The Use of Neuromuscular Electrical Stimulation (NMES) as Part of the Postoperative Care Regime in Orthopaedic Patients

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Abstract

Total Knee Arthroplasty (TKA) is an extremely beneficial procedure carried out primarily as a treatment for end-stage knee osteoarthritis to improve both quality of life and physical functioning. Limitations in physical function and daily physical activity due to osteoarthritis are among the primary reasons for undergoing TKA. As the average age of the world population increases, so will the prevalence of TKA. TKA is generally a very effective and successful procedure but complications can occur and post-surgical functional outcomes can be less than desired. Neuromuscular Electrical Stimulation (NMES) is a technology that may be of great benefit in preventing complications and in enhancing functional recovery post-TKA. NMES has many applications and has been reported to provide benefit in areas such as venous haemodynamics and lower limb muscle strengthening.

Within this thesis, the use of NMES as a method of recovery following TKA was examined, focusing on its use in the prevention of venous stasis and as an aid to functional recovery. Regarding the prevention of venous stasis, a systematic review and meta-analysis was carried out to assess the effectiveness of compression therapy, the current mechanical 'gold standard' for venous stasis prevention post-TKA. In addition, a haemodynamic study assessing and comparing the effectiveness of NMES and compression on both velocity and volume measures was carried out in healthy participants. With regard to functional recovery, physical activity was focused upon as one of the main outcomes and as such, an aim within this thesis was to investigate the sensitivity and specificity of a number of activity monitors that have the potential to be utilised by TKA patents post-surgery as a method of monitoring physical activity levels. To assess the effect of NMES on functional recovery, the use of NMES was examined in TKA patients in the acute post-discharge phase. Measures of interest included physical activity levels, joint range of motion and lower limb swelling.

Results presented within this thesis demonstrate that the true effectiveness of compression following TKA is as yet unknown and that its use is completely

unstandardised. Large, multi-centre, randomised trials with improved reporting are necessary. A comparison of compression to NMES revealed significantly greater improvements in lower limb haemodynamics, in terms of both velocity and volume measures,in healthy participants with use of NMES.

With regard to the accurate quantification of physical activity, studies carried out in a range of activity monitors highlight the importance of assessing both the sensitivity and specificity of these monitors. While all monitors tested were found to be sensitive in step detection, both the type of activity carried out and the wear location of the activity monitor had an effect on activity monitor specificity.

Use of NMES in TKA patients in the early post-discharge phase showed promising results with regard to physical activity levels as patients in the NMES group were found to spend significantly lesser time sitting/lying, a significantly greater time upright and to carry out a significantly greater number of Stepping Bouts within the early post-discharge period. These results demonstrate the ability of NMES to enhance functional recovery post-TKA in the early post-discharge period and suggest that use of an optimised NMES protocol will most likely provide excellent benefit in TKA patients with regard to improving functional recovery.

The findings of this thesis demonstrate the potential role of NMES as part of the post-operative care regime in orthopaedic patients and highlights a number of commercial activity that have the potential to be utilised by TKA patents post-surgery as a method of monitoring physical activity levels.

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Authors Declaration

I hereby declare that the work presented in this thesis was carried out in accordance with the regulations of the National University of Ireland, Galway. The research is original and apart from the contributions acknowledged below, the work presented was entirely my own. Dr. Khalid Bashar provided invaluable assistance with carrying out the meta-analysis (Chapter 2). Kevin O'Halloran and Shelly Moloney assisted in collecting haemodynamic data (Chapter 3). Lisa Kelly, Elaine Murphy, Sorcha Beirne, Niall Burke and Orlaith Kilgannon assisted in collecting physical activity data (Chapter 4). Evismar Almeida wrote the code to extract ActivPAL™ data (Chapter 6).

This thesis, or any part of, has not been submitted to the National University of Ireland, Galway, or in any other institution, in connection with any other award. Any views expressed herein are those of the author.

Signed:

Date:

List of Abbreviations

AAOS, American Academy of Orthopaedic Surgeons

BMI, Body Mass Index

CDC, Centers for Disease Control

CI, Confidence Interval

CINAHL, Cumulative Index to Nursing and Allied Health Literature

COPD, Chronic Obstructive Pulmonary Disease

CT, Computed Tomography

DF, Degrees of Freedom

DVT, Deep Vein Thrombosis

EV, Ejected Volume

FN, False Negative

FP, False Positive

FP/MIN, false positives per minute

FP/KM, false positives per kilometer

GCS, Graduated Compression Stockings

GLORY, Global Orthopaedic Registry

ICU, Intensive Care Unit

INR, International Normalised Ratio

IPC, Intermittent Pneumatic Compression

IU, International Units

LMWH, Low Molecular Weight Heparin

MAPE, Mean Absolute Percentage Error

NMES, NeuroMuscular Electrical Stimulation

OR, Odds Ratio

PE, Pulmonary Embolism

PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analysis

PV, Peak Velocity

RCT, Randomised Controlled Trial

ROM, Range of Motion

SCI, Spinal Cord Injured

SD, Standard Deviation

SEM, Standard Error of the Mean

TAMEAN, Time Averaged Mean Velocity

TED, ThromboEmbolic Disease

THA, Total Hip Arthroplasty

TKA, Total Knee Arthroplasty

TP, True Positive

UFH, UnFractionated Heparin

USA/ US, United States of America

UTD, Unable To Determine

VTE, Venous Thromboembolism

WHO, World Health Organization

WMD, Weighted Mean Difference

Publications and Proceedings

Peer Reviewed Articles:

O'Connell S, ÓLaighin G, Quinlan LR (2017) When a Step Is Not a Step! Specificity Analysis of Five Physical Activity Monitors. *PLoS ONE* 12(1): e0169616. doi:10.1371/journal.pone.0169616

O'Connell S, ÓLaighin G, Kelly L, Murphy E, Beirne S, Burke N, Kilgannon O, Quinlan LR (2016) These Shoes Are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps. *PLoS One* 11(5): e0154956.

O'Connell S, Bashar K, Broderick BJ, Sheehan J, Quondamatteo F, Walsh SR, ÓLaighin G, Quinlan LR (2016) The Use of Intermittent Pneumatic Compression in Orthopedic and Neurosurgical Postoperative Patients: A Systematic Review and Meta-analysis. *Annals of Surgery* 263(5):888-9.

Broderick BJ, **O'Connell S**, Moloney S, O'Halloran K, Sheehan J, Quondamatteo F, Quinlan LR, ÓLaighin G (2014) Comparative lower limb hemodynamics using neuromuscular electrical stimulation (NMES) versus intermittent pneumatic compression (IPC). *Physiological Measurement* 35: 1849-59.

Unpublished Abstracts:

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- *NUIG College of Medicine, Nursing and Health Sciences Research Day (May 2013)*
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- *NUIG College of Medicine, Nursing and Health Sciences Research Day (May 2014)*
- *Royal Academy of Medicine in Ireland, Biomedical Science Section Annual Meeting, Dublin (June 2014)*
- *NUI Galway Research Showcase (July 2014)*
- *37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Italy (August 2015)*
- *22nd Annual Conference of the Bioengineering Section of the Royal Academy of Medicine in Ireland, Galway (January 2016)*
- *Irish Orthopaedic Association Annual Conference, Westport (June 2016)*
- *British Orthopaedic Association Annual Conference, Belfast (September 2016)*

Aims

The main aims of this research were:

1. To investigate the use of NMES as a method of preventing venous stasis and DVT.
2. To investigate the sensitivity and specificity of a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery.
3. To investigate the use of NMES in enhancing recovery post-TKA through measures of physical activity, joint range of motion and lower limb swelling.

Chapter 1

General Introduction

1.1 Total Knee Arthroplasty

Surgeries of various types are routinely carried out with the express aim of improving an individual's health. However, with every surgery, even relatively common and uncomplicated procedures, comes the risk of complications both during and after the surgery. Equally, the recovery process and the time required to achieve functional independence after surgery is variable and dependent on many factors. Total Knee Arthroplasty (TKA) is seen as an extremely beneficial procedure, resulting in improved functional capacity and health-related quality of life for patients. TKA was first performed in 1968. Since then, its effectiveness has greatly increased due to both enhanced surgical techniques and materials and it is now widely considered one of the most successful procedures in medicine.

The knee is made up of the lower end of the femur, the upper end of the tibia and the patella, otherwise known as the kneecap. The ends of these three bones are covered with articular cartilage, a smooth substance that both protects the bones and allows easy movement. Menisci, C-shaped wedges, are located between the femur and tibia bones. They act as shock absorbers and cushion the knee joint. Knee stability is provided by ligaments that join the femur and tibia together, while knee strength is provided by muscles of the thigh. The remaining surfaces of the knee are covered by the synovial membrane, a thin lining that releases a fluid to lubricate the cartilage and reduce friction. The need for TKA can arise when rest and other treatments such as anti-inflammatory medication, cortisone injections, lubricating injections and physical therapy fail to improve symptoms of pain, stiffness, inflammation, swelling or deformity that can occur when the knee is injured or diseased.

TKA involves replacing the surface of the knee bones. When carrying out a TKA, the first step is to remove the damaged cartilage surfaces and a small amount of underlying bone at the end of the femur and tibia. This removed cartilage and bone is replaced with metal components that recreate the surface of the bones. The under surface of the patella is then cut and resurfaced with a plastic button. The final step is to insert a medical-grade plastic spacer between the metal components of the knee joint to allow for a smooth gliding surface.

