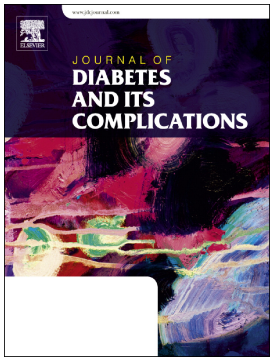

Combined exercise and visual gaze training improves stepping accuracy in people with diabetic peripheral neuropathy

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PII: S1056-8727(19)30424-6
DOI: https://doi.org/10.1016/j.jdiacomp.2019.07.001
Reference: JDC 7404

To appear in: *Journal of Diabetes and Its Complications*

Received date: 17 April 2019
Revised date: 20 June 2019
Accepted date: 2 July 2019

Please cite this article as: J.C. Handsaker, S.J. Brown, M. Petrovic, et al., Combined exercise and visual gaze training improves stepping accuracy in people with diabetic peripheral neuropathy, Journal of Diabetes and Its Complications, https://doi.org/10.1016/j.jdiacomp.2019.07.001

Combined Exercise and Visual Gaze Training Improves Stepping Accuracy in People with Diabetic Peripheral Neuropathy

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Abstract

Introduction: Patients with diabetes and diabetic peripheral neuropathy (DPN) place their feet with less accuracy whilst walking compared to their age-matched controls, which may contribute to the increased falls-risk in this population. This study examines the effects of a multi-faceted intervention on stepping accuracy, in patients with diabetes and DPN.

Methods: Forty participants began the study, of which 29 completed both the pre and post-intervention tests, 8 patients with DPN, 11 patients with diabetes but no neuropathy (D) and 10 healthy controls (C) for reasons unrelated to the study). Accuracy of stepping was measured pre- and post-intervention as participants walked along an irregularly arranged stepping walkway. Participants attended a one-hour session, once a week, for sixteen weeks, involving high-load resistance exercise and visual-motor training.

Results: Patients who took part in the intervention improved stepping accuracy (DPN: +45%; D: +36%) ($p<0.05$). The diabetic non-intervention (D-NI) group did not display any significant differences in stepping accuracy pre- to post- the intervention period (-7%).

Discussion: The improved stepping accuracy observed in patients with diabetes and DPN as a result of this novel intervention, may contribute towards reducing falls-risk, although further research is required to confirm. This multi-faceted intervention presents promise for improving the general mobility and safety of patients with diabetes and DPN during walking and could be considered for inclusion as part of clinical treatment programmes.

Keywords: walking, falls, exercise, eye-tracking, gait.

1. Introduction

Patients with diabetic peripheral neuropathy (DPN) are up to 20-times more likely to fall than age-matched controls, and approximately half of all falls are due to tripping whilst walking (1,2), which is related to the accuracy of stepping. Falling can result in serious injury, and even death (3,4). Further to the consequences of falling, is the considerable economic burden to national health bodies. Therefore, a means by which the number of falls in this population can be reduced is of importance.

The frequency of tripping is a major contributory factor to the probability of falling (5,6). Hence, if the frequency of tripping can be reduced through more accurate foot placements, then likely, so will the risk of falling. A key approach to reducing the risk of tripping is to improve a patient's ability to avoid obstacles before they actually trip over them through improved visual gaze and more accurate stepping. Patients with DPN displayed a decreased stepping accuracy, which is indicative of a reduced ability to avoid observed obstacles (7). This reduced capacity to move the foot where desired with appropriate accuracy is thought to be caused by impaired motor control of the lower limbs and an altered visual gaze strategy with diabetic peripheral neuropathy. We hypothesised that if the motor control and visual gaze strategies can be improved to approach those employed by a healthy population, stepping accuracy may therefore be consequently improved.

Resistance exercise training to increase lower limb muscle strength is expected to improve motor control and increase the accuracy of stepping (6, 8-11). Resistance exercise and balance training can improve walking speed, muscle strength, reduce postural sway and improve activity levels (12-14), but no studies have looked at the effects on stepping accuracy in diabetes patients. Patients with cerebellar and vestibular dysfunction and healthy young adults have displayed improvements in

walking speed, postural stability and stepping accuracy in response to visual gaze-based training (15-17). It is hypothesised that resistance exercise and visual gaze training may be beneficial for stepping accuracy in patients with DPN. The intention was to encourage patients to use vision more with the purpose of planning ahead, as well as their current use for 'feedback' of foot position (6). Visual gaze exercises were performed with the aim of altering visual gaze strategy, teaching patients to visually plan their stepping route before walking. It is hypothesised that such training will improve the use of vision during walking, and motor control of the lower limbs, leading to an improved stepping accuracy.

