**Internet-based vestibular rehabilitation with and without physiotherapeutic support for adults aged 50 years and older with a chronic vestibular syndrome in general practice:**

**a three-armed randomised controlled trial**
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**ABSTRACT**

**Objectives** To investigate the clinical effectiveness and safety of stand-alone and blended internet-based vestibular rehabilitation in the management of chronic vestibular syndromes in general practice.  **Design** Pragmatic, three-armed, parallel group, individually randomised controlled trial.

**Setting** 59 general practices in The Netherlands.

**Participants** 322 adults, aged 50 years and older, with a chronic vestibular syndrome.

**Interventions** Stand-alone vestibular rehabilitation consisted of a six-week, internet-based intervention with weekly online sessions and daily exercises (10-20 minutes per day). In the blended vestibular rehabilitation group, the same internet-based intervention was supplemented by face-to-face physiotherapeutic support (home visits in week one and three). Participants in the usual care group received usual GP care without any restrictions.

**Main outcome measures** The primary outcome was vestibular symptoms after six months as measured by the Vertigo Symptom Scale - Short Form (VSS-SF; range 0-60; clinically relevant difference ≥3 points). Secondary outcomes were impairment due to dizziness, anxiety, depressive symptoms, subjective improvement of vestibular symptoms after three and six months and adverse events.

**Results** In the intention-to-treat analysis, stand-alone and blended vestibular rehabilitation participants had lower VSS-SF scores at six months than usual care participants (adjusted mean difference -4.1 points; 95% confidence interval -5.8 to -2.5; and -3.5 points; 95%-CI -5.1 to -1.9), respectively. Similar differences in VSS-SF scores were seen at three months follow-up. Participants in the stand-alone and blended vestibular rehabilitation groups also experienced less dizziness-related impairment, less anxiety, and more subjective improvement of vestibular symptoms at three and six months. No serious adverse events related to online vestibular rehabilitation occurred during the trial.

**Conclusion** Stand-alone and blended internet-based vestibular rehabilitation are clinically effective and safe interventions to treat patients aged 50 years and older with a chronic vestibular syndrome. Online vestibular rehabilitation is an easily accessible form of treatment with the potential to improve care for an undertreated group of patients in general practice.

**Trial registration** Netherlands Trial Register NTR5712

**Section 1. What is already known on this topic?**

- In chronic vestibular syndromes, patients experience for months to years chronic vestibular symptoms (i.e. vertigo, dizziness, vestibulovisual symptoms or postural symptoms) with features suggestive of persistent vestibular system dysfunction.

- Vestibular rehabilitation is a form of exercise therapy designed to optimise the process of vestibular compensation, which is disrupted in patients with a chronic vestibular syndrome.

- Although considered the preferred treatment for chronic vestibular syndromes, vestibular

rehabilitation is still largely underused in general practice.

**Section 2. What this study adds?**

- This is the first trial that investigated the effectiveness of internet-based vestibular rehabilitation, both with and without physiotherapeutic support, in patients aged 50 years and older with a chronic vestibular syndrome in general practice.

- At six months, internet-based vestibular rehabilitation, both with and without

physiotherapeutic support, resulted in a clinically relevant decrease in vestibular symptoms

compared to usual care.

**PRINT ABSTRACT**

**Study question** Is internet-based vestibular rehabilitation, with and without physiotherapeutic support, more effective than usual care in decreasing symptoms of chronic vestibular syndromes in general practice?

**Methods** This three-armed, individually randomised controlled trial in Dutch general practices included 322 adults, aged 50 years and older, with a chronic vestibular syndrome. Participants received either stand-alone vestibular rehabilitation (n=98), blended vestibular rehabilitation (n=104) or usual care (n=120). Stand-alone vestibular rehabilitation consisted of a six-week, internet-based intervention with weekly online sessions and daily exercises. In blended vestibular rehabilitation, the same internet-based intervention was supplemented by face-to-face physiotherapeutic support. Usual care participants received usual GP care without any restrictions. The primary outcome was vestibular symptoms after six months as measured by the Vertigo Symptom Scale - Short Form (VSS-SF; clinically relevant difference

≥3 points).

**Study answer and limitations** After six months, stand-alone and blended vestibular rehabilitation participants reported clinically relevant lower VSS-SF scores than usual care participants (adjusted mean difference -4.1 points; 95% confidence interval -5.8 to -2.5; and -3.5 points; 95%-CI -5.1 to -1.9, respectively). No serious adverse events related to vestibular rehabilitation occurred during the trial. Patients motivated to treat their vestibular symptoms with exercises may have been more likely to participate in the trial.

**What this study adds** Stand-alone and blended internet-based vestibular rehabilitation are effective and safe interventions to treat patients aged 50 years and older with a chronic vestibular syndrome. Online vestibular rehabilitation is an easily accessible form of treatment that can potentially improve care for an undertreated group of general practice patients.

**Competing interests, funding and data sharing** The Netherlands Organisation for Health Research and Development funded this research. The authors disclosed no other competing interests. Data are available from the corresponding author.

