Side effects in Internet-based interventions for Social Anxiety Disorder

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Abstract

Internet-based interventions are effective in the treatment of various mental disorders and have already been integrated in routine health care in some countries. Empirical data on potential negative effects of these interventions is lacking. This study investigated side effects in an Internet-based treatment for Social Anxiety Disorder (SAD).

A total of 133 individuals diagnosed with SAD took part in an 11-week guided treatment. Side effects were assessed as open formatted questions after week 2 and at post-treatment after week 11. Answers were independently rated by two coders. In addition, rates of deterioration and non-response were calculated for primary social anxiety and secondary outcome measures (depression and quality of life).

In total, 19 participants (14%) described unwanted negative events that they related to treatment. The emergence of new symptoms was the most commonly experienced side effect, followed by the deterioration of social anxiety symptoms and negative well-being. The large majority of the described side effects had a temporary but no enduring negative effect on participants’ well-being. At post-treatment, none of the participants reported deterioration on social anxiety measures and 0–7% deteriorated on secondary outcome measures. Non-response was frequent with 32–50% for social anxiety measures and 57–90% for secondary outcomes at post-assessment.

Results suggest that a small proportion of participants in Internet-based interventions experiences negative effects during treatment. Information about potential side effects should be integrated in patient education in the practice of Internet-based treatments.

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1. Introduction

In the last decade, Internet-based interventions have been developed for a variety of mental and physical health problems (Andersson et al., 2013). Several meta-analyses have summarized the evidence supporting the overall efficacy of Internet-based interventions in the reduction of psychopathological symptoms (e.g. Andrews et al., 2010; Cuypers et al., 2009; Macea et al., 2010; Mureșan et al., 2012; Spek et al., 2007). As a result, Internet-based interventions were integrated into routine mental health care in some countries, for example in Sweden and in the Netherlands (e.g. Hedman et al., 2013). Overall good effects do not, however, capture the proportion of patients who do and who do not benefit from an intervention. Average good effects can include any number of patients who do not respond to treatment, who deteriorate or who experience side effects. No study so far has focused on negative effects in Internet-based interventions (Emmelkamp et al., 2014). In light of the increasing use of Internet-based interventions, research on potential risks of these innovative treatments is highly warranted. The present study focuses on negative effects in Internet-based treatments for Social Anxiety Disorder (SAD). So far, two different Internet-based treatment approaches have been evaluated for SAD with differing success. Trials on guided Internet-based cognitive-behavioural treatments (ICBT) have consistently yielded good effects in reducing symptoms of SAD (for an overview see Ref. (Boettcher et al., 2013b)). In contrast, attempts to apply innovative attention training programmes to the Internet-based setting have produced mixed results (Boettcher et al., 2012; Boettcher et al., 2013d; Carlbring et al., 2012; Neubauer et al., 2013). Whilst ICBT programmes consistently resulted in large effects for social anxiety measures, attention training programmes only yielded small to moderate effect sizes. However, effect sizes are only one indicator of treatment efficacy. So far, nothing is known about potential risks associated with these interventions and empirical data on the frequency of

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deterioration or other unwanted events is still missing. The present report will therefore evaluate unwanted events in ICBT as well as in attention training programmes for patients with SAD.

Linden (2012) defined unwanted events as all events of negative quality that occur parallel to treatment. Unwanted events can be related to treatment or not. In events that are related to treatment, one can distinguish between side effects, which occur in relation to correct state-of-the-art treatment, and the effects of malpractice (malpractice reaction). Whereas malpractice reactions result from incorrect or inappropriately applied treatments and are the direct fault of a therapist, side effects are treatment-inherent and can occur when the treatment is adequate and appropriately delivered (Linden, 2012). Hoffmann et al. (2008) provided an overview of potential side effects in psychotherapy. These include the deterioration or chronification of targeted symptoms, the manifestation of new symptoms, suicidality, decreased self-esteem and self-efficacy due to the failure to achieve (unrealistic) treatment aims, the manifestation of the sick role, dependency on the therapist, negative and enduring personality changes, stigmatisation, and marriage/relationship problems.