This aim of this study was to examine the potential utility of a combined visual gaze and resistance exercise training programme at improving the accuracy of foot placement during walking.

2. Material and methods

2.1 Participants

Ten patients with DPN (4 males) (mean±SD age: 56.8 ± 9.6 years; and BMI: 28.9 ± 4.6 $kg.m^{-1}$), 20 patients with diabetes but no neuropathy (5 males) [D](mean±SD age: 58.9 ± 11.7 years; and BMI: 27.2 ± 3.8 $kg.m^{-1}$) and 10 healthy controls (4 males) [C](mean±SD age: 66.3 ± 11.5 years; and BMI: 25.1 ± 3.1 $kg.m^{-1}$) gave their written informed consent to participate in this study, which was given ethical approval from the UK National Health Service Research Ethics Committee (NHS REC reference: 11/NW/0686). A healthy control group was included to provide a reference condition, displaying 'optimal' performance, providing a comparison to pre- and post-intervention characteristics of patients with diabetes. Inclusion criteria were presence of diabetes for more than 10 years, absence of diabetes for the matched control

group. Patients were excluded if they had open ulcers, required the use of a walking aid, had a history of other disorders affecting gait, or a visual acuity of <6/18 (of any aetiology).

2.2 Neuropathy assessment & classification

The presence and severity of neuropathy was measured using two separate tests: the modified Neuropathy Disability Score (mNDS) (18,19), and the Vibration Perception Threshold (VPT) (18,19) using a neurothesiometer (Horwell, Nottingham UK). Patients were deemed to have moderate to severe neuropathy and grouped as DPN if in either one or both of their feet they displayed either an mNDS score of ≥6, or a VPT of ≥25 Volts (or both). Patients were deemed to have no neuropathy and were grouped as D, if in both feet they displayed scores for the mNDS of ≤5 and for the VPT of ≤24 Volts (18,19).

2.3 Pre- and post-testing procedures

Retro-reflective markers were attached to the participant's feet (8 on each foot) according to standard motion analysis preparation methods. Three-dimensional marker positions were then tracked during the stepping accuracy task described below, by a ten-camera motion capture system recording at 100Hz (Vicon Nexus, Vicon, Oxford, UK). All participants wore specialist diabetic shoes (MedSurg, Darco, Raisting, Germany) with a neutral foot-bed, to standardise footwear between groups, and to ensure that the diabetic patients walked with appropriate footwear.

Participants were asked to walk along a 7m long walkway with stepping targets designed to specifications by Marple-Horvat & Crowdy (20) (Fig. 1) and previously applied to diabetes patients (7), until five trials were captured. Each participant was

given the same instructions: “walk at your natural speed, stepping on each of the targets as accurately as possible.” Participants performed five trials of which three were used for analysis. Kinematic data of foot position were captured from the middle six stepping targets from a total of eighteen (R4, L4, R5, L5, R6, L6) (20) (Fig. 1).

2.4 Multi-factorial intervention

Diabetes patients were randomly allocated into either the intervention group or a control non-intervention group using a random number generator. Twenty-four participants were allocated into the intervention group (D-INT, *n*=17; and DPN-INT, n=7), and seven (D: *n*=4; DPN: *n*=3) were allocated into the diabetic control group (D-NI). Due to the relatively small number of patients within the diabetes control group, data from D and DPN patients were combined and presented as a single diabetic control group (D-NI; *n*=7). Based upon a power calculation, sample size was considered sufficient to analyse the intervention group data separately as D and DPN groups (D-INT and DPN-INT). To determine the adequacy of the group samples, the post-hoc statistical power to detect pre-to-post intervention differences in stepping accuracy (the main study parameter) was tested for the DPN-INT group (*n*=7). The statistical power was found to be 0.81, indicating the study was powered to identify true differences for this specific parameter.