**Trial registration** Netherlands Trial Register NTR5712

**INTRODUCTION**

Vestibular symptoms such as vertigo and dizziness are common in general practice.1 Each year 5% of the general population experiences vertigo symptoms.2 The prevalence, frequency and severity of vertigo generally increases with age.2,3 Four out of five patients with vertigo report that vertigo severely affects their daily functioning.4 Vertigo also represents a substantial economic burden, due to absenteeism, high use of healthcare services and an increased risk of falling.2, 5 Over 80% of patients experiencing vertigo in The Netherlands, UK and USA are primarily treated by their general practitioner/primary care physician and are never referred to a medical specialist for their symptoms.6-8

In the International Classification of Vestibular Disorders (ICVD), developed by the leading international Bárány society for neuro-otology, four types of vestibular symptoms are identified: vertigo, dizziness, vestibulovisual symptoms and postural symptoms. 9, 10 No vestibular symptom is considered pathognomonic in its links to underlying vestibular pathology, and the same patient often experiences more than one vestibular symptom.10, 11 Peripheral vestibular dysfunction due to disorders such as benign paroxysmal positional vertigo (BPPV), vestibular neuritis, vestibular migraine or Menière’s disease is the most important cause of vestibular symptoms.2 Each peripheral vestibular disorder has a distinct initial treatment, and they all have a substantial chance to result in chronic vestibular symptoms.12 When a vestibular disorder damages the peripheral vestibular system, an innate repair mechanism called vestibular compensation is activated that aids functional recovery and decreases vestibular symptoms.13 When vestibular compensation fails, a chronic vestibular syndrome can occur.12 This is defined in the ICVD as a clinical syndrome of chronic vestibular symptoms, lasting months to years, which includes features suggestive of persistent vestibular system dysfunction. Symptoms in chronic vestibular syndromes can either have a progressively deteriorating course; reflect a stable, yet incomplete recovery after an acute vestibular event; or represent persistent, lingering symptoms between episodic vestibular attacks.10, 11

Vestibular rehabilitation (VR), an exercise-based treatment that gradually stimulates the vestibular system, can be used to stimulate vestibular compensation.12 There is moderate to strong evidence that VR is a safe and effective treatment for unilateral peripheral vestibular dysfunction.14 VR is now recommended in US,15, 16 UK,17 and Dutch18 clinical guidelines as the preferred treatment for a chronic vestibular syndrome. Despite the scientific evidence, less than 10% of GPs in the Netherlands19 and UK20 reported using VR. Investigating alternative ways to deliver VR in general practice may stimulate the implementation of VR. Internet interventions are easily accessible, inexpensive and can be tailored to the patient’s individual needs. The University of Southampton used the content of an effective VR booklet21, 22 to develop an online VR intervention.23 In a randomised controlled trial in the UK this fully automated stand-alone internet-based intervention effectively reduced vestibular symptoms compared to usual care. 24 Stand-alone internet-based interventions are prone to non-adherence and attrition, therefore online treatment is often combined with face-to-face therapy by a health care professional. 25-27 Thus, combining online VR with physiotherapeutic support might offer even better results. This guided approach with physiotherapeutic support, known as ‘blended care’, may be especially effective in patients with vestibular symptoms, because anxiety is strongly associated with vestibular disorders. 28-31 Physiotherapists are used to reassure and encourage participants conducting vestibular exercises and regard managing anxiety as an important aspect of their treatment. 16, 32 The objective of this trial was to investigate the clinical effectiveness and safety of stand-alone and blended internet-based VR versus usual care for general practice patients aged 50 years and older with a chronic vestibular syndrome. We hypothesised that both stand-alone and blended internet-based VR would result in a clinically relevant decrease in vestibular symptoms compared to usual care after six months.

**METHODS**

We conducted a pragmatic, three group, parallel arm, individually randomised controlled trial among participants aged 50 years and older with a chronic vestibular syndrome. We compared the clinical effectiveness and safety of stand-alone and blended internet-based VR with physiotherapeutic support with usual care. We published a detailed study protocol, 33 and the trial was registered in The Netherlands Trial Register before recruiting the first patient. We followed the CONSORT reporting guidelines for non-pharmacologic treatment interventions. 34

**Participants**

We recruited participants from 59 general practices in The Netherlands. Eligible participants aged 50 years and older, who had visited their GP with a vestibular symptom in the last two years, were identified by a search in the electronic medical records. The GP screened the list of potentially eligible patients and excluded those with: an identifiable non-vestibular cause of their symptoms; medical contraindications for making the required head movements (e.g. severe cervical arthrosis); serious comorbid conditions precluding participation in an exercise programme; or current enrolment in another—interfering—study. Potential participants received information about the trial and a form to express interest in the trial. In interested patients, one of the physicians in the research team (VAvV or ORM) checked the eligibility criteria by telephone. The inclusion criteria were: a good command of the Dutch language; access to the internet and an email account; persisting vestibular symptoms at time of inclusion that had been present for at least one month and that were exacerbated or triggered by performing head movements. These inclusion criteria allowed us to identify participants with a chronic vestibular syndrome, as defined in the ICVD, 10, 11 who were suitable to receive online vestibular rehabilitation. The research team physician used a checklist (Supplementary Appendix 1) to distinguish a chronic vestibular syndrome from an acute vestibular syndrome and an episodic vestibular syndrome. 10, 11

**Interventions**
*Stand-alone internet-based vestibular rehabilitation (stand-alone VR)*

VR entails specific exercises with the aim of maximising central nervous system compensation for vestibular pathology. Additionally, deliberately provoking vestibular symptoms in a controlled context constitutes a form of exposure-based behaviour therapy. 35, 36 Booklet-based VR is an effective method to reduce vestibular symptoms and dizziness-related impairment.21, 22, 37 VR booklets served as the basis for a British online intervention, called Balance Retraining (freely available from <https://balance.lifeguidehealth.org/>).23, 24, 35 The development of Balance Retraining employed a ‘Person-Based Approach’, drawing on an in-depth understanding of intervention target users. 38, 39 It was built using LifeGuide software. Vertigo Training, the internet-based VR intervention we used in this trial, was a Dutch translation of Balance Retraining.