The occurrence of TKA is increasing due to a number of factors, such as a general increase in the population, an increased incidence of people aged 65 years and older within the population and a high prevalence of obesity, which all contribute to an increased incidence of osteoarthritis and joint degeneration [1, 2]. In the USA, the demand for TKA is estimated to increase by 673% by the year 2030 [2]. Similar projections have been reported in England and Wales with the number of primary and revision TKAs projected to increase by 117% and 332% respectively from 2012 to 2030 [3]. While TKA is extremely beneficial, there are a number of clinical consequences and rehabilitation issues that can negatively affect patient recovery along the continuum of time from surgery to complete recovery (Figure 1). Clinical complications can occur both during and after TKA and include deep vein thrombosis (DVT), bleeding, infection, pain and cardiac events. Beyond these clinical complications, rehabilitation issues can be encountered during the recovery period. Post-TKA, rehabilitation focuses on the recovery of an individual's physical functioning, including an increased knee range of motion and the ability to improve physical activity levels.

1.2 Complications Associated with Total Knee Arthroplasty

The most common in-hospital complications associated with TKA are DVT and cardiac events, with the most common post-discharge complications reported as reoperation due to bleeding, wound necrosis, wound infection and DVT [4]. Venous stasis is a key factor that contributes to the development of DVT, a pathological blood clot that can lead to both morbidity and mortality. Venous stasis is defined as slow or sluggish movement of blood within the veins and is one of three factors proposed by Virchow in 1856 as being responsible for DVT development. The other two factors include hyper-coagulability of the blood and damage to the vascular endothelium. Surgery such as TKA exposes patients to each portion of this triad. The occurrence of venous stasis and subsequent development of DVT can negatively affect both the recovery process and recovery timeline of a patient.

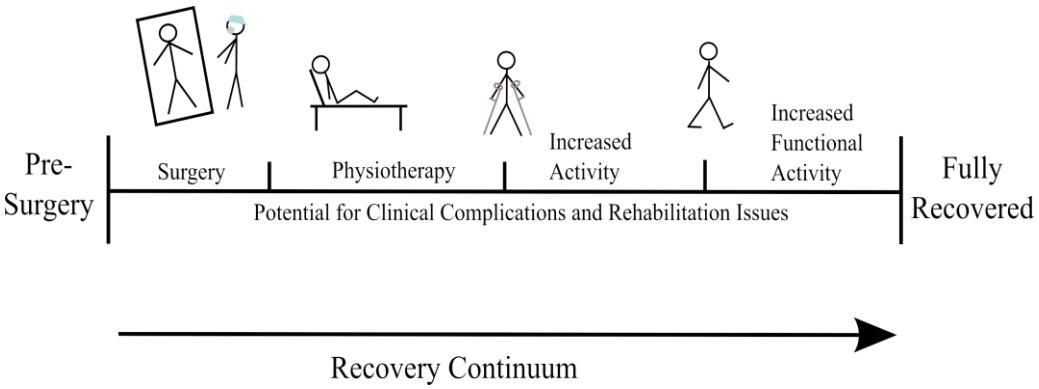


Figure 1 Stages of TKA experienced by patients from pre-TKA to full recovery post-TKA.

1.3 Preventing Complications Post-Total Knee Arthroplasty

This thesis focuses on the complication of DVT, which can arise during or after surgery. Neuromuscular electrical stimulation (NMES) is a mechanical method of venous stasis prevention [5-7]. Unlike pharmacological methods of DVT prevention, NMES is not associated with a risk of bleeding and promising results have been obtained from investigations carried out both during surgery and immediately post-surgery [5, 6]. Faghri et al (1997) investigated the use of electrical stimulation on venous blood flow during total knee/hip arthroplasty. When the tibialis anterior, gastrocnemius, quadriceps femoris and hamstring muscles of patients were stimulated, an increase in the central haemodynamic measures of stroke volume and cardiac output were reported, with the authors concluding that continuous stimulation-induced contractions during surgery could lead to improved venous circulation and blood stasis reduction [5]. When Broderick et al (2013) stimulated the calf muscles of knee and hip arthroplasty patients, who were at least three weeks post-surgery, the authors reported a 5-minute stimulation session to increase lower limb haemodynamic measures of peak venous velocity, mean velocity and volume flow [6].

In a similar study carried out by Yilmaz et al (2015) the authors stimulated the common peroneal nerve for one hour in every four after TKA, reporting a significantly greater peak blood flow velocity in the femoral vein and concluded that stimulation may potentially be of use as a supplementary technique in DVT prophylaxis [7]. The ability of NMES to improve haemodynamic measures may also provide benefit with regard to physical functional recovery. Indeed, NMES has been utilised in combination with physiotherapy as a method of improving functional recovery and rehabilitation post-TKA [8] and has been reported to reduce swelling [9] and improve muscle strength post-surgery [10].

1.4 Rehabilitation Post-Total Knee Arthroplasty

A measurable improvement in physical function following TKA is of the utmost importance and is one of the main reasons knee arthroplasty is performed. Functional recovery is an important aspect of the rehabilitation process following surgery. There are many outcomes that can be utilised as measures of functional recovery following TKA, such as post-operative maximum knee flexion [11]. The normal degree of flexion achieved in a healthy knee, in non-obese individuals, is up to 160 degrees. However, TKA patients rarely achieve a flexion beyond 120 degrees following surgery [12-16]. Knee flexion is an important consideration following TKA. Not only is it of the utmost importance for achieving functional health, the degree of post-surgical knee flexion influences fulfilment of expectations, functional ability, knee perception, and patient satisfaction [11, 17]. In turn, it has been demonstrated that patient expectations and perceptions may influence the success rate of knee arthroplasty [18-20]. When an adequate knee flexion cannot be achieved following TKA, activities of daily living are limited and patient satisfaction is lowered [21].

Furthermore, physical activity levels are an outcome that can be utilised to assess functional recovery following TKA. Physical activity is a major component of a healthy lifestyle and increased levels of physical activity are positively correlated with patient satisfaction following knee arthroplasty [22, 23]. Physical activity is often prescribed following surgery as a method of assisting in rehabilitation and improving functional recovery. An increase in physical activity will improve blood flow, hence reducing venous stasis and the risk of DVT, and will reduce swelling, helping to improve function. In a positive feedback way, an improvement in all of

the above-mentioned factors will allow for greater levels of physical activity to be achieved.

1.5 Monitoring Physical Activity Levels

When utilising physical activity as a method of measuring functional recovery, its accurate quantification is essential. While activity diaries and questionnaires can be utilised, physical activity monitors are often chosen in their stead. Physical activity monitors provide objective data and are unaffected by either recall or response bias. One of the main outputs utilised to quantify physical activity levels with the use of these monitors is that of step count. Step count provides an easy-to-understand measure of physical activity. Indeed, it is now commonly accepted that a daily step count of 10,000 steps is the number of steps required to achieve appropriate physical activity levels and represent 'active' behaviour [24-26]. However, although this level of activity is recommended, it is a more appropriate guide for healthy adults than those with osteoarthritis or post-knee replacement. Adults with osteoarthritis, for example, the most common precursor to lower limb orthopaedic surgeries, perform less physical activity than age-matched healthy subjects [22, 23, 27], with these individuals rarely achieving recommended physical activity levels [28]. Indeed, Tudor-Locke et al (2009) have reported a median expected value of 4,086 steps/day for adults with arthritis and 4,892 steps/day for adults who have undergone joint arthroplasty [29]. These figures are not completely surprising and are in agreement with studies assessing physical activity post joint arthroplasty. These studies have reported that although an increase in physical activity can be observed, this increase is often less than expected and less than that achieved by healthy controls [30-34].

There are many physical activity monitors available. They are commonly small in size, easy-to-wear and easy-to-use. These monitors provide quantification of physical activity on a screen interface and/or through use of a smartphone application. The ability to access real-time physical activity levels would be of great use to patients following TKA. This would allow patients, and their clinicians, to keep track of physical activity levels with regard to improving functional recovery.

However, when utilising physical activity monitors, it is of the utmost importance that they be accurate in their measurements. When utilising step count as an output, activity monitors must be sensitive enough to detect a step when a step is taken but also specific in disregarding non-stepping movements.

1.6 Research Objectives

The main objectives of this research were to investigate the use of NMES as a method of preventing venous stasis and DVT and in enhancing recovery following TKA. Although NMES has been reported to prevent venous stasis in both healthy and patient populations [6, 35- 38] it has yet to be fully elucidated or compared to other methods of venous stasis prevention. Currently, intermittent pneumatic compression (IPC) devices are the technology of choice for venous stasis and DVT prevention post-TKA despite their true efficacy being unknown [39]. Further to assessing its effects on venous stasis prevention, this thesis aims to assess the use of NMES as a method of enhancing functional recovery through outcomes of physical activity levels, knee range of motion and lower limb swelling. These measures play a major role in functional recovery post- TKA, with improvements in physical activity an important goal for many patients following surgery. When the measurement of physical activity is utilised as an indicator of functional recovery, its accurate quantification is of the utmost importance. As such, a further aim within this thesis was to investigate the sensitivity and specificity of a number of activity monitors that have the potential to be utilised by TKA patents post-surgery as a method of monitoring physical activity levels.

Specifically, three main areas of investigation were focused upon:

1. The use of NMES and IPC as mechanical methods of preventing venous stasis and hence preventing DVT.

2. The sensitivity and specificity of a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery.

3. The use of NMES as a method of enhancing functional recovery post-TKA, with a focus on measures of physical activity, joint range of motion and lower limb swelling.

The use of NMES and IPC as mechanical methods of preventing venous stasis and DVT is addressed within Chapters 2 and 3. To gain an understanding of IPC and evaluate its efficacy in preventing DVT, Chapter 2 comprehensively evaluates its use in high-risk surgical patients for DVT prevention through a systematic review and meta-analysis. Further to this, Chapter 3 investigates and compares the haemodynamic capabilities of both NMES and IPC.

