

Long-Term Clinical Trial: Study Design Overview

www.clinicaltrials.gov | NCT 03538756

Rationale

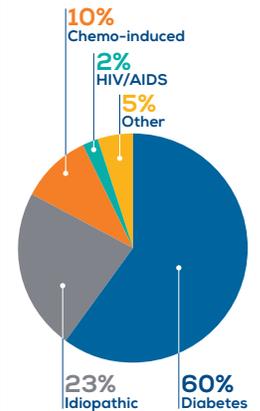
Approximately 20 million Americans suffer from peripheral neuropathy (PN)¹. Leading causes of PN include diabetes, unknown causes (idiopathic), and chemotherapy induced. The incidence increases with age.



Epidemiological evidence has linked PN to an increased risk of falling². There is a need for developing cost-effective interventions for improving mobility and balance to manage fall risk. Walkasins[®], a lower limb sensory neuroprosthesis that mimics lost foot pressure sensation with tactile sensory information around the lower leg, can address this need.

Recent research has demonstrated short-term improvements in gait and balance function in patients with PN using the Walkasins device³. The walk2Wellness clinical trial investigates the long-term effects of wearing Walkasins on a continuous basis as a balance prosthesis for replacing lost foot pressure sensation.

LEADING CAUSES OF PN⁵



Study Purpose

Investigate long-term effects of Walkasins use on clinical and patient-reported outcomes of gait function, balance confidence, physical activity, and social participation in patients with sensory peripheral neuropathy. Fall-rates are monitored and compared to pre-study data.



Hypothesis

Patients using Walkasins every day, who receive tactile sensory balance information, will improve outcomes of gait function, balance confidence, physical activity, and social participation.

Study Design Summary

Assessment of Walkasins through a randomized cross-over study followed by pre- and post-assessments as well as periodic follow-ups. Multiple clinical sites across the country with up to 120 subjects participating. Assessment of subject response long-term (see figure below) vs. response in-clinic (after initial baseline assessment). **Individual study results are not shared with subjects. Subjects may not begin any additional gait, balance intervention or treatment for the first ten weeks of the trial.**

Outcome Measures⁴

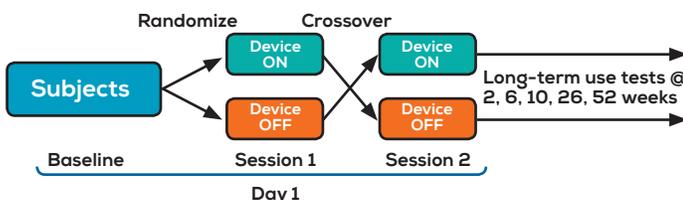
A set of reliable and valid measures of gait function will be used to assess patients for inclusion in the study and for assessing improvement over time. Outcomes captured include gait function, balance confidence, physical activity, social participation, quality of life, as well as tracking falls.

- 1. Functional Gait Assessment (FGA)** – The FGA is the recommended outcome measure for gait function and is used in predicting unexplained falls in community-dwelling older adults.
- 2. Walking Speed** – A simple test often termed “the Sixth Vital Sign” is routinely done in rehabilitation and is highly predictive of long-term survival in older adults.
- 3. 4-stage Balance Test** – Part of a test protocol for balance function that is recommended by the Centers for Disease Control (CDC).
- 4. Timed-Up-and Go (TUG)** – Part of a test protocol for balance function that is recommended by the Centers for Disease Control (CDC).

Several patient-reported outcomes are included to measure balance confidence, social participation and depression at multiple measurement points.

- PROMIS forms for pain and social participation
- Activities-specific Balance Confidence (ABC) scale
- Vestibular Activities of Daily Living (VADL)
- Patient Health Questionnaire (PHQ-9)

Figure. Study design of walk2Wellness clinical trial for each of the sites.

