncertain if
the ineffectiveness of the CBM intervention (Chapter 5) can be attributed to the findings in Chapter 3.

A further limitation is that the dropout in our RCT was substantial, which could have affected both the baseline data (Chapter 3) and the results of CBM intervention (Chapter 5). In the former study we only analyzed complete cases, while in the latter we imputed missing data. Individuals who dropped out were younger and completed fewer CBM sessions, but they did not differ from completers in baseline alcohol use, most of the secondary outcomes measures, or motivation to change. In spite of the data-imputation, the extent of the dropout means that there is some uncertainty with respect to the results of the CBM study. For example, the non-specific reductions that we found in alcohol use and most of the secondary outcome measures may have been less pronounced in individuals who dropped out of the study. Due to the high dropout rate we did not analyze the data of the 12-month follow-up. Both from a scientific and an ethical perspective, it would be preferable to reduce the number of follow-ups and invest more research efforts in minimizing dropout.

As mentioned above, our studies are also limited by the insufficient reliability of some of the behavioral measures, which introduced alternative explanations for a number of our findings. The inadequate reliability of certain cognitive bias measures is not specific to our study (Ataya et al., 2012; Hedge et al., 2018; Schmukle, 2005). The choice to use these measures nonetheless was based on theoretical, empirical and practical considerations. Theoretically, it was important to assess change in the specific biases that were targeted during CBM. Empirically, the selected CBM tasks were those for which the evidence was considered promising. Practically, the web-based nature of our study somewhat restricted the choice of outcome measures. For example, we
could not use more reliable eye-tracking measures to assess attentional bias (Christiansen et al., 2015), or a joystick to measure approach bias (Wiers et al., 2009). As argued above, the reliable assessment of cognitive biases is needed to ensure progress in the field of CBM and should be prioritized in future research.

**General conclusions and clinical implications**

Recent studies showed that CBM is not effective in reducing problem drinking when implemented as a stand-alone intervention or as an add-on to a motivational intervention (Chapter 5, Clerkin et al., 2016; Cox et al., 2015; Jones, A. et al., in press; Wiers et al., 2015). Few of these studies have reliably assessed whether the investigated CBM procedure succeeded in changing the targeted cognitive bias. Therefore, it is unclear whether the fact CBM does not reduce alcohol use beyond non-specific effects is due to a lack of change in the cognitive bias, or to the absence of a causal relation between cognitive biases and alcohol use in problem drinkers. Theoretically, this underlines the indispensability of measuring change in cognitive biases, using reliable tasks. Clinically, however, these results do not support the implementation or investigation of CBM in problem drinkers, unless combined with a more extensive, evidence-based treatment.

The promising findings of CBM as an add-on to in-patient treatment do support the further examination of CBM in this context (Eberl et al., 2013; Manning et al., 2016; Rinck et al., 2018; Schoenmakers et al., 2010; Wiers et al., 2011). There is a need for more RCTs to confidently determine if CBM can help prevent relapse over and above clinical treatment (Boffo et al., in press). Given the low costs of CBM, both financially and in terms of the required effort from patients, CBM would be clinically relevant even if the added effect on relapse
were small. Furthermore, research in this context can test theoretical predictions on the nature (Gladwin et al., 2011; Wiers & Gladwin, 2016) and role (Field, M. et al., 2016) of cognitive processes in addiction, thereby contributing to a better understanding of the maintenance of AUDs.