The sensitivity and specificity of a range of physical activity monitors is focused upon in Chapters 4 and 5. Chapter 4 comprehensively assesses a number of physical activity monitors for their step detection sensitivity under conditions that could be encountered while achieving the recommended daily step goal of 10,000 steps. Further to this, Chapter 5 focuses on evaluating the specificity of a number of activity monitors, i.e. their ability to distinguish stepping from non-stepping movements, while carrying out a range of non-stepping physical activities.

The use of NMES as a method of enhancing functional recovery in the short-term post-TKA discharge phase is assessed within Chapter 6, with a focus on measures of physical activity levels, knee joint range of motion and lower limb swelling.

1.7 References

[1] Badley, E. and Crotty, M., "An international comparison of the estimated effect of the aging of the population on the major cause of disablement, musculoskeletal disorders," , *J Rheumatol,* vol. 22, no. 10, pp. 1934-40, Oct 1995.

[2] Kurtz, S., Ong, K., Lau, E., Mowat, F., and Halpern, M., "Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030," , *J Bone Joint Surg Am,* vol. 89, no. 4, pp. 780-5, Apr 2007.

[3] Patel, A., Pavlou, G., Mujica-Mota, R. E., and Toms, A. D., "The epidemiology of revision total knee and hip arthroplasty in England and Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset," , *Bone Joint J,* vol. 97-B, no. 8, pp. 1076-81, Aug 2015.

[4] Cushner, F., Agnelli, G., FitzGerald, G., and Warwick, D., "Complications and functional outcomes after total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY)," , *Am J Orthop (Belle Mead NJ),* vol. 39, no. 9 Suppl, pp. 22-8, Sep 2010.

[5] Faghri, P., Meerdervort, H. V., Glaser, R., and Figoni, S., "Electrical stimulation-induced contraction to reduce blood stasis during arthroplasty," , *IEEE Trans Rehabil Eng,* vol. 5, no. 1, pp. 62-9, Mar 1997.

[6] Broderick, B., Breathnach, O., Condon, F., Masterson, E., and ÓLaighin, G., "Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty," , *J Orthop Surg Res,* vol. 8, pp. 3-10, 2013.

[7] Yilmaz, S., Calbiyik, M., Yilmaz, B., and Aksoy, E., "Potential role of electrostimulation in augmentation of venous blood flow after total knee replacement: A pilot study," , *Phlebology,* Apr 6 2015.

[8] Avramidis, K., Karachalios, T., Popotonasios, K., Sacorafas, D., Papathanasiades, A., and Malizos, K., "Does electric stimulation of the vastus

medialis muscle influence rehabilitation after total knee replacement?," , *Orthopedics*, vol. 34, no. 3, p. 175, Mar 2011.

[9] Bogachev, V., Golovanova, O., Kuznetsov, A., Shekoyan, A., and Bogacheva, N., "Electromuscular stimulation with VEINOPLUS(R) for the treatment of chronic venous edema," , *Int Angiol*, vol. 30, no. 6, pp. 567-90, Dec 2011.

[10] Stevens-Lapsley, J., Balter, J., Wolfe, P., Eckhoff, D., and Kohrt, W., "Early neuromuscular electrical stimulation to improve quadriceps muscle strength after total knee arthroplasty: a randomized controlled trial," , *Phys Ther*, vol. 92, no. 2, pp. 210-26, Feb 2012.

[11] Devers, B., Conditt, M., Jamieson, M., Driscoll, M., Noble, P., and Parsley, B., "Does greater knee flexion increase patient function and satisfaction after total knee arthroplasty?," , *J Arthroplasty*, vol. 26, no. 2, pp. 178-86, Feb 2011.

[12] Aglietti, P., Buzzi, R., and Gaudenzi, A., "Patellofemoral functional results and complications with the posterior stabilized total condylar knee prosthesis," , *J Arthroplasty*, vol. 3, no. 1, pp. 17-25, 1988.

[13] Goldberg, V., Figgie, M., Figgie, H. r., Heiple, K., and Sobel, M., "Use of a total condylar knee prosthesis for treatment of osteoarthritis and rheumatoid arthritis. Long-term results," , *J Bone Joint Surg Am*, vol. 70, no. 6, pp. 802-11, Jul 1988.

[14] Dennis, D., Clayton, M., O'Donnell, S., Mack, R., and Stringer, E., "Posterior cruciate condylar total knee arthroplasty. Average 11-year follow-up evaluation," , *Clin Orthop Relat Res*, no. 281, pp. 168-76, Aug 1992.

[15] Emmerson, K., Moran, C., and Pinder, I., "Survivorship analysis of the Kinematic Stabilizer total knee replacement: a 10- to 14-year follow-up," , *J Bone Joint Surg Br*, vol. 78, no. 3, pp. 441-5, May 1996.

[16] Sultan, P., Most, E., Schule, S., Li, G., and Rubash, H., "Optimizing flexion after total knee arthroplasty: advances in prosthetic design," , *Clin Orthop Relat Res*, no. 416, pp. 167-73, Nov 2003.

[17] Matsuda, S., Kawahara, S., Okazaki, K., Tashiro, Y., and Iwamoto, Y., "Postoperative Alignment and ROM Affect Patient Satisfaction After TKA," *Clinical Orthopaedics and Related Research®*, journal article vol. 471, no. 1, pp. 127-133, 2013.

[18] Hilding, M., Backbro, B., and Ryd, L., "Quality of life after knee arthroplasty. A randomized study of 3 designs in 42 patients, compared after 4 years," , *Acta Orthop Scand*, vol. 68, no. 2, pp. 156-60, Apr 1997.

[19] Dawson, J., Fitzpatrick, R., Murray, D., and Carr, A., "Questionnaire on the perceptions of patients about total knee replacement," , *J Bone Joint Surg Br*, vol. 80, no. 1, pp. 63-9, Jan 1998.

[20] Heck, D., Robinson, R., Partridge, C., Lubitz, R., and Freund, D., "Patient outcomes after knee replacement," , *Clin Orthop Relat Res*, no. 356, pp. 93-110, Nov 1998.

[21] Sugitani, K. *et al.*, "Factors affecting range of motion after total knee arthroplasty in patients with more than 120 degrees of preoperative flexion angle," *International Orthopaedics*, journal article vol. 39, no. 8, pp. 1535-1540, 2015.

[22] Ethgen, O., Bruyere, O., Richy, F., Dardennes, C., and Reginster, J., "Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature," , *J Bone Joint Surg Am*, vol. 86-A, no. 5, pp. 963-74, May 2004.

[23] Kahn, T. and Schwarzkopf, R., "Does Total Knee Arthroplasty Affect Physical Activity Levels? Data from the Osteoarthritis Initiative," , *J Arthroplasty*, vol. 30, no. 9, pp. 1521-5, Sep 2015.

[24] Tudor-Locke, C. and Bassett, D. J., "How many steps/day are enough? Preliminary pedometer indices for public health," , *Sports Med,* vol. 34, no. 1, pp. 1-8, 2004.

[25] Tudor-Locke, C., Hatano, Y., Pangrazi, R., and Kang, M., "Revisiting "how many steps are enough?"," , *Med Sci Sports Exerc,* vol. 40, no. 7 Suppl, pp. S537-43, Jul 2008.

[26] Kang, M., Marshall, S., Barreira, T., and Lee, J., "Effect of pedometer-based physical activity interventions: a meta-analysis," , *Res Q Exerc Sport,* vol. 80, no. 3, pp. 648-55, Sep 2009.

[27] Grant, P., Dall, P., Mitchell, S., and Granat, M., "Activity-monitor accuracy in measuring step number and cadence in community-dwelling older adults," , *J Aging Phys Act,* vol. 16, no. 2, pp. 201-14, Apr 2008.

[28] Taraldsen, K., Chastin, S., Riphagen, I., Vereijken, B., and Helbostad, J., "Physical activity monitoring by use of accelerometer-based body-worn sensors in older adults: a systematic literature review of current knowledge and applications," , *Maturitas,* vol. 71, no. 1, pp. 13-9, Jan 2012.

[29] Tudor-Locke, C., Washington, T., and Hart, T., "Expected values for steps/day in special populations," , *Prev Med,* vol. 49, no. 1, pp. 3-11, Aug 2009.

[30] de Groot, I., Bussmann, H., Stam, H., and Verhaar, J., "Small increase of actual physical activity 6 months after total hip or knee arthroplasty," , *Clin Orthop Relat Res,* vol. 466, no. 9, pp. 2201-8, Sep 2008.

[31] Brandes, M., Ringling, M., Winter, C., Hillmann, A., and Rosenbaum, D., "Changes in physical activity and health-related quality of life during the first year after total knee arthroplasty," , *Arthritis Care Res (Hoboken),* vol. 63, no. 3, pp. 328-34, Mar 2011.

[32] Tsonga, T. *et al.*, "Evaluation of improvement in quality of life and physical activity after total knee arthroplasty in greek elderly women," , *Open Orthop J,* vol. 5, pp. 343-7, 2011.

[33] Vissers, M., Bussmann, J., Groot, I. d., Verhaar, J., and Reijman, M., "Physical functioning four years after total hip and knee arthroplasty," , *Gait Posture,* vol. 38, no. 2, pp. 310-5, Jun 2013.

[34] Keeney, J., Nunley, R., Wright, R., Barrack, R., and Clohisy, J., "Are younger patients undergoing TKAs appropriately characterized as active?," , *Clin Orthop Relat Res,* vol. 472, no. 4, pp. 1210-6, Apr 2014.