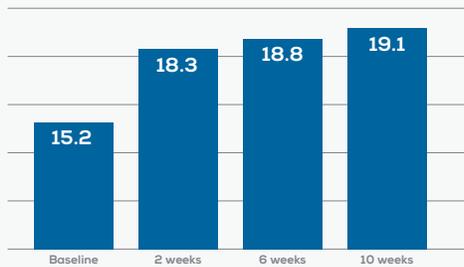


- 1 Peripheral Neuropathy Fact Sheet. (2018, August 16). Retrieved from https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Peripheral-Neuropathy-Fact-Sheet#3208_4IH Peripheral Neuropathy Catalog.
- 2 Richardson JK, HurvitzEA. Peripheral neuropathy: a true risk factor for falls. J GerontolA Biol Sci Med Sci. 1995;50(4):M211-215.
- 3 Koehler-McNicholas SR, Danzi L, Cataldo AY, Oddsson LIE (2019) Neuromodulation to improve gait and balance function using a sensory neuroprosthesis in people who report insensate feet – A randomized control cross-over study. PLOS ONE 14(4): e0216212. <https://doi.org/10.1371/journal.pone.0216212>
- 4 Rehabilitation Measures. Retrieved from <https://www.sralab.org/rehabilitation-measures>
- 5 The Foundation for Peripheral Neuropathy fact sheet. <https://www.foundationforpn.org/what-is-peripheral-neuropathy/types-risk-factors/>.

Long-Term Clinical Trial: Study Status Update 2/2020

Interim study report as presented at APTA CSM^{17,18}

Mean FGA Score, 37 Subjects at 10 Weeks

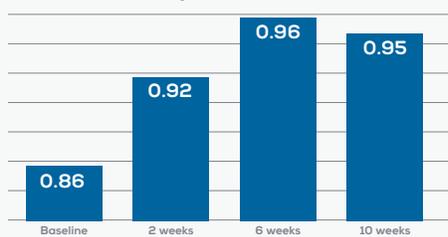


Functional Gait Assessment scores (30 points max) for 37 subjects following Walkasins daily use for 10 weeks.

An increase in the Functional Gait Assessment score with the use of Walkasins®, which may decrease the risk of falls.

- The Functional Gait Assessment is an excellent metric for classifying fall risk and predicting future falls and has been shown to be low in individuals with peripheral neuropathy^{9,10}.
- A history of falls has been linked to reduced confidence with mobility, decreased activity levels, ultimately contributing to decreased quality of life¹¹.

Mean Normal Gait Speed m/s, 37 Subjects at 10 Weeks

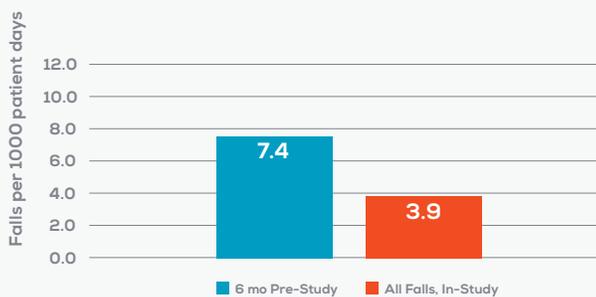


Gait Speed (meters per second) for 37 subjects following Walkasins daily use for 10 weeks.

An increase in gait speed with the use of Walkasins.

- Gait speed typically **declines** with age and it declines faster in those with peripheral neuropathy^{12,13}.
- Slower gait speed is related to increased disability, need for fall prevention interventions, greater likelihood to be hospitalized, and reduced access to the community¹⁴.

Patient Reported Fall Rate at 182 Average Use Days, 52 Subjects¹⁸



A reduction in fall rate and number of fallers with the use of Walkasins^{15,16,17,18}.

- According to the Centers for Disease Control and Prevention, more than 25% of individuals over the age of 65 fall each year, which results in total medical costs that exceed \$50 billion each year⁶.
- Individuals with peripheral neuropathy are up to 15 times more likely than healthy older adults to have a fall-related injury^{7,8}.
- At 182 average use days with 52 subjects enrolled, 19 subjects have fallen post-enrollment with Walkasins use, compared to 30 subjects reporting falls during 180 days pre-study participation¹⁸.