Patients in the intervention group attended a weekly, one-hour session, at a private exercise facility within the university, for a 16-week period. Within this session, a series of resistance training exercises and visual gaze training strategies were performed with the aim to improve the visual and motor limitations in patients with diabetes and DPN (7). After the 16-week intervention period, patients in both control

(D-NI) and intervention (D-INT and DPN-INT) groups repeated the stepping accuracy task.

Visual gaze and motor control training

A visual gaze and motor control training task was performed in which participants negotiated a small stepping walkway, comprising of six stepping targets. The arrangement of these stepping targets was randomized and changed each week to avoid any learning of the stepping pattern, but the principal of the irregularly spaced targets was similar to the stepping walkway used pre- and post-testing and shown in Fig. 1. Before participants began each walkway negotiation and while standing at the start, they were instructed to visually trace their upcoming walk three times before they walked through the stepping task. This was performed in an effort to improve visual gaze strategy by encouraging patients to look at targets in advance of stepping onto them, promoting use of a strategy of visually planning their route. The stepping task (with the necessary visual trace) and walk were performed five times in each direction.

Resistance exercise training

Exercise training sessions followed the same format as used with diabetes patients (21). Participants spent the first two weeks practicing the correct technique and becoming familiarised with the movements of the exercise by using low load. Before progressing towards a suitable load required to yield improvements in strength. In the first session following the initial two-week period, patients gradually increased the load until it was sufficiently challenging to perform no more than twelve repetitions. One repetition consisted of lifting and lowering the load under control in

approximately 2 and 3 seconds, respectively. In the following fourteen weeks, patients were asked to perform three sets of up to twelve repetitions on three different machines; a leg extension (extending the knee from 90˚ of flexion to 0˚ [full extension] to lift the load and flexing to lower under control), a seated leg press (extending the ankle, knee and hip from a flexed position [knee at >90˚] to a more extended position [knee ending close to full extension] and returning while lowering the load under control), and a seated ankle press (plantar flexing the ankle from a dorsi flexed angle and returning to lower the load under control). If the participants could perform three sets of twelve repetitions or more in any one session, the load was increased for the subsequent week to maintain the training stimulus.

2.5 Data analysis

Foot stepping accuracy

Stepping accuracy was calculated as the difference between the position of the distal aspect of the 2nd metatarsal head (2MH), and the calibrated centre of the stepping targets, at foot-ground contact, using the same methods as we have described in our previous study with diabetes patients (7).

Visual gaze

The effects of the visual gaze intervention on visual gaze parameters was measured in a subset of intervention patients, grouped as DPNVA-INT (*n*=3; D-INT=2 and DPN-INT=1). Data were obtained from a sub-sample of the cohort due to the time-consuming nature of these measurements precluding assessment in all participants; non-spherical corneal shape as the result of surgery in some participants, and eyelashes covering the eyes

during the tests. Because of the small cohort of participants, this aspect of the results is presented as preliminary.

Two time-points in the horizontal signal of the eye movement trace were identified: the initial visual acquisition of the target (start of visual acquisition), and the point at which gaze was subsequently directed away from the target (visual acquisition end). These events were identified using the second derivative of the eye position signal, i.e., the eye acceleration peak at saccade onset. By using the timing of when each individual target was visually acquired, and when gaze was subsequently directed away, four separate variables were obtained: 1) the time between visual acquisition of the target and foot-target contact; 2) the time between the subsequent saccade away from the target with respect to foot-target contact; 3) the time spent looking at the target (fixation duration); and 4) the time taken to transfer gaze between targets. This data is considered only as pilot data due to the small sample size and therefore no statistical analysis was performed on the results. Furthermore, it is not presented in the main body of the results for this reason.

2.6 Statistics

Pre- to post-intervention differences were tested using a repeated measures Student's *t*-test with significance set at $p<0.05$. Between group differences for the baseline measures, including the non-diabetic controls were performed using a one-way ANOVA, with a Bonferoni post-hoc test, with significances reported with respect to the C-group. Values are presented as means ± SD.

3. Results

3.1 Neuropathy scores

Patients within the DPN-INT group displayed greater severity of peripheral neuropathy as shown by significantly higher measures of the modified Neuropathy Disability (mNDS) score (Table 1) compared to the D-INT and C groups, and significantly higher vibration perception thresholds (VPT) than the D-INT, D-NI and C groups.