[35] Faghri, P., Votto, J., and Hovorka, C., "Venous hemodynamics of the lower extremities in response to electrical stimulation," , *Arch Phys Med Rehabil,* vol. 79, no. 7, pp. 842-8, Jul 1998.

[36] Griffin, M., Nicolaides, A., Bond, D., Geroulakos, G., and Kalodiki, E., "The efficacy of a new stimulation technology to increase venous flow and prevent venous stasis," , *Eur J Vasc Endovasc Surg,* vol. 40, no. 6, pp. 766-71, Dec 2010.

[37] Izumi, M., Ikeuchi, M., Mitani, T., Taniguchi, S., and Tani, T., "Prevention of venous stasis in the lower limb by transcutaneous electrical nerve stimulation," , *Eur J Vasc Endovasc Surg,* vol. 39, no. 5, pp. 642-5, May 2010.

[38] Corley, G., Breen, P., Birlea, S., Serrador, J., Grace, P., and ÓLaighin, G., "Hemodynamic effects of habituation to a week-long program of neuromuscular electrical stimulation," , *Med Eng Phys,* vol. 34, no. 4, pp. 459-65, May 2012.

Chapter 2

The Use of Intermittent Pneumatic Compression in Orthopaedic and Neurosurgical Post-Operative Patients: A Systematic Review and Meta-Analysis

Published Reference:

O'Connell S, Bashar K, Broderick BJ, Sheehan J, Quondamatteo F, Walsh SR, ÓLaighin G, Quinlan LR. The Use of Intermittent Pneumatic Compression in Orthopedic and Neurosurgical Postoperative Patients: A Systematic Review and Meta-analysis. *Annals of Surgery*. 2016;263(5):888-9.

Background

Venous stasis is a factor involved in the development of Venous Thromboembolism (VTE). VTE is a complication of importance associated with surgeries such as hip and knee arthroplasties and neurological surgeries. VTE encompasses both Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE). DVT involves the development of a pathological blood clot in a deep vein, primarily of the lower limb. PE is a travelling blood clot thought to succeed DVT and can prove fatal in the pulmonary vessels. The development of VTE is a major source of morbidity that can impede recovery following surgery [1]. Management of VTE focuses on prevention rather than cure. Both pharmacological and mechanical methods of prophylaxis are utilised. Mechanical methods target the prevention of venous stasis and are often employed alongside pharmacological methods in surgeries considered to be high-risk for DVT development. These surgeries are considered high-risk as they expose patients to venous stasis, hypercoagulability of the blood and damage to the blood vessel endothelium, the triad of factors necessary for DVT development.

Mechanical methods utilised to prevent venous stasis include Graduated Compression Stockings (GCS), Intermittent Pneumatic Compression (IPC) devices and Neuromuscular Electrical Stimulation (NMES). While GCS and IPC are currently used for venous stasis prevention in hospital and in the home, the use of NMES is not widespread. An aim of this thesis is to investigate the use of NMES as part of a post-operative care regime in orthopaedic patients as a method of preventing venous stasis. However, before assessing the use of NMES, it is first important to assess the currently used methods of venous stasis prevention for their effectiveness. IPC devices, for example, are recommended for use following surgeries such as total hip and knee arthroplasty. However, there is no standardised protocol associated with their usage and their true efficacy remains unknown.

As such, the aim of this systematic literature review and meta-analysis was to carry out an up-to-date evaluation of compression devices and assess their efficacy as venous stasis and hence, DVT prophylaxis methods, in patients with a high-risk of DVT development, i.e. orthopaedic and neurological patients.

Contribution to work

Data collection:Sandra O'Connell, Khalid Bashar.

Data Analysis: Sandra O'Connell, Khalid Bashar.

Interpretation of results: Sandra O'Connell, Khalid Bashar.

Drafting of manuscript: Sandra O'Connell, Khalid Bashar.

Critical review of manuscript: Sandra O'Connell, Khalid Bashar, Barry J Broderick, James Sheehan, Fabio Quondamatteo, SR Walsh, Gearoid ÓLaighin, Leo R Quinlan.

2.1 Abstract

2.1.1 Mini-Abstract

Deep vein thrombosis (DVT) remains an important clinical concern following high-risk surgery despite available prophylaxis methods. Although used in DVT prevention, compression devices have yet to be fully assessed in effectiveness and their use has yet to be standardised for DVT prevention. Further research is required.

2.1.2 Structured Abstract

Objective: The objective of this systematic review and meta-analysis was to carry out an up-to-date evaluation on the use of compression devices as DVT prophylaxis methods in orthopaedic and neurological patients.

Summary Background Data: There is an increased risk of DVT with surgery, in particular in patients who are not expected to mobilise soon after their procedures, such as orthopaedic and neurosurgical patients. Compression devices are often employed for DVT prophylaxis in these patients. However, the true efficacy of these devices and the standardisation of use with these devices have yet to be established.

Methods: Medline, CINAHL, Embase, Google Scholar and the Cochrane library electronic databases were searched to identify randomised controlled trials and observational studies reporting on the use of compression devices for DVT prevention.

Results: Nine studies were included for review and meta-analysis. Use of an IPC device alone is neither superior nor inferior to chemoprophylaxis.

Conclusion: In the absence of large randomised multi-centre trials comparing the use of IPC or chemoprophylaxis alone to a combination of both treatments, the current evidence supports the use of a combined approach in high-risk surgical patients.

2.2 Introduction

Deep Vein Thrombosis (DVT), the development of a pathological thrombus in a deep vein, is of particular concern within the orthopaedic and neurological communities, especially following surgeries in these fields, where patients are deemed a high risk for DVT development. The main danger associated with DVT is that of Pulmonary Embolism (PE), which can occur when the clot breaks away from the vessel wall and travels as far as the lungs, where it can be fatal [2]. Together, DVT and PE are known collectively as Venous Thromboembolism (VTE). There is an increased risk of DVT with surgery, in particular in patients who are not expected to mobilise soon after their procedures, such as orthopaedic patients post Total Hip Arthroplasty (THA)/Total Knee Arthroplasty (TKA) surgery, or neurosurgical patients following spinal/head procedures. To this end, prevention of DVT is more important in those who are considered to be a high risk for developing VTE complications, with the continuing debate on the best modality to achieve a reasonable risk reduction, while at the same time avoiding complications associated with chemoprophylaxis, such as major bleeding [3-6].

The increased incidence of osteoarthritis and rheumatoid arthritis in an aging population makes it a particularly worrying concern within the orthopaedic community. Combined with the benefit these surgeries provide with regard to both function and quality of life for patients, their prevalence will only continue to increase. For example, in the U.S.A alone, it has been estimated that the demand for primary THA will increase from 293,094 in 2010 to 511,837 in 2020, an increase of 75%, with the demand for TKA estimated to increase from 655,336 to 1,375,574 over the same period, an increase of 110% [7]. According to data from the Global Orthopaedic Registry (GLORY), the overall incidence of major complications following THA and TKA is low [8]. However, DVT and PE are complications that do occur. Indeed, DVT is one of the most common in-hospital complications, occurring in 0.6% and 1.4% of THA and TKA patients respectively [8]. Overall, DVT was found to occur in up to 1.4% of patients enrolled in GLORY. This would suggest that although many forms of prophylaxis are available, both pharmacological

and mechanical, DVT remains an important clinical burden following these surgeries.

DVT is also a prominent concern within the neurological community. Although anticoagulants such as Low Molecular Weight Heparin (LMWH) and Unfractionated Heparin (UFH) are recommended for DVT prevention in neurological patients, extreme caution must be exercised with their use due to the risk of bleeding in the brain or spine, which could be fatal [9-13]. As such, mechanical methods of prophylaxis including Graduated Compression Stockings (GCS) and Intermittent Pneumatic Compression (IPC) devices are also recommended for neurological patients.

IPC devices are a popular form of mechanical DVT prevention that act to prevent venous stasis. These devices consist of a pneumatic pump that connects to one or more inflatable cuffs/pads via air hoses. The cuffs are wrapped around a patient's foot or leg. With IPC of the foot, rapid, cyclical inflation and deflation of the cuffs give a non-physiological compression of the plantar venous plexus. Expulsion of blood from the foot prevents venous stasis. The blood is pushed through the venous system back towards the heart in order to reduce the risk of DVT development (Supplemental Figure 2.6). IPC of the calf is similar to IPC of the foot, with the inflatable cuff wrapped around the calf compartment as opposed to the foot. Compression of the underlying veins expels blood from these veins in order to prevent venous stasis, and hence, prevent DVT development (Supplemental Figure 2.7).

Many types of IPC devices are available. They differ in terms of inflation and deflation times, cuff pressure, cuff configuration and placement. There are essentially 5 different cuff placements for the lower limb: foot compression, foot and calf compression, calf compression, calf and thigh compression and whole limb compression [14]. Cuff configurations include uniform compression and graduated sequential compression, which uses multiple bladders that inflate from distal to proximal generating a "milking" effect of the limb in question. As well as acting to prevent venous stasis, studies have also shown that IPC appears to stimulate fibrinolytic activity by inhibiting the tissue factor pathway, suggesting that it affects

two of the three criteria of Virchow's triad: reducing stasis and reversing hypercoagulability [15-19]. This is especially important in the orthopaedic and neurosurgical post-operative patient populations who are at an increased risk of DVT development due to the endothelial damage, hypercoagulability and venous stasis present both during and after their surgeries.

As the risk of bleeding is greatly reduced with mechanical methods of prophylaxis, such as IPC devices, they are attractive options, especially in cases of pharmacological contraindication. However, the true efficacy of mechanical prophylaxis methods is yet unknown. As such, the objective of this systematic review and meta-analysis was to carry out an up-to-date evaluation on the use of compression devices as DVT prophylaxis methods in orthopaedic and neurological patients.

