Depression in Visual Impairment Trial (DEPVIT): A Randomized Clinical Trial of Depression Treatments in People With Low Vision

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Submitted: February 15, 2016
Accepted: June 9, 2016

Citation: Nollett CL, Bray N, Bunce C, et al. Depression in visual impairment trial (DEPVIT): a randomized clinical trial of depression treatments in people with low vision. *Invest Ophthalmol Vis Sci*. 2016;57:4247–4254. DOI:10.1167/iovs.16-19345

Purpose. The purpose of this study was to compare two interventions for depression, problem solving treatment (PST) and referral to the patient's physician, with a waiting-list control group in people with sight loss and depressive symptoms.

Methods. This was an assessor-masked, exploratory, multicenter, randomized clinical trial, with concurrent economic analysis. Of 1008 consecutive attendees at 14 low-vision rehabilitation centers in Britain, 43% ($n = 430$) screened positive for depressive symptoms on the Geriatric Depression Scale and 85 of these attendees participated in the trial. Eligible participants were randomized in the ratio 1:1:1 to PST, referral to their physician, or a waiting-list control arm. PST is a manualized talking intervention delivered by a trained therapist who teaches people over six to eight sessions to implement a seven-step method for solving their problems. Referral to the physician involved sending a referral letter to the person's physician, encouraging him or her to consider treatment according to the stepped care protocol recommended by the U.K.'s National Institute of Health and Care Excellence. The primary outcome was change in depressive symptoms (6 months after baseline) as determined by the Beck Depression Inventory.

Results. At 6 months, Beck Depression Inventory scores reduced by 1.05 (SD 8.85), 2.11 (SD 7.60), and 2.68 (SD 7.93) in the waiting-list control, referral, and PST arms, respectively. The cost per patient of the PST intervention was £1176 in Wales and £1296 in London.

Conclusions. Depressive symptoms improved most in the PST group and least in the control group. However, the change was small and the uncertainty of the measurements relatively large.

Keywords: low vision, depression, clinical trial, mental health, intervention

A growing body of evidence suggests that low vision is associated with depression. Results from several studies in North America suggest that the prevalence of depression and depressive symptoms in those accessing visual rehabilitation centers ranges from 22% to 38%.[1–4] Untreated depression has a profound negative impact on quality of life and reduces life expectancy.[5–7] What is less clear, however, is how to treat the depressive symptoms in this vulnerable group.

In otherwise healthy adults, about 50% of those who receive psychological treatments or antidepressants recover fully.[8,9] However, the effects of depression treatment in people with chronic health conditions are somewhat less clear. For example, a recent meta-analysis of psychological interventions for depression in people with coronary heart disease concluded that although psychological treatments work, the effects are only small (typical effect size 0.3).[10]

A myriad of psychological interventions have been developed for depression, but perhaps the best known and most useful approaches in the context of those with chronic health problems are cognitive behavioral therapy (CBT), behavioral

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activation (BA), and problem-solving treatment (PST).[10–13] Antidepressant drugs are not recommended for the treatment of subthreshold depressive symptoms or mild depression in people with chronic health problems.[7] However, they may be of value in those with long-standing subthreshold symptoms or a past history of moderate or severe depression.[7]

In those with sight problems and depression, there is some evidence that psychological treatments for depression work. For example, in a clinical trial comparing PST to usual care in people with age-related macular degeneration (AMD), PST halved the incidence of a depressive disorder at 2 months, although the effect had reduced by 6 months.[14] Recently, the Low Vision Depression Prevention Trial, which studied AMD patients with subthreshold depressive symptoms, showed that BA combined with occupational therapy halved the incidence of depressive disorders at 4 months.[15]

In the United States, access to mental health care services has been improved by the Affordable Care Act and expansion of Medicaid, particularly for those most in need.[16,17] In Britain, mental health care is provided by the National Health Service (NHS) and accessed via the patient's physician. Within the NHS, the treatment of people with chronic health problems and depressive symptoms is supposed to adhere to the detailed guidelines published by the National Institute for Health and Care Excellence (NICE).[7]

To obtain data on the effectiveness of a manualized PST intervention and a pragmatic referral to the physician to invoke the NHS's stepped care approach to depression treatment, we established the Depression in Visual Impairment Trial (DEPVIT).

DEPVIT sought to establish the prevalence of significant depressive symptoms in people attending visual rehabilitation centers in Britain and undertake an exploratory trial to find out if PST or physician referral were effective at reducing depression in people with impaired vision and significant depressive symptoms.

Methods

The methods for DEPVIT have been previously described in detail.[18] In brief, the study was a multicenter, individually randomized, parallel group, exploratory clinical trial. Two interventions, PST and physician referral, were evaluated alongside a waiting-list control. All participants had a follow-up low-vision appointment 6 weeks after the initial low-vision assessment.