Deterioration and non-response (no clinical change through treatment) are the most frequently researched side effects of psychotherapy. In their review of face-to-face psychotherapy research, Lambert and Ogles (2004) estimated that 5–10% of the patients in psychotherapy deteriorate. Unfortunately, only very few studies directly provide empirical insight into rates of non-response and deterioration. Kraus et al. (2011) reported on 6960 patients treated in regular outpatient care for a mean of 16 sessions. In panic/anxiety, 25% of the patients deteriorated significantly and 34% showed no clinical change (Kraus et al., 2011). Results from a cognitive-behavioural university-based outpatient clinic are more encouraging. Jacobi et al. (2011) reported that 0.8–3% of the 1776 patients experienced reliable deterioration, and 27–49% showed no significant clinical change. Some additional evidence on negative effects on a group level has been reported in meta-analyses. Two early meta-analyses on psychotherapeutic treatments showed that 9–11% of the calculated effect sizes were negative (Shapiro and Shapiro, 1982; Smith and Glass, 1977). With regard to Internet-based interventions, only one meta-analysis reported the proportion of negative effects. Barak et al. (2008) found that 75 out of 746 calculated effect sizes were zero or negative (10.1%).

Empirical studies on the nature and frequency of side effects other than non-response and deterioration are extremely rare. One study was conducted with psychotherapists who reported on their own training psychoanalysis/psychotherapy. Twenty-one percent experienced side effects (Buckley et al., 1981). Examples of side effects were “deleterious to my marriage”, “allowing destructive acting out”, and “fostering too much withdrawal from the outside world” (Buckley et al., 1981, p.304). One recent study on former psychotherapy patients (CBT, psychoanalysis and other therapies) showed that 3–23% reported prolonged periods of depression after treatment termination (Nestoriuc and Rief, 2012). Other frequent side effects in this study were: negative changes of the personality (2–15%), deteriorated coping with negative events of the past (0.5–16%), strained relationship to family members and more marital conflicts (1–11%), as well as fear of stigmatisation (1–4%) and problems with insurance companies due to having been in therapy (8–13%) (Nestoriuc and Rief, 2012).

Side effects are experienced by only a minority of patients in psychotherapy. Patient variables that might be associated with a higher risk of negative treatment outcome include high initial symptom severity, high comorbidity, low social support, low motivation, low outcome expectations, and inadequate treatment process expectations (Bohart and Greaves Wade, 2013; Mohr, 1995). Therapist characteristics that showed an association with poor therapeutic outcome included lack of empathy, hostility, and anger (Beutler et al., 2004; Mohr, 1995). It is yet unclear how these therapist characteristics may affect negative outcomes in Internet-based interventions. Web-based treatments differ in regard to the amount and intensity of therapist contact. Unguided Internet-based attention training programmes do not include any therapist–patient interaction at all. In ICBT, therapists usually provide weekly feedback and encouragement via e-mail and answer direct questions of the patients. Paxling et al. (2012) studied specific therapist behaviours in the e-mail correspondence with patients in ICBT for Generalized Anxiety Disorder. The authors found that specific therapist behaviours, e.g. the demonstration of ‘deadline flexibility’, were negatively related to treatment adherence and outcome. At the same time, the influence of the overall working alliance between patient and therapist seems less pronounced in Internet-based treatments compared to face-to-face treatments (Andersson et al., 2012) even though alliance ratings are positive and comparable to those in traditional therapies (Preschl et al., 2011).

It is so far unknown how the differences between face-to-face and Internet-based therapies might influence the occurrence of negative effects. Whilst research on side effects in face-to-face therapy is scarce, it is non-existent in Internet-based interventions. The frequency and nature of side effects in Internet-based treatments are unknown.