3.2 Stepping accuracy (Fig. 2)

Patients within the DPN-INT and D-INT groups were significantly more accurate at stepping post-intervention compared to pre-intervention, contacting the ground significantly closer to the centre of the target (pre- *vs* post-Intervention – DPN-INT: 57 ± 33 *vs* 31 ± 15 mm [45% increase in accuracy]; and D-INT: 64 ± 29 *vs* 41 ± 14 mm [36% increase in accuracy]). In contrast, the stepping accuracy of the D-NI group was unchanged pre- to post-intervention (pre- *vs* post-Intervention – D-NI: 33 ± 9 *vs* 35 ± 7 mm [7% decrease in accuracy]; $p>0.05$).

Pre-intervention, the DPN-INT and D-INT groups were significantly less accurate at stepping than the C group, whereas the D-NI group displayed a similar level of stepping accuracy (DPN-INT: 57 ± 33; D-INT: 59 ± 28; D-NI: 33 ± 9; and C: 38 ± 31 mm). Post-intervention, no differences in stepping accuracy were observed between the groups (DPN-INT: 31 ± 22 mm D-INT: 41 ± 24mm; D-NI: 35 ± 20 mm; and C: 38 ± 31 mm; $p>0.05$).

4. Discussion

This novel intervention study shows that combined resistance exercise and visual gaze training can increase stepping accuracy during walking in patients with diabetes and DPN. Whilst this was a controlled laboratory study, the general concept from our findings of improved movement control may have application in the real-world for reducing falls-risk in people with DPN through more accurate foot placements, but this requires confirmation from future work.

Accurate stepping is dependent upon the combined use of vision and motor control, to identify the intended position of foot placement, and subsequently control accurate movement of the lower limb. Motor control of the lower limbs is affected by neuropathic damage, as DPN affects not only cutaneous sensation and muscle response, but also lower limb position sense (proprioception), often resulting in a reduced postural stability (22, 23). Impaired proprioception in patients with DPN is likely to impact upon of lower limb and orientation during stepping, as well as the swing limb movement speed (22). Another important element of motor control is the ability to accurately and consistently develop an appropriate level of muscle force, to control joint movement. Whilst no research into the effects of diabetes on muscle force steadiness has been performed, it has been shown that frail older adults (another population at a high risk of falling), show reduced force steadiness during isometric contractions (24). This is particularly important during the swing phase of walking, where the muscles controlling the ankle, knee and hip need to move the limb accurately through space and position it accurately on the ground ahead of the body (25). Furthermore, variability in lower limb motor performance during low and medium effort tasks is exacerbated by increased cognitive demand (26). The stepping task examined is likely to increase cognitive demand and is expected to particularly affect patients with DPN.

Strength training has previously been shown to improve force accuracy and steadiness in elderly patients, increasing maximal strength as well as control of submaximal strength and reduces force fluctuations, which are expected to improve force steadiness and consequential motor control (27, 28). It is expected that as well as increasing strength of the ankle and knee flexors, the resistance training exercises may have improved force steadiness and increased the control of muscle force during movement of the lower limbs.

In addition to improvements to motor control, visual gaze strategy is expected to have improved as a result of the visual gaze training task. Previous studies have shown positive responses to visuomotor training by improving postural stability, dynamic visual acuity, and stepping accuracy in both healthy young and elderly populations (15, 17, 20, 29). The visual gaze training task performed over the 16-week intervention required participants to map the route using their eyes before stepping onto the irregularly placed stepping targets. This was expected to encourage a more optimal planning of the stepping route, which during walking, would cause patients to continuously survey the upcoming environment. This allowed participants to consider the location of upcoming targets as well as the next immediate target, allowing more time to co-ordinate appropriate responses (30). The intervention participants improved their stepping accuracy by an average of 173%.

In pilot data from a subset of participants, visual gaze timings were altered as a result of the intervention, with patients looking away to the subsequent target earlier, and taking less time to look between targets, consequently resulting in patients acquiring the next target earlier (Fig. 3). These visual gaze characteristics indicate that patients

were able to spend longer assessing the target position on approach, and may at least in part, have contributed to the improved stepping accuracy observed. These are, however, only preliminary observations in a small sample size, but the consistent and clear direction of the changes at least provide some insight into the potential mechanism for the improved stepping accuracy.