The intervention period lasted six weeks. The Vertigo Training intervention consisted of six weekly online sessions and daily VR exercises (Supplementary Appendix 2). In the first session, written instructions and video demonstrations were used to teach participants the six core VR exercises. Participants were asked to perform these exercises twice daily for 10 minutes during the intervention period. VR exercises were tailored to the individual needs by taking the participants’ symptoms and balance capabilities into account. At the start of the intervention participants performed all exercises sitting down and directly afterwards scored the level of vestibular symptoms caused by each of the six exercises. Vertigo Training used these scores to automatically produce an exercise prescription for the coming week, custom-built to the participant’s vestibular symptoms. Every week, the participant scored the vestibular symptoms caused by each of the six exercises again in a new online session. When performing an exercise sitting down would not elicit vestibular symptoms (anymore), the difficulty level would be increased by an instruction to perform that specific exercise while standing or eventually even when walking around. Through this personalised approach, participants gradually increased the intensity of their exercises and continued to challenge their vestibular system. Vertigo Training also provided information and advice on coping and symptom control strategies (Supplementary Appendix 2). 37 Muscle relaxation and breathing techniques can decrease psychophysiological arousal, while cognitive restructuring and problem solving may lessen anxiety provoked by vestibular symptoms. 40 In addition, Vertigo Training included several features to increase engagement. To increase participants’ expectations regarding Vertigo Training’s content, scientific studies supporting the effectiveness of VR were summarised in plain language. Participants received e-mail messages to remind them to log in to the website each week. All participants also received the standard level of care provided by their own GP without restrictions.

*Blended internet-based vestibular rehabilitation with physiotherapist support (blended VR)*

Participants in the blended VR group received access to the same Vertigo Training intervention as participants in the stand-alone VR group. In addition, the blended VR participants were visited twice at home by a trained physiotherapist. These physiotherapeutic sessions occurred in week one and three of the six-week intervention period and lasted for 45 minutes each. During these sessions, the physiotherapist: a) provided information about the background of vestibular symptoms and VR; b) elicited and addressed doubts and concerns about vestibular symptoms and VR; c) taught the patient how to use the online intervention; d) described and took the patient through a set of VR exercises; e) advised on how to anticipate and cope with obstacles to adherence; and f) provided support and encouraged adherence. The first session was used to make the patient feel comfortable with the VR exercises, while the second session focussed on adherence to the treatment. Every participant in this group also received the standard level of care provided by their own GP without restrictions.

*Usual care*

Participants in the usual care group received the standard level of care provided by their own GP without restrictions. Participants had access to any treatment available in primary care or (after referral) in secondary care. All usual care participants were offered access to stand-alone internet-based VR after the trial was completed. Participating GPs received a written instruction, asking them to diagnose causes of vestibular symptoms and treat identified disorders for all trial participants according to the guidelines of the Dutch College of GPs.18

**Outcomes**
Measurements were collected at baseline, three months and six months follow-up. The primary outcome measure was vestibular symptoms as measured by the Vertigo Symptom Scale-Short Form (VSS-SF)41, 42 six months after baseline. The VSS-SF has been used effectively in a number of previous VR trials, 21, 22, 24, 37 and has demonstrated excellent discriminative ability (AUC 0.87), high internal consistency (Cronbach’s alpha 0.90), and high test-retest reliability (ICC 0.88).42 It measures the frequency of 15 vestibular symptoms on a scale from 0 (no symptoms) to 4 (symptoms most days) during the past month (total range 0-60 points). Improvement can reflect either fewer or less frequent symptoms. A total score of 12 points or more has been classified as severe vestibular symptoms,22 and a change in score of three points or more has been defined as clinically significant.21, 22, 24, 37 A clinically relevant improvement on the VSS-SF can represent either marked improvement on one symptom (e.g. vertigo), or some improvement on three symptoms (e.g. vertigo, nausea and unsteadiness). Secondary outcome measures included the Dizziness Handicap Inventory (DHI),43 which measures dizziness-related impairment; subjective improvement in vestibular symptoms37; a single dichotomous item that indicated whether participants felt improved or not (i.e. worse or the same), compared to baseline; and the Patient Health Questionnaire (PHQ)44 to determine the presence of a panic disorder, generalised anxiety disorder or major depressive disorder, and measure the severity of anxiety (GAD-7 subscale)45  and depressive symptoms (PHQ-9 subscale).46 In stand-alone and blended VR participants, we also assessed self-reported perceived barriers to adherence with the Problematic Experiences of Therapy Scale (PETS).47 At baseline, we asked participants to report demographic characteristics (age, gender, level of education and living situation), comorbidities, the vestibular diagnosis, the frequency and average duration of their vestibular symptoms, and the time since their vestibular diagnosis. Engagement of Vertigo Training was measured by automatically collected detailed data with regard to intervention usage, number of sessions completed and time spent on each page. We reported all serious adverse events that occurred during the trial to the Medical Ethics Committee. The relationship of all serious adverse events with vestibular symptoms and/or the intervention was judged, after contacting the participant and/or GP.