The aim of the current study was twofold. First, we wanted to investigate what kind of unwanted events occur in Internet-based interventions for SAD and how frequent they are in attention training and guided ICBT for SAD. We aimed at analysing their relatedness to treatment, their impact on patients’ well-being as well as their association with treatment outcome. We also explored potential predictors of unwanted events. Second, we aimed at providing an estimate of rates of deterioration and non-response on standardised outcome measures in Internet-based attention training and ICBT.

2. Methods

2.1. Participants and procedure

Participants were recruited for a randomised controlled trial on the combination of attention bias modification (ABM) training and ICBT (registration number at clinicaltrials.gov: NCT01570400) (Boettcher et al., 2013c). The study compared two groups: one group received attention training in addition to ICBT and the other group received a control training programme in addition to ICBT. A detailed description of the selection of participants, randomisation procedures, and interventions is provided elsewhere (Boettcher et al., 2013a). Participants were recruited via the Internet and via advertisement in regional and national newspapers. After registering with their e-mail address, participants obtained detailed information on the study and were asked to return written informed consent by mail.

The selection of the participants followed two steps. First, participants were asked to fill out the outcome questionnaires which included the Liebowitz Social Anxiety Scale — self report (LSAS-SR; Baker et al., 2002) and additional questions regarding current and past treatment. In the second step, participants who scored above the cut-off of 30 on the LSAS-SR were invited to take part in a telephone-administered diagnostic interview. Two advanced MSc clinical psychology students conducted the social anxiety and depression section of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I, First and Gibbon, 2004). All interviewers had received training in using the SCID-I. We applied the following inclusion criteria: (a) being at least 18 years old, (b) having access to the Internet, (c) meeting diagnostic criteria for a primary diagnosis of SAD according to the DSM-IV (d) no suicidal ideation (e) not participating in any other psychological treatment for the duration of the study, and (f) if on prescribed medication for anxiety/depression, dosage had to be constant for 3 months prior to the start of the treatment.

A total of 133 participants met all inclusion criteria and were randomised to one of two groups (see flowchart in Fig. 1). After randomisation, participants received access to a website where the respective tasks of the attention training/control training were presented and where the ICBT manual was accessible from weeks
The combined intervention took 11 weeks. During weeks 1 and 2, participants were asked to carry out the attention training/control training exercises once a day for a total of 14 days. From week 3 to week 11, participants of both groups were asked to complete the nine modules of the ICBT manual, with one module each week. Unwanted events were assessed after the attention training/control training at the end of week 2 and after ICBT at the end of week 11.

Outcome measures were administered prior to the treatment (pre-assessment), immediately after the attention training/control training after week two (mid-assessment), after the completion of the ICBT programme after week 11 (post-assessment), and at four months follow-up. Six participants (4.5%) did not complete self-report measures at week 2, 7 participants (5.3%) failed to complete the post-assessment and 15 participants (11.3%) failed to fill out self-report measures at follow-up-assessment.

Participants were, on average, 33 years old (SD = 10). Forty-eight percent were male and 58% lived in a stable relationship. The majority (71%) of the participants had a high level of education. Fifty percent reported former experiences with psychotherapy and 13% were on stable medication for anxiety/depression (Boettcher et al., 2013c).