Eligible participants were adults (aged 18 and older) attending participating low-vision centers (two hospitals in London and 12 primary care clinics in South Wales) who scored ≥ 6 on the Geriatric Depression Scale (GDS-15).[19] To ensure the applicability of the results to the target population, exclusion criteria were kept to a minimum. We excluded those who (1) had a low-vision assessment within the previous 12 months, (2) were referred to the clinic in error, (3) were already receiving depression treatment, (4) were unable to understand English, (5) were unable to use the telephone as a result of poor hearing, (6) had a severe medical illness that would preclude participation, (7) reported suicidal ideation, (8) were outside the catchment area, or (9) screened positive for significant cognitive/memory problems. The trial followed the tenets of the Declaration of Helsinki and was approved by the NHS National Research Ethics Service (11/WA/0014) and an independent trial steering committee provided study oversight. The trial was registered prior to recruitment of the first participant (ISRCTN registry no. 46824140).

The PST implemented in this trial was a brief manualized cognitive behavioral therapy based on that used by Rovner et al.[14] Trained psychological therapists worked with participants on an individual basis in their own home or at one of the research centers to teach them a seven-step method for approaching and solving their problems. The only differences between the intervention studied here and that in the original publication were that the intervention also included large-print self-help materials on depression and a list of vision-related organizations. The optometrists providing the low-vision assessment also shared the patient's treatment plan with the therapist via a brief report so that the therapist could help the patient implement the optometrist's recommendations via the PST framework if these were problems that the participant wanted to address.

To ensure standardization, all three therapists delivering PST undertook rigorous training and certification before seeing trial participants. All PST sessions were recorded and a random sample was reviewed for fidelity purposes.

The referral condition consisted of a standardized letter (letter 1) sent to the participant's physician within 2 weeks of randomization. It informed the physician that their patient had screened positive for significant depressive symptoms and asked them to offer treatment according to NICE guidelines.[7] The letter was sent by the research team but appeared to come from the participant's optometrist. This strategy was used to mask the fact that the participant was in a research study, which may have altered the physicians' behavior. Physicians were informed about their patients' participation in this trial 6 months after randomization and asked for information about any depression treatments offered to the patient during this period. This was a pragmatic intervention that aimed to determine the impact of a typical referral, not specifically the stepped care approach to depression treatment recommended by the NICE guidelines. The recommended stepped care approach provides a framework in which to provide services where the least intrusive, most effective intervention is provided first. If patients do not respond to the intervention offered initially, the treatment is stepped up to the next level.

Participants in the waiting-list control arm received no intervention other than the 6-week follow-up low-vision assessment.

Any participant who reported severe symptoms (a Beck Depression Inventory [BDI-II] score of 29 or more) at baseline or follow-up was referred to their physician for a medication review using a standardized medication referral letter (letter 2).

The primary outcome was change in depressive symptoms from baseline to 6 months as measured by the BDI-II. Secondary outcomes included (1) change in BDI-II baseline to 3 months and 3 to 6 months; (2) change in visual disability since baseline interview, as measured by the seven-item National Eye Institute Visual Function Questionnaire (NEI VFQ); (3) change in near-visual function as measured using the near-vision subscale of the Visual Function Questionnaire (VFQ-48); (4) change in generic health-related quality-of-life as measured by the EuroQol five dimensions questionnaire (EQ-5D); and (5) the proportion of participants screening positive for depression at 6 months using GDS-15.

The randomization sequence was created by the senior data manager using permuted blocks of varying sizes and was concealed from the optometrists enrolling participants and the researchers who obtained the outcomes via telephone interview. The chief investigator (CI) consulted the allocation sequence and assigned participants to the next available allocation.

As a result of the nature of the interventions, participants were aware of their treatment assignment. The therapists were aware which participants were assigned to PST; the GPs were unaware that the participant was in a trial so as not to bias their actions, and the optometrists were masked to treatment

assignment but may have been unmasked through discussions with the participant, although this was actively discouraged. Outcome assessors were masked and reminded participants at the beginning of each outcome assessment not to discuss allocation. All masking violations were recorded and the assessors were asked to guess each participant's allocation before the 6-month interview.

DEPVIT included a concurrent health economic analysis to determine the cost of the intervention and the overall health and social care service use costs of participants in the trial. Measurement and analysis of costs was undertaken from a multiagency public-sector perspective. Local authority and NHS service use costs were collected at baseline and 6 months using the Client Service Receipt Inventory.[20] Service use costs were determined using published national unit costs.[21,22] All costs are reported in £ Sterling for 2013. Mean differences in cost per patient were calculated for the different types of service use, and 95% confidence intervals were estimated using nonparametric bootstrapping methods, run on 5000 iterations.

Service use and related costs for both the intervention and control arms were collected using the Client Service Receipt Inventory. Intervention costs for the PST intervention were collected using cost diaries completed by the therapists. Using employer data, therapist salary for South Wales was costed at £39 per hour (including on-costs and overheads) and estimated to be £49 per hour for London. Mileage was calculated at £0.67 per mile.[21] Because of the more rural nature of South Wales, average mileage per session was reduced by 25% for London.

A statistical analysis plan was developed before the study started, and a dedicated Microsoft Access database (Microsoft Corp., Redmond, WA, USA) was constructed. Trial data was double entered, and all data queries were resolved.

At the outset there were no data on people with sight loss and significant depressive symptoms on which to power the clinical trial component of the study, and hence DEPVIT was an exploratory study. However, working on the assumption that participants with a mean BDI-II score of 30 (SD 10.5) would enter the trial and that 60 would provide outcome data at the 6-month outcome point, the study had 83% power to detect a moderately large clinically important 10-point reduction in depressive symptoms at the 5%, two-sided significance level. The trial analysis was undertaken on an intent-to-treat basis based on an available case analysis.