2.3 Methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines [20]. There is no published protocol for this review.

2.3.1 Eligibility Criteria

We searched for randomised controlled trials (RCTs) and observational studies that compared the use of an intermittent pneumatic compression device – with or without an additional pharmacological agent – to the more conventional use of pharmacological agents in patients undergoing major orthopaedic, general and neurosurgical procedures. Case series and review articles were excluded from this review.

2.3.2 Search Strategy

We searched the literature for relevant citations in December 2014 using the following terms: ([“deep venous thrombosis” OR “DVT”] AND [“prophylaxis” OR “prophylactic” OR “prevention” OR “thrombo-prophylaxis”] AND [“compression” OR “device” OR “sequential compression” OR “intermittent compression” OR “pneumatic compression”]. We searched the databases of Medline, CINAHL, Embase, Google Scholar and the Cochrane library. No restrictions were applied in terms of publication status or language. We restricted our search to studies conducted on human subjects only between 2004 and 2014. Bibliographies of included studies were searched for possible citations. A summary of the study selection process can be found in the PRISMA flow diagram in Figure 2.1.

Two researchers (SOC and KB) independently determined eligibility for inclusion for each study following an examination of the relevant abstracts. Any differences regarding the possible inclusion of individual citations were settled by downloading the full article. A third reviewer (SRW) was consulted to settle any remaining differences.

The main outcome measures for this systematic review were the reported rate of developing DVTs and/or PEs in included studies, both symptomatic and asymptomatic as reported by the individual studies. Secondary outcome measures were death related to a thromboembolic event and the need for blood transfusions following enrolment of patients in each study. Criteria used for the detection of DVT/PE were those mentioned in individual studies, and were reported separately.

2.3.3 Data Collection

Data were collected independently by SOC and KB and extracted to a Microsoft Excel spread sheet. Differences in data extraction were discussed between the two researchers, and any remaining differences were resolved following consultation with the third reviewer (SRW). The following baseline characteristics of participants were recorded: sex, age and history of DVT, in addition to reported rates of DVT, PE, number of patients requiring blood transfusion, number of units used for blood transfusion and death related to DVT/PE. Studies were not restricted based on the duration of follow-up. The individual inclusion and exclusion criteria of the studies included in this review are summarised in Table 2.1.

Table 2.1 Inclusion & Exclusion Criteria and Main Outcomes for Included Studies

Study	Inclusion criteria	Exclusion criteria	Reported primary outcome(s)	Main results
Kurtoglu [21]	Patients with severe head or spinal trauma	Younger than 14 years, hepatic/urinary dysfunction, spinal cord injury, history of DVT, high bleeding risk (platelets < 100,000 µl or INR > 1.5) and use of anti-coagulants. Also patients with CT evidence of continuing bleeding and those requiring craniotomy were excluded	DVT, PE	No statistically significant difference regarding a reduction in DVT, PE, or mortality between groups ($P = 0.04$, $P > 0.05$, $P > 0.05$, respectively). Similar rates of postoperative wound/urine infections and pneumonia. Blood transfusion when required was significantly less in the IPC group (0.9±1.7 vs. 2.8±1.3 units, $P = 0.03$)
Pitto [22]	Patients undergoing uncemented total hip arthroplasty	History of DVT/PE, heart disease. Age groups < 18 and > 80 years, active malignant tumour, long term anticoagulation treatment, gastrointestinal ulceration and painful joints in the foot. 16 excluded after initial randomisation for not tolerating the use of the foot pump	DVT	DVT occurred significantly less frequently in the IPC group ($P < 0.05$). The mean post-operative drainage was 259 mL in the foot-pump group and 328 mL in the LMWH group ($P < 0.05$). Less swelling measured in the thighs of patients in the IPC group (10mm compared with 15mm; $P < 0.05$)
Silbersack [23]	Patients > 18 years undergoing primary unilateral total hip replacement or total knee replacement	Patients with stage III chronic renal insufficiency, history of significant cardiac insufficiency, severe peripheral arterial disease, neurological disorders or arthrodesis of the lower limbs, recent anticoagulation acute thrombophlebitis, haemorrhagic diathesis, allergy to heparins and active malignant disease	DVT, PE	DVT risk significantly lower in the IPC group: 0/68 in IPC and LMWH group, vs. 18/63 in the LMWH and GCS ($P < 0.0001$)
Gelfer [24]	Unilateral primary THA or TKA. All included women were post-menopausal	Refusal of consent, long-term anticoagulant therapy, treatment with anti-aggregant medication for the last 10 days, known hypersensitivity to contrast medium or aspirin or low molecular weight heparin, previously diagnosed venous thromboembolism (VTE), concurrent thrombosis process, enrolment in another clinical trial	Thromboembolism	Overall risk for DVT and proximal DVT were both significantly higher in the Enoxaparin group ($P = 0.002$ and $P = 0.049$, respectively). IPC appeared to have prevented more DVTs in patients undergoing total hip arthroplasty (0/4 DVTs in the IPC group in those patients, compared to 13/17 DVTs in the Enoxaparin group)
Eisele [25]	Age > 20 and < 86 years, and a surgical site in an area other than the upper extremity	If the surgical site interfered with the application of the IPC. One patient was excluded based on history of acute DVT	Not clearly stated. Development of DVT was primary outcome reported on	DVT occurred in 10 patients who had total hip/knee arthroplasty in the LMWH group compared to 3 DVTs in patients with knee surgery in the IPC + LMWH group. Overall difference in rate of DVT in the study was significant between the two groups ($P = 0.007$)

Edwards [26]	Patients undergoing total hip or total knee arthroplasty procedures	33 patients excluded for protocol violations: missed ultrasound (n=9), surgery other than total hip/knee arthroplasty (n=1), previous history of thrombosis (n=12), history of prophylaxis other than LMWH (n=8), and other protocol deviations (n=3)	DVT, PE	5 DVTs and zero PEs occurred in the IPC + LMWH group compared with one PE and 14 DVTs in the LMWH group (P = .018). The difference was not significant for patients who underwent hip replacement procedures
Chin [27]	Low risk patients with no predisposition to thromboembolism who were undergoing elective total knee arthroplasty	The use of anticoagulants or aspirin, a history of DVT/PE in the previous year, obesity (BMI of >30 kg/m^2), prolonged immobilisation, bleeding tendency or a history of gastrointestinal bleeding, surgery in the previous 6 months, cerebrovascular accident in the previous 3 months, uncontrolled hypertension, congestive cardiac failure, renal or liver impairment, allergy to heparin or heparin-induced thrombocytopenia, varicose veins or chronic venous insufficiency, peripheral vascular disease, skin ulcers, dermatitis or wounds, and malignancy	DVT	Numbers of patients requiring transfusion were similar among groups, but the enoxaparin group required more blood volume to be transfused (P = 0.029). Also, two patients in the enoxaparin group suffered major bleeding
Colwell [28]	Patients who had total hip arthroplasty and aged > 18 years	DVT history, a coagulation disorder including the known presence of factor V Leiden, a solid malignant tumour, peptic ulcer disease, and major surgery in the prior three months	Major bleeding	All major bleeding (n=11) occurred in the LMWH group (P = 0.0004). The difference in the rate of DVT/PE was not significant between the groups (P = 0.953)
Windisch [29]	Patients undergoing elective total knee arthroplasty	Age < 60 years, BMI > 40 or <25 (underweight), existing acute DVT, thrombophlebitic varicosis, venous insufficiency	Soft tissue swelling	Reduction of soft tissue swelling around operated knee was better in the IPC + LMWH group (P < 0.05). Improved mobility was associated with the use of IPC and LMWH rather than LMWH only (P <0.01). No evidence of DVT/PE in any of the patients included in the study

BMI, body mass index; DVT, deep vein thrombosis; GCS, graduated compression stockings; INR, international normalised ratio; IPC, intermittent pneumatic compression; LMWH, low molecular weight heparin; PE, pulmonary embolism; THA, total hip arthroplasty; TKA, total knee arthroplasty.

2.3.4 Quality Assessment for Risk of Bias

We used the Downs and Black Tool to measure and report the quality assessment of included studies [30]. The tool has 27 questions assessing the quality of reporting, external validity and internal validity. The original tool generates scores between (0 and 32), however, we simplified the score given for sample size justification (0 – 5) and modified the score to award one point for studies which outlined their methods of sample calculation and zero points for those that did not state their methods of sample size calculation. Thus, the modified tool generates scores between (0 and 27). The higher scores indicate higher quality. Details of the quality assessment can be found on a supplemental table (Supplemental Table 2.3).

2.3.5 Data Analysis

Statistical analyses were performed using Cochrane's Review Manager version 5.3.5 [31]. The random effects model of DerSimonian and Laird was chosen to generate pooled risk ratios for outcomes measured in the meta-analysis section of this review [32]. For continuous outcome variables the weighted mean difference (WMD) was calculated. Statistical heterogeneity among studies was determined by the Cochran's Q test. The confidence interval was measured at the 95% point and P-values < 5% were used to measure statistical significance. Publication bias among studies was examined by comparing between the fixed and random effects measures in a sensitivity test of pooled data [33]. Another sensitivity test aimed to adjust for the small number of PEs reported across studies was performed using a second software package – Biostat's Comprehensive Meta-Analysis – to generate pooled Peto's odds ratio [34]. Peto's odds ratio has been recommended when events being examined are rare or when intervention effects are small [35]. In this latter test, we assumed a value of (0.1) to both groups in trials that reported zero outcome PE events in both groups to force the inclusion of those trials in the pooled estimate of intervention effect. We also performed another sensitivity test by adding the data from one study that was originally omitted from the meta-analysis due to the lack of a clearly defined control group [36].