2.2. Interventions

2.2.1. Attention training and control training (weeks 1–2)

The attention training programme was aimed at normalising the processing of social threat cues through the reduction of attentional avoidance of social threat cues. Participants were randomised to either a 14-day long attention training condition or a control training condition. Tasks for both conditions were based on the dot-probe paradigm and were identical except for the location of the probe. Each training/control session comprised of 192 trials. Each trial consisted of the presentation of a pair of stimuli of different emotional valence followed by a probe. Stimuli consisted either of two words (neutral, negative, or positive words), or of two portrait images of the same person's face expressing two different facial expressions (happy, neutral, or disgust expressions). The pair of stimuli was followed by a probe. The probe presented was either a ‘less-than sign’ ("<") or a ‘greater-than sign' (">").
to treatment on a 5-point Likert scale (1 = unrelated, 2 = probably unrelated, 3 = possibly related, 4 = probably related, 5 = related). We calculated the inter-rater reliability for the categorisation of unwanted events using Cohen’s Kappa (Cohen, 1960). The kappa-coefficient indicated substantial agreement of the two raters after the ABM treatment at week 2 (κ = 0.77) and moderate agreement of the two raters at the combined treatment of ABM and ICBT at week 11 (κ = 0.49) (Landis and Koch, 1977). The inter-rater reliability for the measure of relatedness to treatment was calculated using a two-way mixed agreement, average-measures Intra-Class-Correlation (ICC) (Hallgren, 2012). The resulting ICC was in the excellent range for both the rating at week 2 (ICC = 0.99) and at week 11 (ICC = 0.94) (Cicchetti, 1994).

Deterioration and non-response were calculated according to the reliable change index (Jacobson and Truax, 1991). The reliable change index classifies individual change scores as ‘deteriorated’, ‘no change’ or ‘improved’ in accordance to a critical difference which takes into account the psychometric properties of the applied instrument and normative data. As suggested by Lambert and Ogles (2009), we used internal consistencies rather than re-test-reliabilities to calculate critical differences. Psychometric properties and normative data were taken from a study on the Internet administration of social anxiety and related questionnaires (Hedman et al., 2010). In this study, internal consistencies and standard deviations were reported for a sample of individuals with SAD. Critical differences were as follows: LSAS-SR: 15.26 (SD1 = 22.48, α = .94), SPS: 14.43 (SD1 = 15.60, α = .89), SIAS: 13.04 (SD1 = 12.57, α = .86), MADRS-S: 7.53 (SD1 = 7.26, α = .86), and QoL: 2.22 (SD1 = 1.84, α = .81). We also calculated an overall deterioration index for each assessment point that distinguished between participants that showed no deterioration on any measure and participants that showed deterioration on at least one outcome measure. We report data both for the complete sample and the intention-to-treat sample. Missing values were replaced according to the Last-Observation-Carried-Forward-method. This method implies that participants with missing values are classified as non-responder (‘no change’).

3. Results

3.1. Preliminary analyses

The randomised controlled trial on the combination of ABM and ICBT did not result in significant differences between the attention training and the control group on primary outcome measures or on clinical change rates. Participants in both groups benefited from the combined treatment approach and showed, on average, large within-group improvements of social anxiety symptoms from pre- to post-assessment (d = 0.97–1.50). Treatment benefits were stable at four months follow-up (Boettcher et al., 2013c). Data on unwanted events as well as rates of deterioration and non-response are therefore reported for the total sample. Seven participants (5.3%) indicated at post-assessment that they had initiated psychological or medical treatment during the course of the study (see flowchart in Fig. 1). As three of them also reported unwanted events, we included these participants in our analyses even though we could not rule out that the reported negative effects were associated with the additional treatments.

3.2. Frequency and nature of reported unwanted events

At mid-assessment, after the ABM procedure, six participants (4.5%) indicated that they had experienced unwanted events. Two unwanted events were excluded as the independent raters agreed that these were either ‘unrelated’ or ‘probably unrelated’ to the treatment resulting in a total of 4 reported unwanted events. Table 1 depicts the classification of the unwanted event. At mid-assessment, one participant reported an increase of discomfort in
social situation (‘deterioration of symptoms’), one described frequent headaches and stomach aches (‘emergence of new symptoms’), and one reported that he was observed by a colleague whilst doing the exercises and feared that the therapeutic nature of the exercises became obvious (‘stigmatisation’). One participant described a trivial accident caused by lack of concentration (‘other’). At post-assessment, after the combined treatment of ABM and ICBT, 17 participants (12.9%) reported unwanted events. Most of the unwanted events were classified as the ‘emergence of new symptoms’. New symptoms included insomnia, anxiety, and depression. Two participants reported feelings of grief when facing the extent and impact of social fears in their lives. The ‘deterioration of symptoms’ was also experienced by some of the participants. Here, participants described an increase in focus on social fears and more negative expectations, which led not only to an increase of negative cognitions but also to the development of social fears in new situations such as talking to authorities. One participant also mentioned that the awareness that social behaviours had to be analysed in the treatment led to an increase of discomfort in social situations. Some unwanted events were classified as ‘negative well-being’. These included the perceived stress to comply with the treatment programme in a limited amount of time, as well as feelings of nervousness, anger, and frustration. Table 1 lists examples of unwanted events in all categories.