The GDS-15, BDI-II, and EQ-5D surveys were scored traditionally to ensure that the scores would be comparable with other studies using these measures. The seven-item NEI VFQ and near-vision subscales of the VFQ 48 were scored using Rasch analysis implemented with Winsteps version 3.58.1 (Linacre, Chicago, IL, USA).

Baseline characteristics were summarized using means and standard deviations for continuous (Gaussian) variables and medians with interquartile ranges for non-Gaussian continuous variables. Categorical variables were summarized as numbers and percentages. Although the study was not powered to detect significant differences, we provide 95% confidence intervals with treatment effect estimates.[23–25]

Results

In total, 1008 consecutive patients were screened for eligibility. Of these, 430 (43%, 95% CI 40%–46%) screened positive for significant depressive symptoms (GDS-15 $\geq$6). Of those who screened positive, 75% were not receiving any treatment for their depressed mood.

A total of 85 people with significant depressive symptoms took part in the clinical trial. Figure 1 depicts the CONSORT flow diagram and identifies the reasons for excluding people.

Table 1 describes the demographic characteristics by treatment assignment.

Table 2 shows the primary and secondary outcomes by treatment group. At 6 months, depressive symptoms had reduced in all three arms. In the waiting-list control arm, depressive symptoms were reduced by −1.05 (95% CI −4.33 to 2.23), in the referral arm by −2.11 (95% CI −4.98 to 0.76), and in the PST arm by −2.68 (95% CI −6.00 to 0.63). In all cases, the 95% CI spanned zero, suggesting that change was not significant at the 5% level.

Post hoc analyses suggest that depressive symptoms reduced most in those with moderate to severe depressive symptoms at baseline, that is, a BDI-II > 20. Specifically, in the waiting-list control, referral, and PST arms, depressive symptoms reduced by −2.4, −5.0, and −6.1, respectively, in those with moderate to severe depression at baseline, and by only 0.3, 2.3, and −0.3, respectively, in those with mild or minimal symptoms at baseline.

At 6 months, the proportion of people still screening positive for depression according to the GDS-15 had decreased to 33.3% (95% CI 15.5–51.1), 38.5% (95% CI 19.8–57.2), and 40.9% (95% CI 20.4–61.5) of those in the waiting-list, referral, and PST arms, respectively.

Table 3 summarizes the action taken by physicians in response to the referral letters. Letter 1 was for those in the referral arm. Letter 2 was used to refer all those who had severe depressive symptoms (BDI-II >29). Of the physicians who responded (32 of 36), approximately 65% indicated that they had at least met the patient, and 25% of patients were offered antidepressants.

On average, South Wales participants received 6.15 PST sessions (SD 1.21), lasting an average of 1.37 hours (SD 0.41). Allowing for travel time, the total estimated therapist time was 3.48 hours per session (SD 1.12), giving an average cost per session of £196 in Wales and £216 for London.

Table 4 summarizes the health and social care service use costs in each study group for 6 months. The total health and social care costs, excluding the cost of the interventions, incurred by those in the waiting-list, referral, and PST arms of the trial during the 6-month study period were £1444 (SD £1941), £1362 (SD £1842), and £962 (SD £1051), respectively.

Of the PST recordings, 16% were randomly selected and reviewed by D.S. using the PST Therapist Adherence and Competence Scale to ensure fidelity of the intervention.[26] The therapist in Wales received an average score of 4/5, indicating that the sessions delivered were rated as good. The first therapist in London conducted only four sessions and was not reviewed. The second therapist received an average rating of 3.3/5, indicating that the sessions were satisfactory to good.

The researchers were inadvertently unmasked by comments made by participants during 6.8% of interviews, and the researcher guessed the allocation arm correctly in another 41.9% of cases, that is, only a little higher than by chance alone.

Participants in the waiting-list control group were asked to refrain from consulting their physician for depression until after the 6-month interview. Despite this, two participants, one in Wales and one in London, received depression treatment from their physicians by 6 months.

Two adverse events were reported, and one was considered to be related to their prescribed treatment: the participant experienced dizziness and fell after taking newly prescribed antidepressant medication. Ten serious adverse events were reported during the trial, but none were related to the trial.

One participant in the control group reported suicidal ideation during the 3-month outcome assessment. As per protocol, he was withdrawn from the trial and urgently referred to his physician.