**Randomisation and blinding**

Participants who completed the informed consent procedure received an email message with a link to the trial website. After filling out the baseline questionnaire, the LifeGuide software allocated participants to stand-alone VR, blended VR or usual care. A simple randomisation algorithm stratified participants by vertigo severity using a cut-off of 12 or higher on the Vertigo Symptom Scale–Short Form (VSS-SF). The automated randomisation process took place online and was concealed from the research team. Due to the nature of the interventions in the trial, blinding of participants, physiotherapists and research assistants was not possible. The trial statistician (JWRT) remained blind to allocation until analyses were complete.

**Sample size**

Our sample size calculation was based on the comparison between participants allocated to stand-alone VR and participants allocated to usual care. We chose this comparison because, based on previous blended internet-based research projects,25-27 we anticipated that blended VR would be just as effective or more effective than stand-alone VR. In a previous VR trial with VSS-SF as primary outcome measure, booklet-based VR alone compared with usual care showed an effect size (Cohen’s d) of 0.45, favouring booklet-based VR.21 In order to be able to detect such an effect, and assuming that stand-alone internet-based VR would produce the same effect size as booklet-based VR, we needed 80 participants per group for a two-sided test with alpha=0.05 and beta=0.20. As attrition from internet-based interventions can be substantial,25 we decided to recruit a minimum of 100 participants per group (300 total sample) to allow for up to 20% loss-to-follow-up.

**Statistical analyses**

We used descriptive statistics to compare the baseline characteristics of participants in the three trial arms. For the primary intention-to-treat analysis, participants were analysed according to their randomisation group. Two comparisons were made: stand-alone internet-based VR versus usual care and blended internet-based VR with physiotherapist support versus usual care. In a secondary per-protocol analysis, we only included stand-alone VR participants who completed all six online sessions and blended VR participants who completed all six online sessions and both physiotherapist visits. We used a linear mixed models analysis for continuous outcome variables and generalised estimating equation analysis for binary outcome variables. These techniques can account for repeated measures within one patient and are also capable of handling missing data in a longitudinal data set without performing multiple imputations.48 For each outcome measure, we reported a crude and an adjusted analysis. The crude analysis included the group variable (using the usual care group as reference), time and the interaction between the group variable and time. Furthermore, we adjusted for the baseline values of the outcome, as is customary in randomised controlled trials, 49 and for other pre-specified potential confounders i.e. age (continuous)50-54; gender (categorical)50, 55; level of education (categorical)54; living situation (categorical)54, 56; number of chronic diseases (categorical)50, 54, 56, 57; time since diagnosis (categorical)55, 56, 58; and the presence of a panic disorder, generalised anxiety disorder or major depressive disorder at baseline (categorical).50, 56-59 Lastly, we conducted a post-hoc analysis to assess possible effect modification in the primary intention-to-treat analysis for each potential confounder by using interaction terms in the model. SPSS 22.0 and Stata 14.1 were used for statistical analyses.

**Patient and public involvement**

Patients played an important role in the development of Vertigo Training. Detailed feedback by patients with vestibular symptoms on the content, usability and Dutch translation in prototype versions led to some amendments of the online intervention. No patients advised on interpretation of the results, nor were they involved in writing the manuscript. A lay summary of the research findings will be distributed to all participants in the study and the results will be disseminated to the relevant patient community.

**RESULTS**

Participants were recruited between June 2017 and July 2018 from 59 Dutch general practices. Figure 1 shows the patient flow during the trial. At baseline 322 participants were randomised: 98 participants were allocated to the stand-alone VR group, 104 to the blended VR group, and 120 to the usual care group. Follow-up data on our primary outcome was complete at three and six months for 91% and 89% of participants, respectively. The baseline characteristics of participants are shown in Table 1. The groups were generally well balanced, although there were relatively more men in the usual care group. In the stand-alone VR group, 71% of participants completed at least one online session and 48% completed all six sessions. In the blended VR group, 80% completed at least one online session, 82% of participants received both physiotherapist visits, and 53% completed all six sessions and were visited twice by the physiotherapist.

**Primary outcome**

In the intention-to-treat analysis, after three and six months participants in both the stand-alone VR group and the blended VR group reported less vestibular symptoms than participants in the usual care group (Table 2). After controlling for baseline values and pre-specified confounders, stand-alone VR participants scored 4.3 points lower on the VSS-SF compared to usual care participants at three months (95% confidence interval -5.9 to -2.6) and 4.1 points lower at six months (-5.8 to -2.5). Blended VR participants scored 3.9 point lower than usual care participants at three months (-5.5 to -2.3) and 3.5 points lower at six months (-5.1 to -1.9). The differences between groups were statistically significant and exceeded the clinically relevant difference of 3 points. In the per protocol analysis, the participants in the stand-alone VR group reported a 5.4 point lower VSS-SF score at six months compared to participants in the usual care group (95% CI -7.4 to -3.4), and the blended VR group scored 3.5 points lower than the usual care group (95% CI -5.4 to -1.6). In a post-hoc analysis, we found no effect modification for our primary outcome (Supplementary Appendix 3).