### Table 1

<table>
<thead>
<tr>
<th>Classification</th>
<th>Example</th>
<th>Mid-assessment</th>
<th>Post-assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emergence of new symptoms</strong></td>
<td>“Sleep has been worse, had trouble sleeping.”</td>
<td>1.0</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>Deterioration of symptoms</strong></td>
<td>“I have become more aware of situations and therefore I experience new situations as annoying with which I have not had problems before because I now reflect more and analyse situations more. Suddenly it’s hard to contact a lecturer and talk to him, eye contact has suddenly become difficult and I think too much when I have eye contact and it gets tough.”</td>
<td>1.0</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>Negative well-being</strong></td>
<td>“Perhaps that I was frustrated/angry sometimes. Might be linked to setting limits (assertiveness training).”</td>
<td>0.0</td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Lack of clear treatment result</strong></td>
<td>“In my situation, where I mainly suffer from anxiety and fear of blushing in front of other people I thought that the treatment did not help me with techniques for dealing with those tough situations, but I had to sit for hours and ponder my negative automatic thoughts and how I could challenge them, but none of it worked.”</td>
<td>0.0</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Non-compliance</strong></td>
<td>“I got tired of it and terminated treatment”</td>
<td>0.0</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Changes in work situation</strong></td>
<td>“I got an increased workload during the treatment”</td>
<td>0.0</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Stigmatisation</strong></td>
<td>“Once, a buddy passed by in the library when I was in the middle of an exercise, I cancelled the exercise, not least out of fear that he would look at and understand what it was about (…) which would have made me very embarrassed.”</td>
<td>1.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td>1.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

* N number of negative events was averaged across two independent raters.

3.2.2. Impact of unwanted events

After the ABM treatment at week 2, most participants rated the negative impact of the unwanted event as moderate at the time the event occurred (Md=2, M=1.25, SD=0.96), whereas they indicated that the occurred unwanted event had no longer a negative impact on their well-being at the time of the mid-assessment (Md=0, M=0.50, SD=1.00). Similarly, after the combined treatment of ABM and ICBT at post-assessment, most participants experienced the negative impact of the unwanted events as small at the time the event occurred (Md=1, M=1.59, SD=1.12) and as no longer negative at the time of the post-assessment after week 11 (Md=0, M=0.76, SD=0.90).

3.2.3. Predictors of unwanted events

To identify potential predictors of the occurrence of unwanted events, we calculated a logistic regression analysis. The experience of unwanted events (yes/no) was entered as dependent variable. Influenced by former reviews of patient variables and negative effects (see the Introduction section), we included the following predictors (forced entry): initial symptom severity as assessed by the LSAS-SR, relationship status (single/in stable relationship), former experience with psychotherapy (yes/no) as well as age and gender. None of these potential predictors was significant (all p>0.11) and all odds ratio confidence intervals included 1.

3.2.4. Association with outcome on standard questionnaires

To examine whether the reporting of unwanted events was associated with the deterioration on standard questionnaires, we tested the equal distribution between unwanted events (yes/no) and deterioration on any outcome measure (yes/no) at mid-, post-, and follow-up-assessment in three separate $\chi^2$-tests. Results indicated that those participants who experienced unwanted events were not necessarily prone to report deterioration on outcome questionnaires (all $\chi^2(1)$<2.25, all p>0.15).