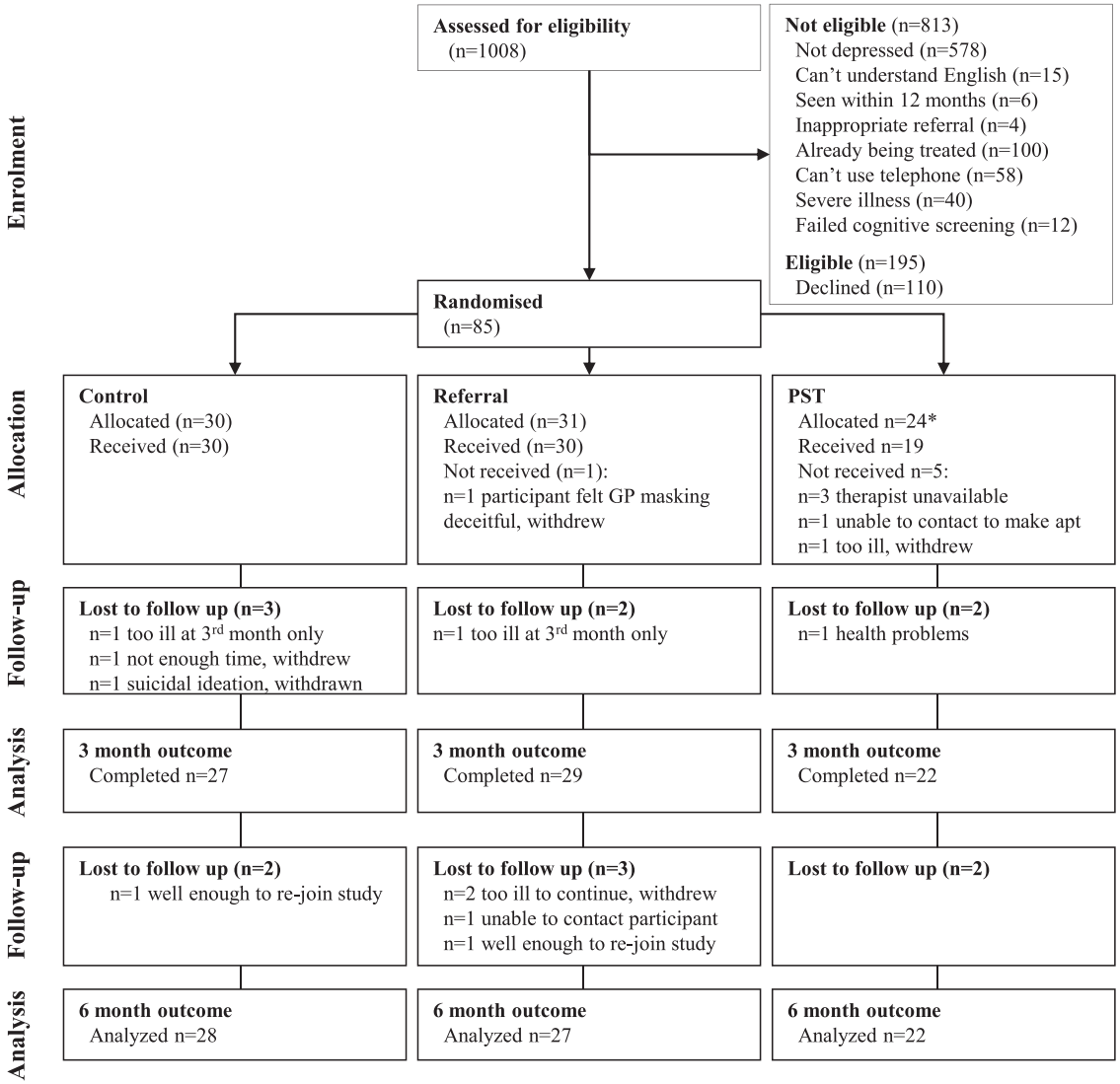

Figure 1. CONSORT flow diagram. *The delivery of PST in London was problematic. The original therapist resigned after having seen just 3 patients. It then took approximately 9 months to recruit and train a replacement therapist. After several visits to participants' houses, the second therapist reported feeling intimidated by some of the locations that were visited. A volunteer was found to accompany the therapist, but after two more sessions the therapist resigned. It was too late in the trial to recruit a third therapist, so the decision was made to skip all future PST allocations in the London area only. Hence the relatively low number of people assigned to PST.

Table 1. Baseline Participant Characteristics

Characteristic	Waiting List (n = 30)	Referral (n = 31)	PST (n = 24)
Gender, n (%)			
Female	14 (46.7)	20 (64.5)	16 (66.7)
Male	16 (53.3)	11 (35.5)	8 (33.3)
Age			
Mean years (SD)	72.3 (13.1)	67.1 (19.6)	71.8 (16.7)
Ethnicity, n (%)			
Asian/Asian British	1 (3.3)	1 (3.2)	1 (4.2)
Black/Black British	4 (13.3)	10 (32.3)	1 (4.2)
Other ethnic group	0 (0.0)	1 (3.2)	0 (0.0)
White	25 (83.3)	19 (61.3)	22 (91.7)
Depressive symptoms			
Baseline GDS-15 (SD)	10.1 (2.9)	9.5 (2.9)	9.1 (2.7)

Discussion

Those randomized to receive PST experienced the greatest reduction in depressive symptoms, and those in the waiting list the least, but the results were not compelling. The study suggests that neither active intervention would reduce depression by the minimal clinically important difference, although both did appear better than current standard care. Working on the basis of the primary outcome measure results alone, power calculations suggest that we would need a sample size of > 400 participants per arm to be reasonably confident of demonstrating a statistically significant difference between participants on the waiting list and those in receipt of PST.