**Secondary outcomes**

The comparison between the groups on impairment due to dizziness, anxiety, depressive symptoms and subjective improvement of vestibular symptoms is shown in Table 3. Stand-alone and blended VR participants experienced less impairment due to dizziness than usual care participants at three and six months (adjusted mean difference DHI at 6 months: -4.9 points; 95% CI -8.4 to -1.3, and -4.5 points; 95% CI -8.0 to -0.9). They also experienced less anxiety symptoms at three and six months (adjusted mean difference GAD-7 at 6 months:

-1.2 points; 95% CI -2.0 to -0.4, and -1.2 points; 95% CI -2.0 to -0.4). There were no significant differences in depressive symptom severity between the VR groups and the usual care group at three and six months. At six months, 46/87 (53%) of stand-alone VR participants, 48/93 (52%) of blended VR participants and 43/110 (39%) of usual care participants reported subjective improvement of vestibular symptoms compared to the start of the trial. Over the course of the trial, stand-alone VR participants and blended VR participants were more likely to experience subjective improvement than usual care participants (adjusted odds ratio stand-alone VR versus usual care 2.2; 95% CI 1.2 to 4.1; blended VR versus usual care 2.1; 95% CI 1.2 to 3.8). There were no significant differences in self-reported perceived barriers to adherence between stand-alone and blended VR participants (Supplementary Appendix 4).

**Serious adverse events**

A total of 16 serious adverse events occurred during the trial. There were two deaths (one stand-alone VR (1); blended VR (1)), five participants were admitted to an intensive care unit (ICU) (stand-alone VR (4); usual care (1)) and nine participants were hospitalised for non-ICU care (stand-alone VR (3); blended VR (2); usual care (4)). None of the serious adverse events were judged to be related to vestibular symptoms or the treatment interventions.

**DISCUSSION**

**Principal findings**

This three-armed randomised controlled trial provides strong evidence for the effectiveness of online VR in general practice for patients with a chronic vestibular syndrome. After three and six months, participants in both the stand-alone internet-based VR group and the blended internet-based VR group with physiotherapeutic support experienced significantly less vestibular symptoms than participants in the usual care group. They also experienced less dizziness-related impairment, less anxiety and more subjective improvement of vestibular symptoms. In the intention-to-treat-analysis the effects of stand-alone VR and blended VR were comparable. In a per protocol analysis that only included participants who adhered fully to the intervention, the treatment effects of stand-alone VR were notably better than the intention-to-treat-analysis. No serious adverse events related to either stand-alone or blended VR occurred during the trial. To conclude, in this trial stand-alone and blended VR show significantly better effects than usual care at three and six months on both the primary outcome measure and three out of four secondary outcome measures, which points to the robustness of these findings.

**Comparison with existing literature**

The positive effects of VR seen in this trial are in line with the results of previous VR randomised controlled trials in general practice.21, 22, 24, 60 Internet-based VR was previously investigated in only one RCT in general practice.24 The stand-alone intervention Balance Retraining, the English version of our online intervention Vertigo Training, significantly reduced vestibular symptoms and dizziness-related impairment compared to usual care in British patients aged 50 years and older.24 The adjusted mean difference at six months in the VSS-SF score in that trial was 2.3 points (95% CI 0.4 to 4.1), favouring the online intervention. Our trial confirms the effectiveness of stand-alone online VR in general practice. The larger difference we found in our stand-alone VR group (4.1 points; 95% CI 2.5 to 5.8) may be explained by better adherence to treatment (71% completed ≥ 1 session versus 61%) and a higher follow-up rate (87% versus 70%). Our trial was the first to assess the value of guidance in internet-based VR. Compared to usual care, blended VR was not different from stand-alone VR in our trial in terms of effectiveness, self-reported perceived barriers to adherence and actual adherence to the online intervention. In treating patients with stress, anxiety and depression, blended online interventions have shown benefits over stand-alone internet-based interventions.61-63 However, a review that examined blended internet-based interventions in chronic somatic disorders showed inconsistent effects.64 The optimal quantity (number of face-to-face sessions) and quality of guidance (type of therapist) in internet-based interventions is still unclear and may be dependent on the condition.65 The added value of support by a health care professional in chronic vestibular syndromes might be less than in anxiety or depressive disorders. In stand-alone VR, participants received automated emails to promote adherence and treatment was tailored to the participant’s vestibular symptoms, which might have been enough to encourage them to continue. Further research is needed to determine the added value of guidance in internet-based VR. A qualitative interview study and a prediction study, announced in the published study protocol,33 are still in progress. Interviews with blended VR participants will provide insights in participants’ experiences and a prediction rule may help to determine which type of patient will benefit most from therapeutic guidance.

**Strengths and limitations**

Our study has several strengths. The trial was well-powered, follow-up rates were high and participants displayed a good adherence to treatment interventions. The primary outcome measure we used, the VSS-SF, is an established patient-reported outcome measure42, 66 that has been used in a number of VR trials.21, 22, 24, 60 The pragmatic design of this trial with relatively broad inclusion criteria and no restrictions in usual care, allows GPs to directly apply the trial results in daily practice.