2.4 Results

2.4.1 Study Selection

The results of the study selection process are summarised in the PRISMA flow diagram (Figure 2.1). Initially, we found a total of 2,075 citations. After we removed duplicates and limited the search to studies on humans, we were left with 1,018. We screened the titles of those citations and were left with 84 potentially relevant papers. The abstracts of those citations were examined for relevant measures. Finally, we downloaded the full articles of the remaining seventeen citations and found that nine studies satisfied our inclusion criteria for this systematic review [21-29].

All included studies were RCTs published between 2004 and 2010. One study was excluded from the meta-analysis for not having a clearly defined control group, however, we added the data extracted from this study in a sensitivity test for both of our main outcomes (DVT and PE) to increase the rigour of our review [36]. An IPC device was used in all studies; six studies reported the use of a device around the calf muscles [21, 23-26, 28], whereas a foot-pump device was used in two studies [22, 29], and one study did not report the type of device used for intermittent pneumatic compression [27]. Four studies used an IPC device in the intervention group [21, 22, 27, 28], including one study which reported the additional use of Aspirin in 63% of patients randomised to receive compression [28], whereas another four studies combined the use of an IPC device with a LMWH agent [23, 25, 26, 29], and finally one study reported the use of Aspirin in all patients in the compression group [24]. A LMWH was used in the controls of all included studies as follows: Enoxaparin in seven studies [21, 23, 24, 26-29], Fraxiparin in one study [22], and Certoparin in one study [25]. Overall four studies used the same pharmacological agent type, dose, and frequency of dosing in the IPC group as in the control group [23, 25, 26, 29]. Three studies used IPC alone [21, 22, 27], with the control groups receiving LMWH (enoxaparin or fraxiparin). Two studies compared the use of IPC plus aspirin to LMWH [24, 28]. A detailed description of the criteria for each study is shown in Table 2.2. Of the included studies, one study included neurosurgical patients with severe head or spinal trauma [21], while the remaining studies were with orthopaedic patients; four studies in patients who underwent either THA or TKA surgery [23-26],

two studies in patients who had THA [22, 28] and two studies in patients who had TKA procedures [27, 29].

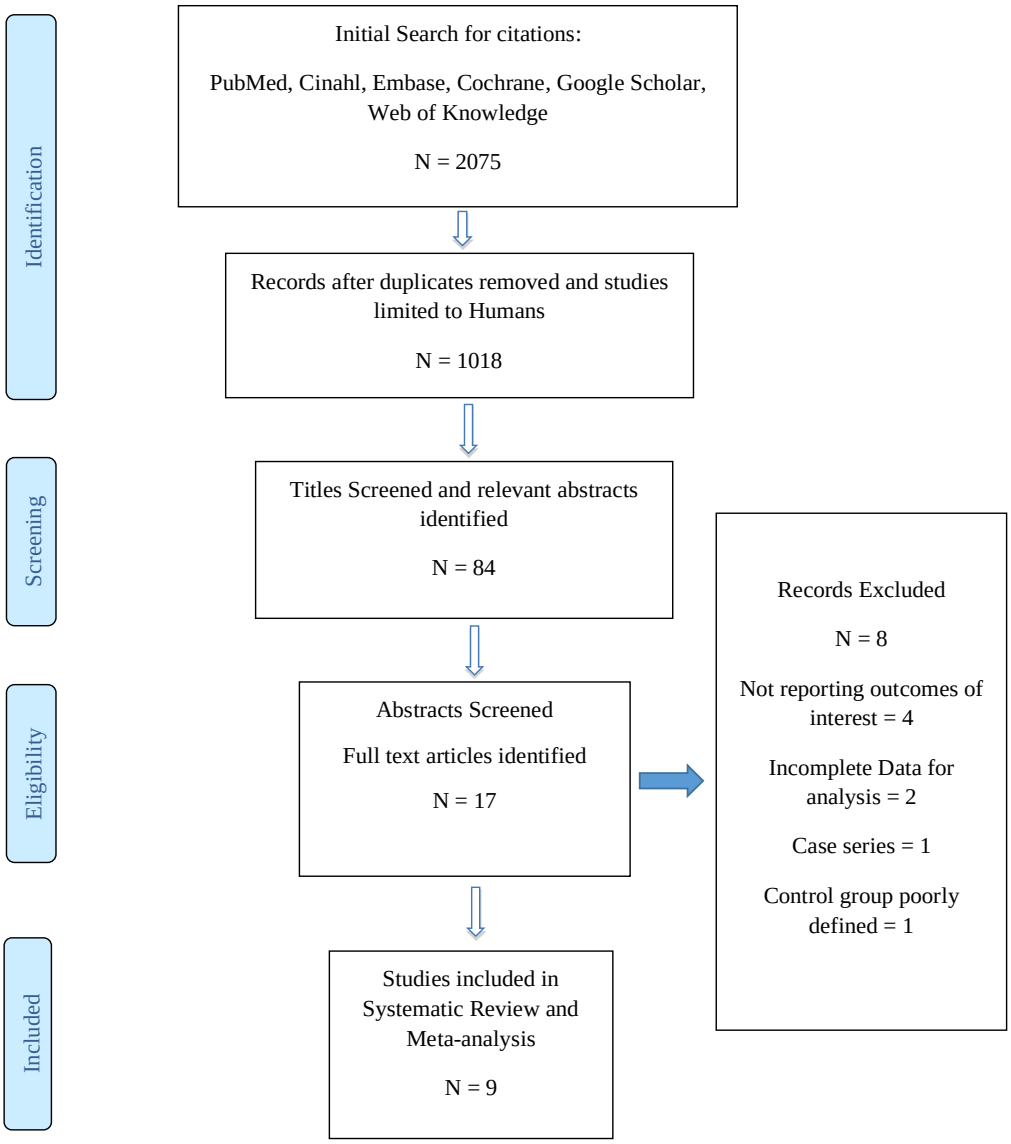


Figure 2.1 PRISMA flow diagram.

We performed a sensitivity test by including the data from the study by Sobieraj-Teague et al. [36]. This study did not include clearly defined intervention or control groups; both groups had a mixture of patients who were put on different pharmacological agents (aspirin, warfarin or a LMWH) and some of the patients

were treated with conventional GCS only. This study included patients who were admitted for cranial or spinal neurosurgery, as well as patients admitted with intracranial haemorrhage and evidence of a motor deficit who were not planned for surgery.

2.4.2 Participants

The nine studies included in this review had a combined total of 3,347 patients. The IPC group consisted of 1,680, while the control group was formed by the remaining 1,667 patients. Age was not reported in all studies; however, all patients were above 18 years. Kurtoglu et al had the youngest patients (median 37.1 (18 - 76) for both groups) [21], whereas Edwards et al had the oldest patients (IPC group median of 66.2 (31.6 - 87.7), and 68.2 (33.7 - 86.6) for controls) [26]. The remaining studies reported an average age in the late 50s to 60s for patients in both groups [22-25, 27-29]. Two studies did not report the male-to-female ratio [25, 29], and one study reported an overall ratio of 47 male subjects to 73 females [21]. The remaining six studies reported the ratio separately for the two groups, with a ratio of 232:440 males: females in the IPC group, compared to 229:437 males: females in the controls [22-24, 26-28].

Table 2.2 Criteria of Individual Studies

Study	Date published	Design	Characteristics of the intervention group	Number of cases	Characteristics of the control group	Number of controls	Method and time of DVT assessment	Duration of hospital stay (days)	Duration of follow-up (weeks)	Time to mobilise	Study quality score	Comment
Kurtoglu [21]	2004	RCT	*Age:* overall 37.1 (18-76) yrs *Gender M/F:* overall 47/73 *Excluded patients:* continuing haemorrhage within 24 hrs admission, requiring craniotomy *IPC started:* admission to ICU *Hrs/day:* - *Application:* below-knee	60	*Age:* overall- 37.1 (18-76) yrs *Gender M/F:* overall 47/73 *Excluded patients:* continuing haemorrhage within 24 hrs admission, requiring craniotomy *LMWH started:* determined following CT scans within 24 hrs admission *Time on LMWH:* - *Dose of LMWH:* 40mg/day	60	Duplex colour-flow ultrasound on admission to ICU, each week in hospital and 1 week after discharge	Case: 10.3± 3.6 Control: 10.7± 4.4	1	Case: 12.1± 2.1 hrs Control: 13± 1.9 hrs	14	Time using IPC or LMWH is unclear. 14 patients had suspected DVT; 5 of these patients were diagnosed with DVT by ultrasound. PEs were not reported to be symptomatic.
Pitto [22]	2004	RCT	*Age:* 57.3 ± 12 yrs *Gender M/F:* 30/70 *Excluded patients:* if use of foot pump was stopped for more than 4 consecutive hours *IPC started:* in recovery room *Hrs/day:* mean of 19.4 *Application:* foot IPC	100	*Age:* 58.1± 11 yrs *Gender M/F:* 32/68 *Excluded patients:* - *LMWH started:* 12 hrs before operation *Time on LMWH:* 13 days *Dose of LMWH:* 0.2 to 0.6ml; 0.1ml = 950 IU of anti Xa	100	Duplex ultrasound at pre-op, day 3 and day 10 post-op	Case: 12± 2 Control: 13± 1.5	6	By day 2 (usually)	22	The only study that used Fraxiparin as the LMWH. Patients who stopped using the pump > 4 hours were excluded from study. The foot pump group had 3 DVT in total, 1 was symptomatic. The control group had 6 DVT in total, 1 was