So why was PST not more effective? One possibility is that this intervention was not well matched with the sample studied. The inclusion criteria were wide ranging; DEPVIT included people with mild, moderate, and severe depressive symptoms. A post hoc analysis suggested that those with

Table 2. Primary and Secondary Outcomes

Outcome Measure	Waiting List	Referral	PST
Depressive symptoms (BDI-II)			
Mean baseline value (SD)	20.30 (10.33)	21.06 (7.61)	19.04 (10.62)
Change from baseline to 3 months (SD)	−2.83 (10.38)	−1.14 (8.49)	−2.27 (5.81)
Change from baseline to 6 months (SD)	−1.05 (8.85)	−2.11 (7.60)	−2.68 (7.94)
Screening positive at 6 months (GDS-15)	33.3%	38.5%	40.9%
Reading ability (LV VFQ-48)			
Mean baseline value (SD)	−1.20 (1.64)	−1.02 (1.96)	−0.83 (1.52)
Change from baseline to 3 months (SD)	0.17 (1.35)	−0.05 (1.05)	−0.10 (1.78)
Change from baseline to 6 months (SD)	−0.09 (1.79)	−0.08 (1.17)	−0.09 (1.67)
Visual disability (seven-item NEI-VFQ)			
Mean baseline value (SD)	0.90 (1.35)	0.43 (1.88)	0.52 (1.39)
Change from baseline to 3 months (SD)	−0.25 (1.26)	0.19 (1.21)	0.13 (1.58)
Change from baseline to 6 months (SD)	−0.34 (1.68)	0.22 (0.99)	0.35 (1.51)
Health status (EQ-5D)			
Mean baseline value (SD)	0.47 (0.32)	0.43 (0.40)	0.43 (0.34)
Change from baseline to 3 months (SD)	0.02 (0.26)	0.03 (0.25)	−0.07 (0.23)
Change from baseline to 6 months (SD)	0.02 (0.37)	−0.34 (0.29)	−0.07 (0.29)

Mean change in depressive symptoms at 3 and 6 months, proportion screening positive for depression at 6 months (GDS-15 score of 6 or more), mean change in near reading ability (Near Vision subscale of the LV VFQ-48), and mean change in visual disability (seven-item NEI-VFQ). Both sets of results are in logits, but the scales work in different directions. More positive scores on the LV VFQ 48 indicate greater ability. More positive scores on the seven-item NEI-VFQ indicate greater disability; mean change in health status (EQ-5D).

moderate to severe depressive symptoms at baseline (BDI-II score $\geq$20) derived the greatest benefit from the active treatment interventions. Hence, we may have observed larger effects had we included only those with moderate to severe symptoms at baseline.

Another possible explanation for the apparent lack of effectiveness is that PST was not delivered as intended. The fidelity check of audio recording suggests that PST delivery in Wales was good and in London satisfactory to good. However, in Wales it was not possible to deliver PST as per protocol in 30% of cases, and in London only one person allocated to PST received it as described in the protocol. In Wales, the main barrier to the per-protocol delivery of PST was participant health. In London, a range of problems were experienced. The first therapist was very experienced but resigned abruptly citing unacceptable travel times to participants' homes as being an issue. The second therapist was less experienced and found the delivery of PST challenging. She reported several problems: some participants denied having problems and therefore felt that PST was inappropriate; the emotional and psychological issues could be overwhelming, and this made it difficult to stick to the manualized intervention; communicating with people whose first language was not English was problematic; and the therapist felt physically vulnerable in some of the more deprived parts of South London. The second therapist in London resigned 15 months after the trial started. When it became clear that there was no possibility of delivering PST as intended, the trial management group agreed to close this arm of the trial in London.

Table 3. Physician's Responses to Referral Letters

Action Taken by Physician	Referral Letter 1, % (*n*)	Referral Letter 2, % (*n*)
Patient offered medication	12.9 (4)	60 (3)
Patient offered other	19.4 (6)	20 (1)
Patient offered medication and other	12.9 (4)	
Appointment with physician but no treatment	9.7 (3)	
Offered appointment but patient declined	3.2 (1)	20 (1)
No appointment	6.5 (2)	
Did not receive letter	22.6 (7)	
No response from physician	12.9 (4)	
Total	100 (31)	100 (5)

Two types of letters were sent to physicians during the trial. Referral letter 1 was a carefully crafted letter and was the intervention in the referral arm of the trial. The trial was stratified for severe/not severe depressive symptoms (BDI-II score of 29 or more). For all of those with severe depressive symptoms in any arm of the trial, referral letter 2 was sent to the physician. This letter indicated that the patient had severe depressive symptoms and requested a medication review.

Another explanation is that PST is just not very effective at reducing depressive symptoms over longer follow-up periods such as 6 months. In the original study by Rovner et al.,[14] positive effects were reported at 2 months, but they were substantially diminished by 6 months. That study did suggest that booster treatments for all PST participants may be beneficial. Had we modified the PST intervention in this way, it is possible that more positive effects would have been observed at 6 months.