There were also some limitations. First, only a small percentage (<10%) of patients, who were invited to participate, enrolled in the trial which may represent a selection bias. 61% of invited participants did not respond to our invitation. The low uptake may partly be caused by inviting patients who visited their GP for vestibular symptoms in the last two years. Since 60% of patients who declined to participate (Figure 1) reported that they no longer experienced vestibular symptoms, this may also be true for a large proportion of non-responders. In 10% of patients the reason for declining participation was that they had no access to a computer or the internet. When we compared our trial sample to vestibular subgroup data from representative Dutch general practice studies on dizziness,8, 54 our participants were more often men, and the group aged 85 years and older was underrepresented. Lastly, patients motivated to treat their vestibular symptoms with exercises may have been more likely to participate in the trial, which should be taken into account for implementation in daily general practice.

Secondly, we chose to include participants with a chronic vestibular syndrome, and not with a specified vestibular disorder. The effectiveness for vestibular rehabilitation was first shown in selected populations with various vestibular disorders including BPPV, vestibular neuritis, Menière’s disease, unilateral and bilateral vestibulopathy.14, 37, 67, 68 This formed the basis for later VR trials that applied a syndrome-based approach to include patients who experienced symptoms related to these disorders.21, 22, 24 These studies showed that VR can be effective when applied in patients with a syndrome diagnosis, which is important for general practice where a final vestibular diagnosis may not be available. In our trial 66% of participants reported that they were never diagnosed with a specific vestibular disorder. Previous studies in general practice have shown that GPs record a symptom diagnosis in one third of all patients who present with vertigo or dizziness. 8, 54 As we endorse the importance of a specific vestibular diagnosis in general practice, all participating GPs received a written instruction to diagnose and treat vestibular symptoms according to the Dutch guideline18 and all participants received usual care without restrictions. Nevertheless, the absence of a specific vestibular diagnosis should not be a reason to withhold patients VR when a chronic vestibular syndrome is present. We acknowledge that including participants with chronic vestibular syndromes instead of specified vestibular disorder diagnoses entailed a higher risk of diagnostic uncertainty. However, we believe that VR is a low-risk therapy, which according to the ICVD makes a lower level of diagnostic certainty acceptable.10 Since over 80% of patients with vestibular symptoms are treated by GPs without referral to secondary care,6-8 using a syndrome diagnosis over a disorder diagnosis may increase the uptake of VR because it is more applicable to daily general practice.
Thirdly, stand-alone and blended VR were compared to usual care, which is an inactive comparator group. In pragmatic trials it is common to use usual care as a control group to maximise applicability of the results of the trial in daily practice.69 Nevertheless, not providing any experimental treatment to participants in the usual care group could have affected the results. Unfortunately, it was not possible to blind participants to this exercise-based treatment. Therefore, the difference in treatment effects between the intervention groups and usual care might be partly explained by including an “inactive” control group. In Menière’s disease patients with chronic vestibular symptoms, booklet-based VR has been compared to both an inactive control group and an active control group where participants received a booklet to teach them how to control their symptoms.37 Compared to the inactive control group in this trial, both vestibular symptoms (VSS-SF) and impairment due to dizziness (DHI) decreased in the VR group and only impairment due to dizziness decreased in the active control group. Also, previous trials have shown that improvement in subjective, patient-reported outcomes after VR are accompanied by improvements in objective measures of balance function.14, 22, 70 Therefore, it is unlikely that the findings of our study are explained solely by providing any form of experimental treatment.

Fourthly, the absence of serious adverse events related to online VR indicates this treatment is safe to use in general practice, but harms may have been underreported. Participants were asked about adverse reactions at three and six month follow-up, and were encouraged to report these directly to the trial team. Since contact with the trial team during the trial was minimal, participants might have forgotten to mention some harmful side effects. Because our results are consistent with previous VR studies where serious adverse events were also absent, 14, 24 online VR can probably be considered to be a safe form of treatment.

**Conclusions and implications for research and/or practice**

Internet-based VR is a safe and effective treatment for patients of 50 years and older with a chronic vestibular syndrome. Although further research is needed to determine if certain participants may benefit more from either stand-alone or blended VR, this trial shows that both forms of internet-based VR can reduce vestibular symptoms. By providing GPs with an easily accessible, low-cost form of treatment, online VR has the potential to substantially improve care for a largely undertreated group of patients with a chronic vestibular syndrome in general practice.

**ADDITIONAL INFORMATION**

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**Competing interests**

All authors have completed the [Unified Competing Interest form](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare: support from The Netherlands Organisation for Health Research and Development (ZonMw) for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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**Ethical approval**

The study protocol was approved by the Medical Ethics Committee of the VU University

Medical Center. All participants included in the study provided written informed consent.

**Data sharing**

De-identified individual participant data and data analysis plan available from the corresponding author on reasonable request.