This study has shown that stepping accuracy can be improved in patients with diabetes, and particularly in those with DPN, through a combination of high-load resistance exercise and visual gaze training. Future studies should look to elucidate the separate effects of the high-load resistance exercise and visual gaze training components on motor control and visual gaze strategy. Such work may help to further focus exercise regimens and aid the production of an all-encompassing, yet short and enjoyable intervention regimen that patients with diabetes and DPN can perform to improve their safety in a real-world environment. Although demonstrated in a controlled laboratory study, the observed improvements in stepping accuracy may have real-world application in contributing to reduce the high falls-risk reported in this population, through a more controlled movement strategy with fewer foot placement errors. However, this real-world application (reduced falls-risk) was not tested in the present study and remains an area for confirmation by future research.

In conclusion, this study provides evidence for the benefits of a novel intervention for improving stepping accuracy in patients with diabetes and DPN involving resistance exercise and visual gaze training and could be considered as part of a clinical treatment programme to improve the general health and safety of patients with diabetes.

Funding Statement

This work was supported by a Clinical Research Grant from the European Foundation for the Study of Diabetes (EFSD).

Conflict of interest

All the authors declared no conflicts of interest in association with the present study.

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Table 1. Data showing values for two separate tests used in the assessment for the presence and severity of peripheral neuropathy – the modified neuropathy disability score (mNDS) and the vibration perception threshold (VPT).

	DPN-INT	D-INT	D-NI	C
mNDS, score /10	6.2 (2.6)	2.4 (2.1)*	4.8 (4.5)*	2.0 (1.4)*
VPT, V	31.0 (5.9)	8.5 (2.7)*	11.8 (6.0)*	11.9 (7.0)*

Values are means (SD). The modified neuropathy disability score (mNDS) is a test for sensory neuropathy consisting of assessments of pain sensation (pin-prick), vibration, temperature and Achilles tendon reflexes. The vibration perception threshold (VPT) is a semi-quantitative test assessing participant's ability to detect a given level of vibration applied at the Hallux (Volts). *denotes significantly different ($p<0.05$) from the C group.

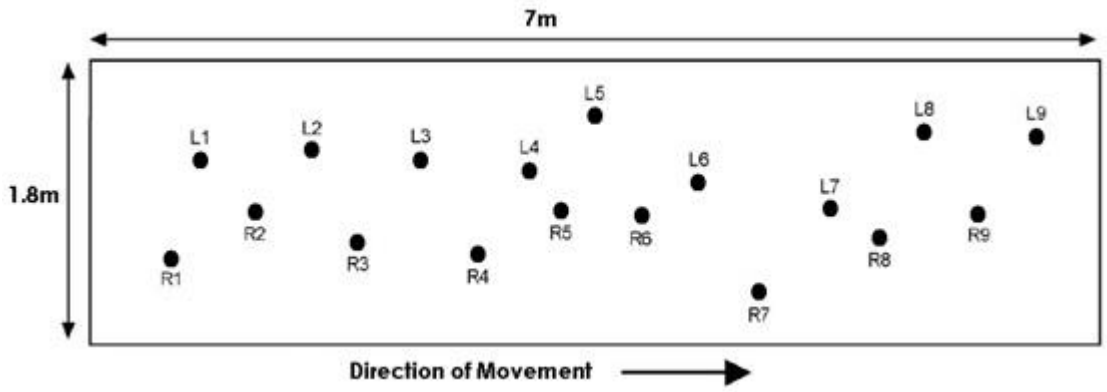

Figure 1. Diagram showing an over-head schematic view of the stepping walkway used for the stepping accuracy task in the study. The dimensions of the stepping walkway were 1.8 by 7 metres. The irregularly arranged stepping targets are shown by the black dots and are numbered in order of contact, i.e., the participant started before the targets indicated L1 and R1 and walked in the direction shown, finishing at L9 and R9. 'L' and 'R' on the targets denotes that they should be contacted by the left and right foot, respectively.