Caution: Prior to using this device, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, and precautions. Walkasins is an external lower limb sensory prosthesis intended to replace the nerve function used for detection and signaling of foot pressure sensation. Walkasins is indicated for patients with lower limb sensory peripheral neuropathy who present with gait and balance impairments. Walkasins is indicated for patients who can feel the tactile stimuli from the Leg Unit on the lower leg. This device is contraindicated for patients with untreated lymphedema; untreated lesion of any kind, swelling, infection, inflamed area of skin or eruptions on the lower leg near product use; acute thrombophlebitis including deep vein thrombosis; untreated fractures in the foot and ankle; and severe peripheral vascular disease.

6 Important Facts about Falls | Home and Recreational Safety | CDC Injury Center. Retrieved from <https://www.cdc.gov/HomeandRecreationalSafety/Falls/adultfalls.html>

7 Richardson JK, Hurvitz EA. Peripheral neuropathy: a true risk factor for falls. J Gerontol A Biol Sci Med Sci. 1995;50(4):M211-215.

8 Cavanagh PR, Derr JA, Ulbrecht JS, Maser RE, Orchard TJ. Problems with gait and posture in neuropathic patients with insulin-dependent diabetes mellitus. DiabetMed. 1992;9:469-74

9 Diane M. Wrisley, Neeraj A. Kumar, Functional Gait Assessment: Concurrent, Discriminative, and Predictive Validity in Community-Dwelling Older Adults, Physical Therapy, Volume 90, Issue 5, 1 May 2010, Pages 761-773, <https://doi.org/10.2522/ptj.20090069>

10 Koehler-McNicholas SR, Danzl L, Cataldo AY, Oddsson LIE (2019) Neuromodulation to improve gait and balance function using a sensory neuroprosthesis in people who report insensate feet – A randomized control cross-over study. PLoS ONE 14(4): e0216212. <https://doi.org/10.1371/journal.pone.0216212>

11 Dionysiotti Y. (). Analyzing the problem of falls among older people. International journal of general medicine, 5, 805-813. doi:10.2147/IJGM.S32651

12 Studenski, S. (2011). Gait Speed and Survival in Older Adults. Jama, 305(1), 50. doi:10.1001/jama.2010.1923

13 Lipsitz, L. A., Manor, B., Habtemariam, D., Ilpoutaife, I., Zhou, J., & Trivison, T. G. (2018). The pace and prognosis of

peripheral sensory loss in advanced age: association with gait speed and falls. BMC geriatrics, 18(1), 274. doi:10.1186/s12877-018-0970-5 Gait speed is predictive of survival with slower gait speeds indicative of earlier mortality.

14 Middleton A., Fritz, S. L., & Lusardi, M. (2015). Walking speed: the functional vital sign. Journal of aging and physical activity, 23(2), 314-322. doi:10.1123/japa.2013-0236

15 Oddsson, LIE. (2019, April). Improving Physical Function in Persons with Peripheral Neuropathy Using Sensory Neuromodulation – Clinical Trial Update, Poster Session presented at the Peripheral Nerve Society Annual Meeting, Genoa, Italy.

16 Oddsson, LIE., Cohen H., Wrisley, DM. (2019, Nov.) A Wearable Device for Sensory Motor Recovery, Function and Balance. Presentation presented at the 96th Annual meeting of the American Congress of Rehabilitation Medicine (ACRM), Chicago, IL.

17 Oddsson, LIE., Bisson T., Cohen, HS., Koehler-McNicholas, SR., Kung, D., Lipsitz, L., Manor, B., McCracken, P., Wrisley, D. (2020, Feb.) Walk2Wellness Update: Sustained Effects of Sensory Neuromodulation on Gait Function in Persons with Peripheral Neuropathy. Poster presented at 2020 American Physical Therapy Association Combined Sections Meeting (APTA CSM), Denver, CO.

18 Oddsson, LIE., Bisson T., Cohen, HS., Koehler-McNicholas, SR., Kung, D., Lipsitz, L., Manor, B., McCracken, P., Wrisley, D. (2020, Feb.) On Certain Patients, a Wearable Plantar Sensory Neuroprosthesis Appears to Decrease Falls! Poster presented at 2020 American Physical Therapy Association Combined Sections Meeting (APTA CSM), Denver, CO.