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**Transparency declaration**
Vincent van Vugt affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

**Contributors**
Contributors: ORM obtained the funding and coordinated the study. ORM, VAvV, JCvdW, HEvdH and LY were involved in the design of the study. RE and LY advised in the development of the Vertigo Training treatment intervention. VAvV collected the data. VAvV and JWRT analysed the data. VAvV wrote the first substantial draft of the article and is the guarantor. ORM, JCvdW, RE, LY, HEvdH and JWRT critically revised the manuscript. All authors read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

**Table 1. Baseline characteristics. Figures are numbers (percentages) unless stated otherwise.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Stand-alone VR (N=98) | Blended VR (N=104) | Usual care (N=120) | Total sample (N=322) |
| Mean (SD) age (years) | 66.7 (9.5) | 67.4 (9.8) | 67.0 (9.4) | 67.0 (9.5) |
| Female | 64 (65) | 69 (66) | 64 (53) | 197 (61) |
| Level of education |  |  |  |  |
|  | Low | 33 (34) | 37 (36) | 36 (30) | 106 (33) |
|  | Middle | 25 (26) | 31 (30) | 30 (25) | 86 (27) |
|  | High | 40 (41) | 36 (35) | 54 (45) | 130 (40) |
| Living situation |  |  |  |  |
|  | Alone | 34 (35) | 33 (32) | 35 (29) | 102 (32) |
|  | With partner | 64 (65) | 71 (68) | 85 (71) | 220 (68) |
| Number of chronic diseases\* |  |  |  |  |
|  | 0 | 59 (60) | 64 (62) | 63 (53) | 186 (58) |
|  | 1 | 28 (29) | 32 (31) | 41 (34) | 101 (31) |
|  | 2 | 8 (8) | 4 (4) | 12 (10) | 24 (7) |
|  | ≥3 | 3 (3) | 4 (4) | 4 (3) | 11 (3) |
| Time since vestibular diagnosis\*\* |  |  |  |  |
|  | One to six months | 15 (15) | 22 (21) | 13 (11) | 50 (16) |
|  | Six months to two years | 28 (29) | 27 (26) | 39 (33) | 94 (29) |
|  | Two years to 10 years | 31 (32) | 44 (42) | 48 (40) | 123 (38) |
|  | More than 10 years | 23 (24) | 11 (11) | 18 (15) | 52 (16) |
| Self-reported vestibular diagnosis\*\*  |  |  |  |  |
|  | No known diagnosis | 67 (68) | 69 (66) | 77 (64) | 213 (66) |
|  | BPPV | 11 (11) | 17 (16) | 22 (18) | 50 (16) |
|  | Menière’s disease | 9 (9) | 9 (9) | 10 (8) | 28 (9) |
|  | Vestibular neuritis | 6 (6) | 4 (4) | 7 (6) | 17 (5) |
|  | PPPD | 0 (0) | 1 (1) | 0 (0) | 1 (0) |
|  | Other^ | 4 (4) | 4 (4) | 2 (2) | 10 (3) |
| Panic disorder, generalised anxiety disorder or major depressive disorder at baseline according to PHQ | 14 (14) | 16 (15) | 23 (19) | 53 (17) |
|  | Panic disorder | 2 (2) | 3 (3) | 5 (4) | 10 (3) |
|  | Generalised anxiety disorder | 12 (12) | 15 (14) | 19 (16) | 46 (14 |
|  | Major depressive disorder | 5 (5) | 6 (6) | 9 (8) | 20 (6) |

\* Chronic diseases included chronic non-specific lung disease, cardiac disease, peripheral arterial disease, stroke, diabetes mellitus, arthritis and cancer.
\*\* Data on this variable missing for three participants (N=1 stand-alone VR; N=2 usual care).

^ Other diagnoses reported by patients consisted of traumatic brain injury, cerebrovascular accident, Parkinson’s disease, bacterial meningitis and vestibular organ surgical procedures.

VR = vestibular rehabilitation; BPPV = benign paroxysmal positional vertigo; PPPD = persistent postural-perceptual dizziness

**Table 2. Comparison of primary outcome between treatment groups.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Treatment group (mean score (standard deviation))** | **Comparison (crude mean difference (95% CI))\*\*\*** | **Comparison (adjusted mean difference (95% CI))\*\*\*\*** |
|  | **Stand-alone VR**  | **Blended VR** | **Usual care**  | **Stand-alone VR versus usual care** | **Blended VR versus usual care** | **Stand-alone VR versus usual care** | **Blended VR versus usual care** |
| **VSS-SF (intention-to-treat)\*** | *N=98* | *N=104* | *N=120* | *N=218* | *N=224* | *N=218* | *N=224* |
|  | Baseline | 14.1 (8.9) | 13.8 (8.3) | 13.2 (8.6) | **-** | **-** | **-** | **-** |
|  | 3 months | 8.1 (7.4) | 8.6 (7.1) | 11.5 (9.9) | -4.2 (-5.9 to -2.5) | -3.9 (-5.5 to -2.2) | -4.3 (-5.9 to -2.6) | -3.9 (-5.5 to -2.3) |
|  | 6 months | 7.5 (7.8) | 8.7 (6.9) | 10.9 (9.3) | -4.0 (-5.8 to -2.3) | -3.5 (-5.1 to -1.8) | -4.1 (-5.8 to -2.5) | -3.5 (-5.1 to -1.9) |
|  |
| **VSS-SF (per- protocol)\*\*** | *N=47* | *N=55* | *N=120* | *N=167* | *N=175* | *N=167* | *N=175* |
|  | Baseline | 13.2 (6.2) | 15.0 (8.6) | 13.2 (8.6) | **-** | **-** | **-** | **-** |
|  | 3 months | 6.0 (4.0) | 10.0 (8.0) | 11.5 (9.9) | -6.0 (-8.1 to -4.0) | -3.4 (-5.3 to -1.4) | -6.0 (-8.0 to -3.9) | -3.3 (-5.2 to -1.4) |
|  | 6 months | 5.9 (5.0) | 9.4 (7.4) | 10.9 (9.3) | -5.4 (-7.5 to -3.4) | -3.6 (-5.6 to -1.7) | -5.4 (-7.4 to -3.4) | -3.5 (-5.5 to -1.6) |