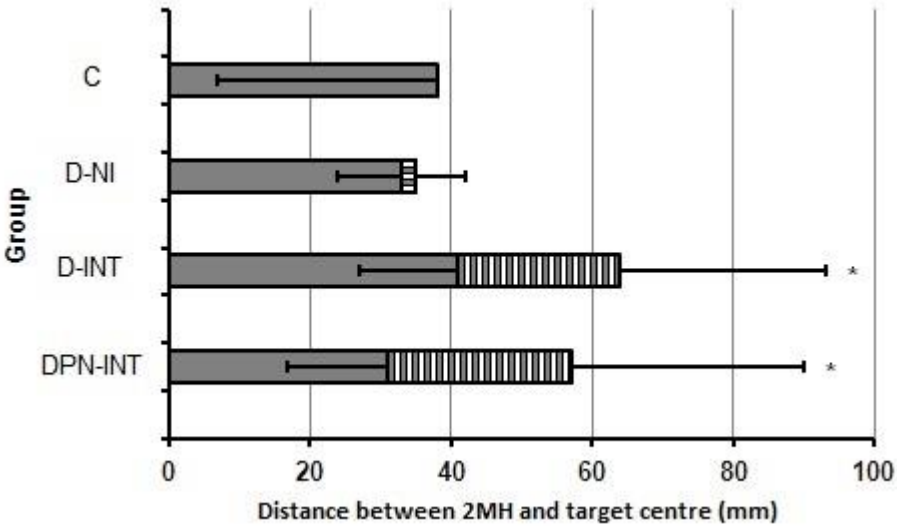

Figure 2. Pre- and Post-intervention results for stepping accuracy. The second metatarsal head (2MH) was identified from pilot work as the part of the foot that defined its placement onto a target. Stepping accuracy was therefore calculated as the distance between the 2MH and the centre of the target (the value shown in mm on the x-axis). Data are shown here for diabetic controls (D-NI; n=6), diabetic intervention (D-INT; n=8), and diabetic peripheral neuropathy intervention (DPN-INT; n=5) groups. The C bar shows the results without any intervention for the healthy control group (C; n=10) as a reference for comparison against the diabetes groups. For the D-NI bar, the grey section shows the pre-intervention results, and the additional horizontal striped section shows the increase in distance (i.e., reduced accuracy post-intervention) post-intervention. For the D-INT and DPN-INT bars, the grey bar shows the post-intervention distance, and the vertical striped bar in addition to the grey bar shows the pre-intervention distance (i.e., improved accuracy post-

*intervention). Values are mean distances and SD; * denotes significantly different distance post-intervention compared to pre-intervention (p<0.05).*

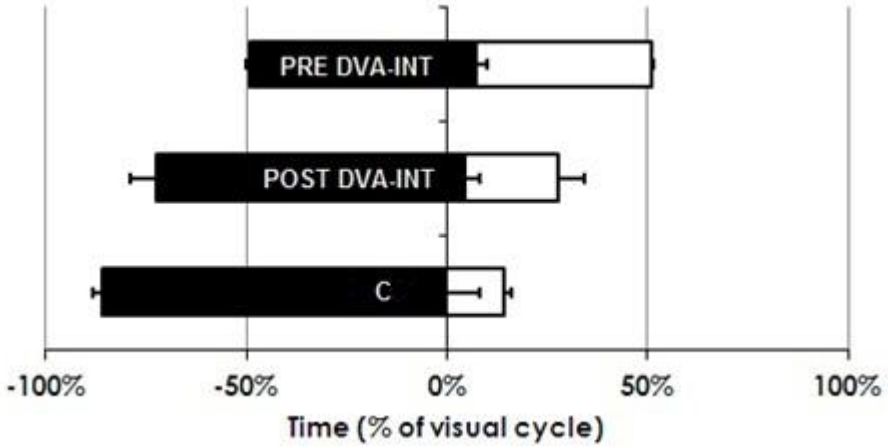

Figure 3. Target visual acquisition parameters during the stepping task, pre- (PRE DVA-INT) and post-intervention (POST DVA-INT) for the combined diabetic visual acquisition patient intervention group, and shown in comparison to healthy controls (C) as a reference. Values are means and standard deviations as a percentage of the visual gaze cycle. The black bars denote visual acquisition of the target, the white bars denote the time looking between targets, and the end of the white bar denotes the acquisition of the next target. Foot-ground contact occurs at 0%.