3.3. Deterioration and non-response

Deterioration and non-response on standardised outcome measures were assessed at mid-, post-, and follow-up-assessment. Table 2 depicts the rates of improvement, non-response, and deterioration for the completer and the intention-to-treat sample. Overall, 19 (14.3% of the ITT sample) participants showed deterioration on any outcome measure after the ABM intervention at week 2, and 9 participants (6.8% of the ITT sample) showed deterioration on any measure after the combined treatment of ABM and ICBT at post-assessment and at follow-up-assessment. On targeted social anxiety symptoms, 1–7 participants (0.8–5.3% of the ITT sample) showed deterioration from pre- to mid-assessment whereas no participant classified as reliably deteriorated at post-assessment. At follow-up-assessment, 1–3 participants (0.8–2.3% of the ITT sample) showed reliable deterioration of social fears. On secondary outcome measures, one participant described a reliable deterioration of quality...
of life from pre- to mid-assessment and two participants deteriorated from pre- to follow-up-assessment. Rates of deterioration were higher on the secondary depression scale with 7 participants (5.3% of the ITT sample) showing reliable deterioration from pre- to mid-assessment, 9 participants (6.8% of the ITT sample) from pre- to post-assessment, and 5 participants from pre- to follow-up-assessment (3.8% of the ITT sample) (see Fig. 2).

Non-response was far more frequent than deterioration, especially at week 2 assessment. After the ABM intervention, 70–87% of the participants in the ITT sample showed no reliable clinical change in social anxiety. Non-response on secondary measures ranged from 81 to 97%. After the combined intervention at post-assessment, one third to one half of the participants in the ITT sample did not experience a reliable change in social fears. Fifty-seven percent of the participants reported no change on the depression scale and 90% failed to report clinical change in quality of life. At four months follow-up, rates of non-response remained fairly similar to those at post-assessment. One third to one half of the participants failed to experience change in social anxiety, about 85% did not achieve reliable change in their quality of life and two thirds of the participants did not experience change in depressive symptoms (see Fig. 2).

### 3.3.1. Predictors of deterioration

To identify potential predictors of deterioration, we calculated logistic regression analyses similar to the one used for the prediction of the experience of unwanted events. The first logistic regression analysis included deterioration on any measure at mid-assessment (yes/no) as dependent variable and initial symptom severity as assessed by the LSAS-SR, relationship status, former psychotherapy experience, age, and gender as predictors. The second and the third logistic regression analysis included the same predictors and, as dependent variable, deterioration at post-assessment and at follow-up-assessment respectively. Deterioration at mid-assessment was not predicted by any of the entered variables (all \(p>.15\)). At post-assessment, deterioration was significantly predicted by initial symptom severity assessed by the LSAS-SR (\(p=.01\), OR = 1.07 (CI: 1.02–1.13)). Participants with higher LSAS-SR scores at pre-assessment were slightly more likely to experience deterioration in at least one outcome domain at post-assessment. At follow-up-assessment, none of the entered predictors significantly affected deterioration (all \(p>.13\)).

### 4. Discussion

The present study was the first to evaluate negative effects in Internet-based interventions for SAD. It investigated what kind of unwanted events participants of a combined web-based treatment approach experienced. The most commonly reported side effect was the emergence of new symptoms, which was experienced by 5% of the participants. New symptoms included, for example, not only insomnia but also grief experienced in the confrontation with the extent of life impairments associated with the social fears. The second frequent side effect was the deterioration of targeted symptoms, which was experienced by 4% of the participants and which was mainly attributed to an enhanced focus on socially anxious thoughts and feelings. Other less frequent side effects reported in the current trial were negative well-being, the lack of clear treatment results, non-compliance to the treatment (and subsequent termination), changes in the work situation and fear of stigmatisation. None of the participants experienced a negative change in interpersonal relations due to the treatment. This finding corresponds with a review on negative interpersonal consequences of individual therapy which found no evidence of a detrimental effect of psychotherapy on marital quality (Hunsley and Lee, 1995).