\* All participants analysed according to allocation.
\*\* Only stand-alone VR participants analysed who completed all six online sessions, and blended VR participants who completed all six online sessions and both physiotherapist visits.
\*\*\* Adjusted for baseline values and repeated measurements within participants.
\*\*\*\* Adjusted for baseline values, repeated measurements within participants, age (1), gender (2), level of education (3), living situation (4), number of chronic diseases (5), time since vestibular diagnosis (6) and the presence of a panic disorder, generalised anxiety disorder or major depressive disorder at baseline (7).
VR = vestibular rehabilitation; VSS-SF = Vertigo Symptom Scale Short-Form (VSS-SF), range 0-60, clinically relevant difference 3 points.

**Table 3. Comparison of secondary outcomes between treatment groups.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Treatment group (mean score (standard deviation))** | **Comparison (crude mean difference (95% CI))\*** | **Comparison (adjusted mean difference (95% CI))\*\*** |
|  | **Stand-alone VR**  | **Blended VR** | **Usual care**  | **Stand-alone VR versus usual care** | **Blended VR versus usual care** | **Stand-alone VR versus usual care** | **Blended VR versus usual care** |
| **DHI** |  |  |  |  |  |  |  |
|  | Baseline | 34.8 (18.5) | 36.0 (21.9) | 35.8 (19.9) | **-** | **-** | **-** | **-** |
|  | 3 months | 24.4 (20.8) | 26.4 (20.6) | 29.2 (21.1) | -4.5 (-8.1 to -0.8) | -3.9 (-7.5 to -0.3) | -4.6 (-8.2 to -1.1) | -3.9 (-7.4 to -0.4) |
|  | 6 months | 21.5 (20.4) | 25.4 (21.6) | 27.6 (21.5) | -4.7 (-8.4 to -1.1) | -4.4 (-8.0 to -0.8) | -4.9 (-8.4 to -1.3) | -4.5 (-8.0 to -0.9) |
| **GAD-7** |  |  |  |  |  |  |  |
|  | Baseline | 3.7 (4.6) | 4.0 (4.3) | 4.5 (4.8) | **-** | **-** | **-** | **-** |
|  | 3 months | 3.1 (3.8) | 2.9 (3.4) | 4.5 (5.0) | -1.0 (-1.9 to -0.1) | -1.3 (-2.2 to -0.5) | -1.1 (-1.9 to -0.3) | -1.4 (-2.2 to -0.6) |
|  | 6 months | 2.6 (3.3) | 2.7 (3.5) | 4.2 (5.0) | -1.1 (-1.9 to -0.2) | -1.1 (-2.0 to -0.3) | -1.2 (-2.0 to -0.4) | -1.2 (-2.0 to -0.4) |
| **PHQ-9** |  |  |  |  |  |  |  |
|  | Baseline | 4.5 (4.7) | 5.4 (4.5) | 5.9 (5.4) | **-** | **-** | **-** | **-** |
|  | 3 months | 4.2 (4.2) | 4.3 (4.2) | 5.3 (5.0) | -0.3 (-1.3 to 0.6) | -0.9 (-1.8 to 0.0) | -0.5 (-1.4 to 0.4) | -0.9 (-1.8 to 0.0) |
|  | 6 months | 3.5 (4.3) | 4.0 (3.7) | 4.9 (5.1) | -0.5 (-1.4 to 0.5) | -0.8 (-1.7 to 0.2) | -0.6 (-1.5 to 0.3)  | -0.8 (-1.7 to 0.1) |
|  |
|  | **Intervention(Patient-reported improvement, No. (%))** | **Comparison (crude odds ratio (95% CI))^ \*** | **Comparison (adjusted odds ratio (95% CI))^ \*\*** |
|  | **Stand-alone VR**  | **Blended VR** | **Usual care**  | **Stand-alone VR versus usual care** | **Blended VR versus usual care** | **Stand-alone VR versus usual care** | **Blended VR versus usual care** |
| **Subjective improvement**  |  |  |  |  |  |  |  |
|  | 3 months | 49/91 (54%) | 54/97 (56%) | 39/107 (36%) | 2.1 (1.2 to 3.6) | 2.2 (1.2 to 3.8) | 2.2 (1.2 to 4.1)  | 2.1 (1.2 to 3.8) |
|  | 6 months | 46/87 (53%) | 48/93 (52%) | 43/110 (39%) |

All analyses reported in this table were performed on an intention-to-treat basis with participants analysed according to allocation.
\*Adjusted for baseline values and repeated measurements within participants.
\*\* Adjusted for baseline values, repeated measurements within participants, age (1), gender (2), level of education (3), living situation (4), number of chronic diseases (5), time since vestibular diagnosis (6) and the presence of a panic disorder, generalised anxiety disorder or major depressive disorder at baseline (7).
**^** Comparison of overall effect over six months follow-up period.
VR = vestibular rehabilitation; DHI = Dizziness Handicap Inventory, range 0-100; GAD-7 = measure for anxiety symptom severity, range 0-21; PHQ-9= measure for depressive symptom severity, range 0-27; Subjective improvement = dichotomous evaluation of vestibular symptoms compared to baseline measurement: improved or not improved (i.e. worse or the same).

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