Referring people to their physician was a pragmatic intervention. It represented the most likely course of action for those delivering rehabilitation services who discover that one of their patients is depressed. At the conclusion of the trial, we asked both the participants and their physicians about any treatments received. Of the 36 referrals to the physicians, we were unable to get a response from four physicians, and seven said that they did not receive the referral letter. Clearly, although the physician's contact details were cross checked with the practice website at the time the referral letter was sent, communication breakdown between the referral center and the physician is a distinct possibility. A phone call to check

Table 4. Mean NHS and Local Authority Costs (£) Over 6 Months by Group

Health Care Service Use	Control ($n = 27$)*	GP Referral ($n = 26$)*	PST ($n = 22$)*	PST vs. Control†	PST vs. GP Referral†
Total primary care	192 (303)	169 (137)	214 (222)	22 (−124 to 162)	45 (−48 to 158)
GP consultations (surgery)	156 (271)	138 (129)	122 (119)	−34	−16
GP consultations (home)	10 (32)	4 (14)	49 (209)	39	45
Practice nurse consultations	25 (58)	24 (76)	43 (67)	18	19
Primary care antidepressant prescribing	1 (4)	3 (11)	<1 (1)	−1	−3
Total community-based services	202 (761)	750 (1540)	415 (948)	213 (−273 to 705)	−335 (−1066 to 349)
Community health workers‡	124 (642)	353 (1302)	212 (908)	88	−141
Mental health support services§	0 (0)	71 (172)	20 (94)	20	−51
Occupational therapy	3 (11)	2 (5)	4 (14)	1	2
Social services	21 (63)	74 (202)	51 (159)	30	−23
Physical rehabilitation services‖	33 (116)	36 (94)	43 (136)	10	7
Other¶	21 (30)	214 (930)	85 (235)	64	−129
Total community-based services	202 (761)	750 (1540)	415 (948)	213 (−273 to 705)	−335 (−1066 to 349)
Total local authority day care services	68 (351)	38 (194)	0	−68 (−248 to 89)	−38 (−144 to 134)
Total secondary care	982 (1826)	405 (622)	333 (583)	−649 (−1421 to 4)	−72 (−404 to 267)
Ophthalmology inpatient	0 (0)	0 (0)	75 (351)	75	75
Ophthalmology outpatient	138 (385)	110 (232)	103 (168)	−35	−7
Low vision assessment (LVA)	30 (49)	7 (24)	20 (47)	−10	13
Inpatient (other)	601 (1824)	166 (601)	0 (0)	−601	−166
Outpatient (other)	202 (371)	107 (158)	128 (228)	−74	21
Day case (other)	0 (0)	15 (76)	0 (0)	0	−15
Accident and emergency	11 (41)	0 (0)	4 (20)	−7	4
Therapy/counseling services	0 (0)	0 (0)	3 (12)	3	3
Total NHS and local authority service use cost	1444 (1941)	1362 (1842)	962 (1051)	−482 (−1334 to 323)	−400 (−1277 to 375)
Total service use cost and intervention cost	1444 (1941)	1362 (1842)	1775 (1044)	331 (−554 to 1099)	413 (−439 to 1193)

All costs rounded to nearest £.
* Reported as mean (SD).
† Reported as mean difference (bootstrapped 95% confidence interval, where appropriate).
‡ District nurse or health visitor.
§ Psychologist, therapist or counselor, or psychiatric nurse.
‖ Physiotherapist or chiropodist.
¶ Dietician, optician, dentist, or meals on wheels.

if the physician has received the referral letter would be helpful in future studies.

It was not part of our analysis plan to determine what happened to participants offered different interventions by the physician, but it is perhaps noteworthy that 25% of those referred to their physician were offered antidepressants. In DEPVIT, depressive symptoms reduced by 13.2 (SD 6.3) points on the BDI-II in the six people who were offered medication and for whom data were available. Antidepressants are an inexpensive, straightforward, and effective means of reducing depressive symptoms. However, antidepressant use may be associated with side effects such as insomnia, nausea, increased weight gain, drowsiness, and agitation, and the rate of relapse is relatively high.

Assuming that six sessions of PST would be offered to each person on average, the overall costs of this intervention were £1176 in Wales and £1296 in London. Total health and social care service use costs during the 6-month trial period were £400 lower in the PST arm of the trial than in the referral arm and £482 lower in the PST arm than in the control arm. However, although there is some suggestion that PST may reduce costs, when the cost of the PST intervention is added, the total cost of those in the PST arm was greater than in the other arms of the trial.

The relatively high number of serious adverse events and difficulties experienced making appointments to deliver PST during the trial reflects the underlying state of health of the participants. Participants were elderly, and comorbidity was common. Interventions aimed at reducing depression in this patient group, including those delivered via a stepped care approach, should consider the practical difficulties associated with intervention delivery. That some participants found engaging with PST difficult because they claimed not to have problems suggests that PST may not be appropriate for everyone.

One important finding from the DEPVIT study was that the prevalence of significant depressive symptoms in visual rehabilitation clinics in Britain, at 43%, is among the highest reported anywhere in the world. To put these findings in perspective, other studies using the GDS-15 and the same cut-off point have estimated that the prevalence of significant depressive symptoms in people with a cancer diagnosis about to start chemotherapy is 45%.[27] We provide a description of the prevalence data in another publication.[28]

Another significant observation from DEPVIT was that the response rate was relatively low. That is, the main reason for nonparticipation ($n = 345$) was refusal ($n = 110$; 32%). Refusal is a common finding in other trials in this population. For example, in the study by Rovner et al.,[14] refusal was the main reason (66%) for nonparticipation, and in the study by van der Aa et al.[29] only 914 of 3000 people invited to take part in the study provided written consent. A better understanding of the reasons why people are declining to take part may improve recruitment rates to future trials and help people accept the offer of treatment.