In total, about 14% of the participants of the current trial reported a side effect of the treatment. This proportion is lower but corresponds to the 21% found in former psychotherapy patients by Buckley et al. (1981). However, only a minority of the participants who reported unwanted events described the events’ consequences as negative and enduring. Only four out of the 21 reported unwanted events were described as having a negative impact on the participants’ well-being at the time of the post-assessment.

Using a different methodological approach, the current study also aimed at evaluating the frequency of deterioration of symptoms and non-response in Internet-based interventions for SAD. Deterioration and non-response are the two most commonly studied side effects of psychotherapy and are usually operationalized by change scores on outcome questionnaires. In summary, the deterioration of social anxiety symptoms was rare and ranged between 1 and 5% at week two and 1–2% four months after treatment termination. A reliable increase of depressive symptoms as a secondary outcome domain was slightly more frequent with rates ranging between 4 and 7% at the three assessment points. As there are no studies expressly focusing on negative effects in SAD treatment, these proportions must be compared to studies examining negative effects of psychotherapy in general. Negative change rates of the current study are lower than those reported by Kraus et al. (2011) for a large community outpatient sample (25% of deterioration on anxiety/panic symptoms). This difference may be partly explained by the structured research setting of the current study, the homogeneity of diagnosis and treatment, and the selected patient population. In general, randomised controlled efficacy trials achieve better clinical outcomes, and therefore less negative effects, than studies in clinical routine (e.g. Westen and Morrison, 2001). However, the rates of deterioration in the current sample are slightly higher than those reported for a large effectiveness study in patients of a university-based outpatient clinic (1–3%) (Jacobi et al., 2011).

### Table 2

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mid</th>
<th>Post</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Completer</td>
<td>ITT</td>
<td>Completer</td>
</tr>
<tr>
<td></td>
<td>(N=127)</td>
<td>(N=133)</td>
<td>(N=126)</td>
</tr>
<tr>
<td>Liebowitz Social Anxiety</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scale – Self-rated</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Deterioration</td>
<td>7</td>
<td>5.5</td>
<td>7</td>
</tr>
<tr>
<td>No change</td>
<td>87</td>
<td>68.5</td>
<td>93</td>
</tr>
<tr>
<td>Social Phobia Scale</td>
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<td>Deterioration</td>
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<td>0.8</td>
<td>1</td>
</tr>
<tr>
<td>No change</td>
<td>109</td>
<td>85.8</td>
<td>115</td>
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<td>Social Interaction Anxiety Scale</td>
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<td>Deterioration</td>
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<td>4.7</td>
<td>6</td>
</tr>
<tr>
<td>No change</td>
<td>108</td>
<td>85.0</td>
<td>114</td>
</tr>
<tr>
<td>Quality of Life Inventory</td>
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<tr>
<td>Deterioration</td>
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<td>0.8</td>
<td>1</td>
</tr>
<tr>
<td>No change</td>
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<td>96.9</td>
<td>129</td>
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<td>Montgomery Åsberg</td>
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<tr>
<td>Deterioration</td>
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<tr>
<td>No change</td>
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<td>79.5</td>
<td>107</td>
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<tr>
<td>Depression Rating Scale</td>
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<tr>
<td>Reliable deterioration on any measure</td>
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<td>15.0</td>
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</tbody>
</table>
Patients in this setting received on average 30 sessions of individual cognitive-behaviour therapy. Differences in non-response and deterioration between the current Internet samples and the face-to-face outpatient sample could at least partly be explained by the vast differences in treatment sessions (Lambert, 2007).

Rates of deterioration and non-response also highly depend on the definition of critical clinical change. The most frequent measure of clinical change constitutes the reliable change index suggested by Jacobson and Truax (1991). However, even in studies using this method, the definition of critical differences varies widely depending on the outcome measure applied and the normative and psychometric data considered (Lambert and Ogles, 2009). For example, Hiller et al. (2012) compared critical differences for the Beck Depression Inventory (BDI-II; Beck et al., 1996) in 11 psychotherapy trials and found that critical differences varied substantially between 6 and 14 points. Thus, change scores that are classified as reliable deterioration in one study are not necessarily interpreted similarly in the next study.