												symptomatic. No PE reported.
Silbersack [23]	2004	RCT	*Age:* 63 (29- 90) yrs *Gender M/F:* 28/40 *Excluded patients:* non-compliance, premature transfer to different institution, confinement to bed for > 1 week, re-operation or discharge without ultrasound *IPC started:* in recovery room *Hrs/day:* 6- 8 *Application:* calves *LMWH started:* evening prior to surgery *Time on LMWH:* 30 days *Dose of LMWH:* 40mg/day	68	*Age:* 65 (36- 87) yrs *Gender M/F:* 19/44 *Excluded patients:* non-compliance, premature transfer to different institution, confinement to bed for > 1 week, re-operation or discharge without ultrasound *LMWH started:* evening prior to surgery *Time on LMWH:* 30 days *Dose of LMWH:* 40mg/day	63	Ultrasound on day 6 to 12 post-op	Not reported	12	Day 1 post-op	19	Heparin was substituted for enoxaparin in patients with spinal epidural until safe to start LMWH (not stratified by sub-group analysis). Did not report whether DVTs were symptomatic or not. No symptomatic PE reported.
Gelfer [24]	2006	RCT	*Age:* 68 ± 10.4 yrs *Gender M/F:* 21/40 *Excluded patients:* refused venography/ultrasound, late info. about old DVT, early hip prosthesis dislocation, protocol violation *IPC started:* after induction of anaesthesia *Hrs/day:* - *Application*: calf (foot used on TKA patients during surgery) *Aspirin started:* within 12 hrs post-operation *Time on aspirin:* -	61	*Age:* 67 ± 8.7 yrs *Gender M/F:* 23/37 *Excluded patients:* refused venography/ultrasound, late info. about old DVT, early hip prosthesis dislocation, protocol violation *LMWH started:* within 12 hrs post-operation *Time on LMWH:* - *Dose of LMWH:* 40mg/day	60	Venography or duplex ultrasound on day 5 to 8 post-op	Case: 8.8± 1.9 Control: 9.9± 2.7	12	Not reported	22	Duration on pharmacological agents and IPC is not clearly reported. Did not report on whether DVTs were symptomatic or not. However, did state that if thrombosis was suspected before time of scheduled venogram, ultrasound was performed. 1 patient developed symptomatic PE 1 month after

			Dose of aspirin: 100mg/day									operation.
Eisele [25]	2007	RCT	*Age:* - *Gender M/F:* - *Excluded patients:* existing acute DVT *IPC started:* in recovery room after surgery *Hrs/day:* - *Application:* calves *LMWH started:* 12 hrs before surgery *Time on LMWH:* - *Dose of LMWH:* 3000 aXa units/ day	901	*Age:* - *Gender M/F:* - *Excluded patients:* existing acute DVT *LMWH started:* 12 hrs before surgery *Time on LMWH:* - *Dose of LMWH:* 3000 aXa units/ day	902	Duplex color-coded ultrasound on day of discharge	Not reported	Not reported	Not reported	15	Patient characteristics are not reported within the text. Patients in the IPC group were assigned to use IPC for different durations, i.e. some wore the device for 1 to 2 hours daily, others wore it for more than 2 to 4 hours daily etc. 15 DVT reported in control group, 3 were symptomatic. 4 DVTs reported in IPC group, 1 was symptomatic.
Edwards [26]	2008	RCT	*Age:* overall range 32-88 yrs *Gender M/F:* 57/84 *Excluded patients*: protocol violations: missed ultrasound, surgery other than TKA/THA, previous thrombosis, prophylaxis other than LMWH, other deviations *IPC started*: in operating room *Hrs/day:* 20.4 *Application:* calves *LMWH started:* morning after surgery	141	*Age:* overall range 32- 88 yrs *Gender M/F:* 58/78 *Excluded patients;* protocol violations: missed ultrasound, surgery other than TKA/THA, previous thrombosis, prophylaxis other than LMWH, other deviations *LMWH started:* morning after surgery *Time on LMWH:* 7-8 days *Dose of LMWH:*	136	Duplex ultrasound before discharge	3	12	Not reported	19	Mean ages are reported for groups undergoing each type of surgery, not per intervention used. Did not report whether in-hospital DVTs were symptomatic or not. Did report 1 symptomatic PE 29 days after surgery and 1 symptomatic DVT following

			Time on LMWH: 7- 8 days *Dose of LMWH:* 30mg/12 hrs		30mg/12 hrs							discharge.
Chin [27]	2009	RCT	*Age:* 65 (49- 85) yrs *Gender M/F:* 11/99 *Excluded patients:* - *IPC started:* Postoperatively *Hrs/day:* - *Application:* -	110	*Age:* 67 (52- 78) yrs *Gender M/F:* 9/101 *Excluded patients:* - *LMWH started:* Postoperatively *Time on LMWH:* 5- 7 days *Dose of LMWH:* 40mg/day	110	Duplex ultrasound on day 5 to 7 post-op	4 to 24	4	Case: 3.5 Control: 3.8	15	IPC device or place of application was not reported. Did not report on whether DVTs were symptomatic or not. 1 symptomatic PE in the control group, none in the IPC group.
Colwell [28]	2010	RCT	*Age:* 63 (20- 88) yrs *Gender M/F:* 89/109 *Excluded patients:* - *IPC started:* immediately after anaesthesia induction *Hrs/day:* 20 *Application:* calves *Aspirin started:* after the operation *Time on aspirin:* 10 days *Dose of aspirin:* 81mg/day	196	*Age:* 62 (20- 88) yrs *Gender M/F:* 87/103 *Excluded patients:* - *LMWH started:* morning after surgery *Time on LMWH:* 10 days *Dose of LMWH:* 30mg/12 hrs until discharge. 40mg/day thereafter	190	Duplex ultrasound on day 10 to 12 post-op	2 to 10	12	Not reported	21	Patients in the IPC group were allowed to receive aspirin at the discretion of the treating surgeon. Did not report on whether DVTs were symptomatic or not. All 4 PEs were symptomatic.
Windisch [29]	2010	RCT	*Age:* mean 68.93 yrs *Gender M/F:* - *Excluded patients:* - *IPC started:* in recovery room *Hrs/day:* Differs per day *Application:* foot pumps *LMWH started:* 24 hrs prior to surgery *Time on LMWH:* 8 days	40	*Age:* mean 68.15 yrs *Gender M/F:* - *Excluded patients:* - *LMWH started:* 24 hrs prior to surgery *Time on LMWH:* 8 days *Dose of LMWH:* 40mg/day	40	Ultrasound on day 8 post-op	Not reported	12	2	16	Breakdown of patients by gender is not reported. Use of IPC (hrs/day) is not reported clearly. No DVT/PE reported.

			Dose of LMWH: 40mg/day									
Sobieraj-Teague [36]	2012	RCT	*Age:* 61.97± 10.11 *Gender M/F:* 44/31 *Excluded patients:* - *IPC started:* within 4hrs of operation or 24 hrs admission for non-operated patients *Hrs/day*: 82.7 ± 42.9hrs over 6.6 days *Application:* calves	75	*Age:* 62.11± 11.82 *Gender M/F:* 46/29 *Excluded patients:* - *Pharm agent started:* - *Time on pharm agent:* - *Dose of pharm agent:* -	75	Ultrasound or venography on day 9 ± 2 post-op	Not reported	Not reported	Not reported	18	Patients could receive pharmacologic prophylaxis (aspirin, unfractionated heparin, or low molecular weight heparin) at the discretion of the neurosurgeon. Two patients allocated to the Venowave group did not wear the devices (refusal), and were considered to be non-users. These patients were included for analysis. Details of pharmacologic prophylaxis are not specified. 2 symptomatic DVT in control group, none in intervention group. No PE reported.

CT, computed tomography; DVT, deep vein thrombosis; ICU, intensive care unit; IPC, intermittent pneumatic compression; IU, international units; LMWH, low molecular weight heparin; RCT, randomised controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty.

2.4.3 Risk of DVT

The rate of developing DVT was reported in all included studies with a combined total of 3,347 patients divided as 1,680 patients in the IPC group and 1,667 controls [21-29]. The criteria used to identify DVT in individual studies are outlined in Table 2.2. In the IPC group less patients were diagnosed with DVT (38/1680) compared to (89/1667) patients in the control group; analysis of pooled data showed this difference was significant (pooled risk ratio = 0.49 [0.25, 0.96], 95% CI, P = 0.04; Figure 2.2). Heterogeneity was detected statistically (Cochran's Q = 17.68; degree of freedom (DF) = 7; P = 0.01; I_2 = 60%). Heterogeneity was also seen on a funnel plot analysis (Figure 2.3). We carried out a sensitivity test for the possible effect of publication bias, which did not change the significance of the result (pooled risk ratio = 0.42 [0.29, 0.61], 95% CI, P = 0.00001). Additionally, we performed a sensitivity test by including the data from one study, which we excluded from the systematic review for lack of clearly defined groups [36]. The pooled data from all ten studies showed the difference remained significant favouring the use of IPC (pooled risk ratio = 0.45 [0.24, 0.83], 95% CI, P = 0.01).