Table 5. Comparison of Clinical Trials of Depression Treatments in People With Sight Loss

Study	Sample Size	Baseline Depression	Measure	Intervention	Follow-Up, mo	Effect Size
Rovner et al., 2014[15]	188	Mild	PHQ-9	Behavioral activation	4	0.32
Van der Aa et al., 2015[29]	265	Mild	CES-D	Stepped care	24	0.21
Brody et al., 2011[31]	16	Mild/moderate	HAMD-17	Escitalopram	4	0.67
Rees et al., 2015[30]	153	Normal	DASS	LVSMP	6	0.00
DEPVIT	85	Moderate	BDI-II	PST	6	0.19

The results of this trial add to those of other trials recently published in this research area. For example, van der Aa et al.[29] showed that a stepped care approach, which comprised watchful waiting, guided self-help based on cognitive behavioral therapy, problem-solving treatment, and referral to a general practitioner significantly reduced the risk (relative risk 0.63) of a depressive dysthymic and/or anxiety disorder at 24 months.[29] In another study, a relatively simple, low-intensity psychological intervention known as BA, a treatment that helps people recognize the link between action and mood, often delivered in the person's own home by an occupational therapist during an 8-week period, was shown to halve the incidence of depressive disorders in people with AMD at 4 months.[15] In contrast, an 8-week, group-based low-vision self-management program based on cognitive-behavioral approaches and social cognitive theory did not reduce depressive symptoms at 6 months in people with low vision.[30] However, the people in that study were psychologically normal at baseline. Another well designed clinical trial showed the antidepressant therapy, escitalopram, to be effective at reducing depression in a small group of people with AMD and depression at 4 months.[31] Collectively, these studies suggest that psychological and pharmacological interventions can be effective in reducing depression in people with low vision. However, comparisons are complicated because of differences in the samples studied, the interventions tested, the follow-up period, the instruments used to measure depression and outcome measures, for example, change in depressive symptoms versus proportions with a depressive disorder. Table 5 summarizes the differences and outcomes of recent clinical trials in this area. Overall, it appears that the psychological interventions studied to date produce a small effect size (0.19 to 0.32) in people with low vision and depressive symptoms. These modest findings are typical of those observed in other chronic health conditions.[10] The larger effect size (0.67) observed in the small antidepressant trial is consistent with results obtained for those prescribed antidepressants in DEPVIT, but larger studies are needed.[31]

Taken together, these studies and our own experience of trying to deliver psychological interventions to those with the full spectrum of depressive symptoms (from mild to severe) has led us to believe that screening this high-risk group is vital; although PST may be helpful to some, it is not a panacea, and there may be better low-intensity psychological interventions, such as BA. It is unlikely that one intervention will suit everyone, and hence patients should be offered a range of treatment options tailored to their individual needs and the severity of their depression. The stepped care delivery platform can facilitate the delivery of individualized care and provide long-term benefits.

The strengths of this study include publication of the study protocol before recruitment began, an analysis based on prespecified primary and secondary outcomes, relatively successful masking of the outcome assessors, identification of sources of bias, a minimal set of exclusion criteria, and the large number of consecutive participants originally screened. Limitations of this study included a relatively modest sample size ($n = 85$) and practical difficulties experienced trying to deliver PST per protocol.

Conclusions

Our study suggests that PST and referring people to their physician are more effective than doing nothing for the treatment of depression in people with low vision, but the results were not compelling. Those with moderate to severe depressive symptoms benefited most from the interventions at a moderate cost.

Acknowledgments

The authors thank Helen Court who undertook the Rasch analysis of the seven-item National Eye Institute Visual Function Questionnaire and the near vision subscale of the Visual Function Questionnaire 48. Supported by Guide Dogs (Grant OR-2009 07b).

Disclosure: **C.L. Nollett**, None; **N. Bray**, None; **C. Bunce**, None; **R.J. Casten**, None; **R.T. Edwards**, None; **M.T. Hegel**, None; **S. Janikoun**, None; **S.E. Jumbe**, None; **B. Ryan**, None; **J. Shearn**, None; **D.J. Smith**, None; **M. Stanford**, None; **W. Xing**, None; **T.H. Margrain**, None

References

1. Goldstein JE, Massof RW, Deremeik JT, et al. Baseline traits of low vision patients served by private outpatient clinical centers in the United States. *Arch Ophthalmol*. 2012;130:1028–1037.
2. Horowitz A, Reinhardt JP, Boerner K. The effect of rehabilitation on depression among visually disabled older adults. *Aging Ment Health*. 2005;9:563–570.
3. Renaud J, Levasseur M, Gresset J, et al. Health-related and subjective quality of life of older adults with visual impairment. *Disabil Rehabil*. 2010;32:899–907.
4. Rovner BW, Zisselman PM, Shmuely-Dulitzki Y. Depression and disability in older people with impaired vision: a follow-up study. *J Am Geriatr Soc*. 1996;44:181–184.
5. Adamson JA, Price GM, Breeze E, Bulpitt CJ, Fletcher AE. Are older people dying of depression? Findings from the medical research council trial of the assessment and management of older people in the community. *J Am Geriatr Soc*. 2005;53:1128–1132.
6. Covinsky KE, Fortinsky RH, Palmer RM, Kresevic DM, Landefeld CS. Relation between symptoms of depression and health status outcomes in acutely ill hospitalized older persons. *Ann Intern Med*. 1997;126:417–425.
7. National Institute for Health and Clinical Excellence. *Depression in Adults With a Chronic Physical Health Problem: Treatment and Management*. NICE Clinical Guidelines No. 91. London, U.K.: National Institute for Health and Clinical Excellence; 2010.
8. Bollini P, Pampallona S, Tibaldi G, Kupelnick B, Munizza C. Effectiveness of antidepressants - meta-analysis of dose-effect relationships in randomised clinical trials. *Br J Psychiatry*. 1999;174:297–303.