With a combined rate of deterioration and non-response for targeted primary symptoms of 32–50% at post-assessment, results of the current study are comparable to the face-to-face literature. A recent review of 291 meta-analyses on face-to-face CBT reported response rates of 46–77% for anxiety disorders implying that non-response and deterioration varied between 23 and 54% (Hofmann et al., 2012). Hanssen et al. (2002) found that 42% of the patients in 28 analysed psychotherapy trials (CBT and other therapies) showed no clinical significant change after an average of 13 sessions. One could conclude that deterioration, non-response, and other side effects do not seem more frequent in remotely delivered Internet interventions for SAD than in face-to-face treatments.

The current study has limitations. First, the analysis of predictors of unwanted events in general and of deterioration in particular was restricted to a limited set of predictors. With the exception of initial symptom severity in the prediction of deterioration at post-assessment, none of the applied predictors explained the occurrence of unwanted events, a finding consistent with the often very varied results on patient variables in psychotherapy research (Bohart and Gravers Wade, 2013). However, other theoretically important predictors such as outcome and process expectations and motivation were not assessed in the current study and should be addressed in future studies on side effects in Internet-based interventions. Second, the present study did not include an analysis of the interaction of Internet therapists and patients and its impact on negative effects. The analysis of the written correspondence between therapists and participants was beyond the scope of the present report but could, as indicated by the results of Paxling et al. (2012), be highly relevant for the understanding of how deterioration and other side effects develop. Swift et al. (2010) studied different processes of deterioration in face-to-face therapy and reported that an increase of symptoms reliably preceded decreased functioning and decreased well-being. Future studies should explore whether these stages of deterioration occur in a similar way in Internet-based treatments and whether it would be possible for therapists to detect deterioration at an early stage.

In the current study, unwanted events were assessed in an open format question at two assessment points. Answers were then classified into categories (Linden, 2012) by two independent raters. The interrater reliability for this classification was only moderate at post-assessment. To improve the agreement between raters, future studies should train coders to distinguish between categories. The classification by Linden (2012) is based on clinical experience and a review of the literature. The development of an empirically informed catalogue of common side effects of Internet interventions could be a goal of future studies. Future studies should also aim at a standardisation of how to define deterioration and non-response on widely used outcome measures. In the current trial, critical differences were defined on the basis of psychometric properties reported by Hedman et al. (2010) in a study validating common outcome measures for Internet-based interventions in SAD. Although these data seemed most appropriate for defining clinical change in the current trial, the sample size in the Hedman et al. study was small which limits the generalizability of the reported critical differences. Seggar et al. (2002) calculated standard critical differences for the BDI-II using meta-analytic techniques to provide reliable estimates of normative data and psychometric properties. Similar procedures should be applied to instruments commonly used in Internet-based research. Proportions of deterioration and non-response are also crucially affected by the applied method of handling missing values. We imputed missing data with the Last-Observation-Carried-Forward method. This method classifies all missing data as non-responder. As participants with missing data could have reliably deteriorated during the current treatment, the LOCF method may have led to an underestimation of deterioration.

The present trial provides a first estimate on the frequency and nature of unwanted events in Internet-based interventions for SAD. Future studies should focus on evaluating negative effects in Internet-based interventions for other common conditions, including depression. Due to their good performance in efficacy and effectiveness trials and their great potential to address shortages in treatment rates, Internet-based treatments have already been incorporated into standard clinical routine in several countries. The education on potential risks of a treatment is an indispensible part of the patient education as well as of the training of professionals. The current trial allows specifying these risks for the Internet-based treatment of SAD and thus enables clinicians and patients to make fully informed treatment decisions.

Conflict of interest statement

The authors declare no conflict of interest.

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