9. Churchill R, Hunot V, Corney R, et al. A systematic review of controlled trials of the effectiveness and cost-effectiveness of brief psychological treatments for depression. *Health Technol Assess*. 2001;5:1–173.
10. Dickens C, Cherrington A, Adeyemi I, et al. Characteristics of psychological interventions that improve depression in people with coronary heart disease: a systematic review and meta-regression. *Psychosom Med*. 2013;75:211–221.
11. Coventry PA, Hudson JL, Kontopantelis E, et al. Characteristics of effective collaborative care for treatment of depression: a systematic review and meta-regression of 74 randomised controlled trials. *PLoS One*. 2014;9:e108114.
12. Fiske A, Wetherell JL, Gatz M. Depression in older adults. *Ann Rev Clin Psychol*. 2009;5:363–389.
13. Hollon SD, Jarrett RB, Nierenberg AA, Thase ME, Trivedi M, Rush AJ. Psychotherapy and medication in the treatment of adult and geriatric depression: which monotherapy or combined treatment? *J Clin Psychiatry*. 2005;66:455–468.
14. Rovner BW, Casten RJ, Hegel MT, Leiby BE, Tasman WS. Preventing depression in age-related macular degeneration. *Arch Gen Psychiatry*. 2007;64:886–892.
15. Rovner BW, Casten RJ, Hegel MT, et al. Low vision depression prevention trial in age-related macular degeneration a randomized clinical trial. *Ophthalmology*. 2014;121:2204–2211.
16. Gonzalez HM, Vega WA, Williams DR, Tarraf W, West BT, Neighbors HW. Depression care in the United States: too little for too few. *Arch Gen Psychiatry*. 2010;67:37–46.
17. Tsai J, Pilver CE, Hoff RA. Potential mental health needs of US adult residents under different provisions of the Affordable Care Act. *J Clin Psychiatry*. 2014;75:1402–1410.
18. Margrain TH, Nollett C, Shearn J, et al. The Depression in Visual Impairment Trial (DEPVIT): trial design and protocol. *BMC Psychiatry*. 2012;12:57.
19. Margrain TH, Ryan B, Wild JM. A revolution in Welsh low vision service provision. *Brit J Ophthalmol*. 2005;89:933–934.
20. Beecham J, Knapp M. *Costing Psychiatric Interventions: Discussion Paper 1536*. Personal Social Services Unit (PSSRU), University of Kent: Canterbury; 1999. Available at: http://www.pssru.ac.uk/pdf/dp1536.pdf.
21. Curtis L. *Unit Costs of Health & Social Care 2013*. Personal Social Services Unit (PSSRU), University of Kent: Canterbury; 2013. Available at: http://www.pssru.ac.uk/project-pages/unit-costs/2013/index.php?file=full.
22. Department of Health. *National Health Schedule of Reference Costs 2012 to 2013*. Department of Health, London; 2013. Available at: https://www.gov.uk/government/publications/nhs-reference-costs-2012-to-2013.
23. Altman DG, Bland JM. Uncertainty and sampling error. *Br Med J*. 2014;349:g7064.
24. Altman DG, Gardner MJ. Confidence intervals for research findings. *Br J Obstet Gynaecol*. 1992;99:90–91.
25. Gardner MJ, Altman DG. Confidence intervals rather than P values: estimation rather than hypothesis testing. *Br Med J*. 1986;292:746–750.
26. Hegel MT, Dietrich AJ, Seville JL, Jordan CB. Training residents in problem-solving treatment of depression: a pilot feasibility and impact study. *Fam Med*. 2004;36:204–208.
27. Bellera CA, Rainfray M, Mathoulin-Pelissier S, et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. *Ann Oncol*. 2012;23:2166–2172.
28. Nollett C, Bray N, Bunce C, et al. High prevalence of untreated depression in patients accessing low-vision services. *Ophthalmology*. 2016;123:440–441.
29. van der Aa HPA, van Rens GHMB, Comijs HC, et al. Stepped care for depression and anxiety in visually impaired older adults: multicentre randomised controlled trial. *Br Med J*. 2015;351:h6127.
30. Rees G, Xie J, Chiang PP, et al. A randomised controlled trial of a self-management programme for low vision implemented in low vision rehabilitation services. *Patient Educ Couns*. 2015;98:174–181.
31. Brody BL, Field LC, Roch-Levecq A-C, Moutier CY, Edland SD, Brown SI. Treatment of depression associated with age-related macular degeneration: a double-blind, randomized, controlled study. *Ann Clin Psychiatry*. 2011;23:277–284.

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