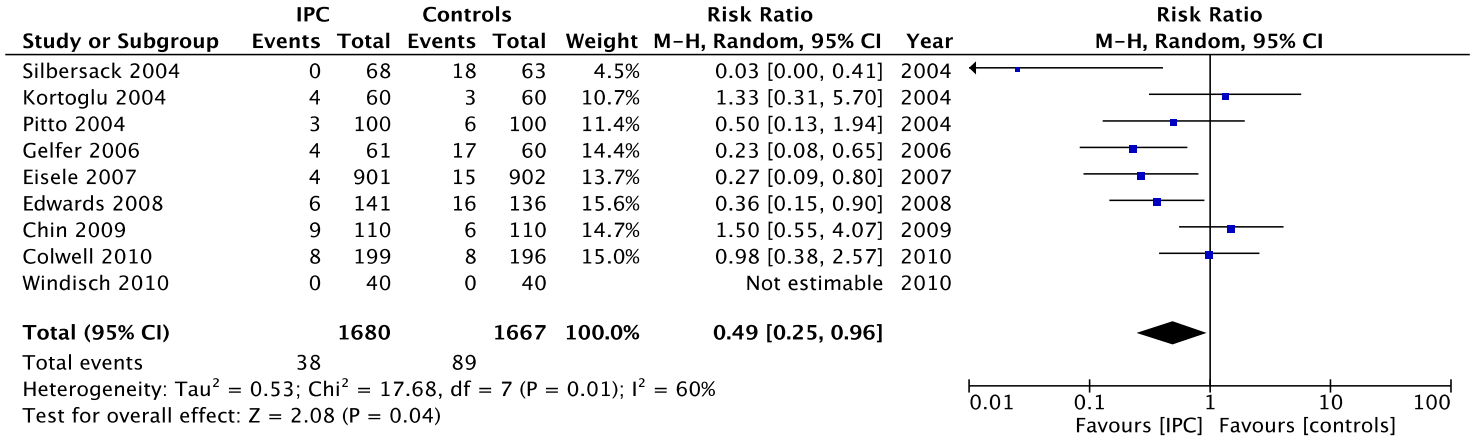


Figure 2.2 Forest plot showing the incidence of DVT.

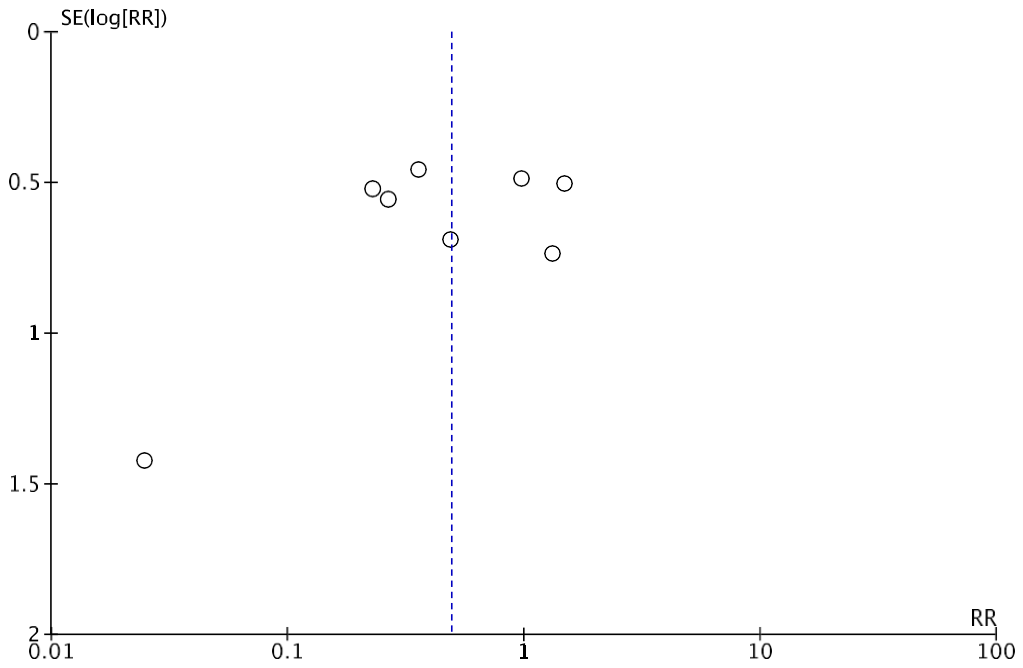


Figure 2.3 Funnel plot of publications bias for DVT outcome.

We also performed a sensitivity test by including studies that randomised cases to receive IPC alone – without additional chemoprophylaxis; 16/270 patients developed DVT in the IPC group compared to 15/270 in the controls (P = 0.42) [21, 22, 27]. Finally, we performed a sensitivity analysis to assess if observed differences were related to pharmacological protocol differences and not necessarily related to IPC by including data from seven studies – using LMWH only; 26/1420 patients developed DVT in the IPC group compared to 64/1411 in the controls. The result was slightly in favour of the IPC group, however the difference remained non-significant (P = 0.10) [21-23, 25-27, 29].

2.4.4 Risk of PE

The risk of developing a PE in included studies was reported in eight studies with 5/779 patients found to suffer from a PE in the IPC group compared to 7/765 in the controls [21-24, 26-29]. However, five of those reported a zero event in both groups and as such were not considered in the pooled analysis by the Cochrane's Review Manager software [22-24, 27, 29], and only three studies were used to generate the

pooled estimates with the difference between the groups not found to be significant (pooled risk ratio = 0.71 [0.22, 2.24], 95% CI, P = 0.56) [21, 26, 28]. Heterogeneity was not detected statistically (Cochran's Q = 2.04; degree of freedom (DF) = 2; P = 0.36; I_2 = 2%).

We performed a sensitivity test by assuming a value of (0.1) to both groups in trials that reported no PEs in both groups; the Peto's odd ratio was used to generate a pooled estimate of the treatment effect (pooled Peto's odd ratio = 0.721 [0.24 – 2.17], 95% CI, P = 0.56) (Figure 2.4).

Another sensitivity test by including studies which randomised cases to receive IPC alone – without additional chemoprophylaxis was performed; 4/530 patients developed PE in the IPC group compared to 6/526 in the controls (P = 0.53) [21, 22, 27, 28].

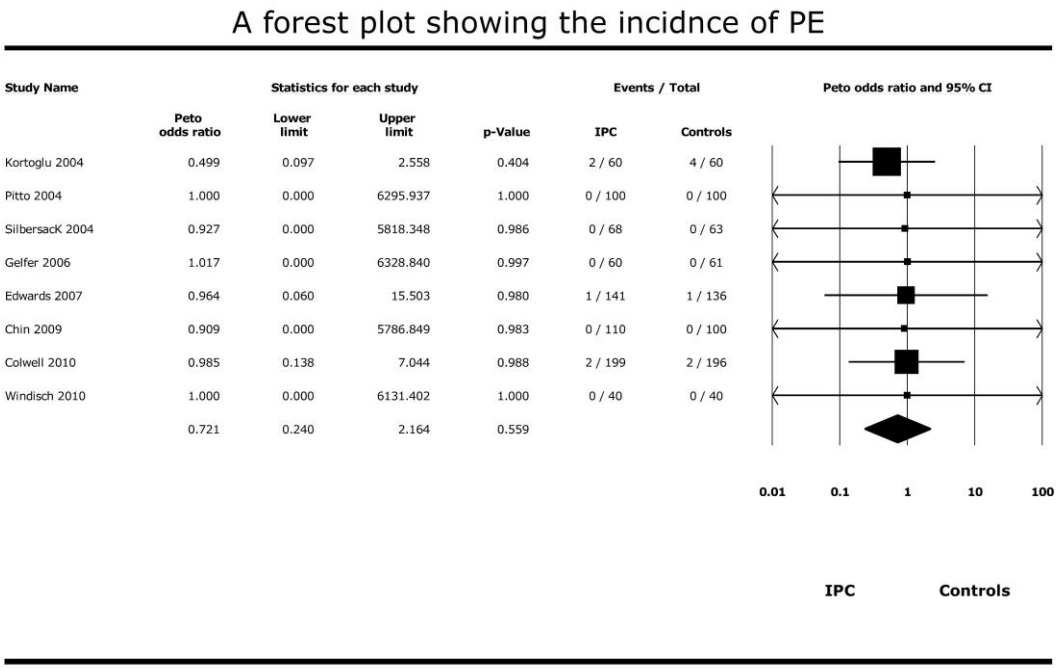


Figure 2.4 Forest plot showing the incidence of PE.

2.4.5 The Need for Blood Transfusion

Three studies reported the number of patients who required blood transfusion following their enrolment with a total number of 158/450 patients that received a blood transfusion in the IPC group compared to 187/442 in the controls; pooled analysis showed this difference to be statistically significant (pooled risk ratio = 0.85 [0.74, 0.97], 95% CI, P = 0.02; Figure 2.5) [26-28].

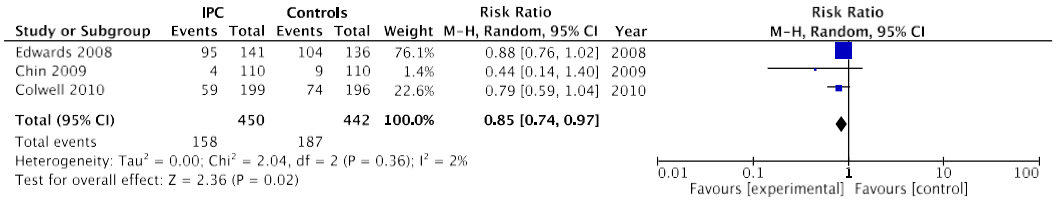


Figure 2.5 Forest plot showing blood transfusion rates.

The amount of blood transfused was reported in another three studies [21-23]: we used the WMD method to pool data from those studies in order to generate pooled risk ratios. The two groups consisted of 228 patients in the IPC group, and 223 controls. Although the difference was not statistically significant, a trend was shown suggesting decreased blood transfusion requirements are associated with the use of IPC (pooled mean difference = –0.69 [-1.90, 0.51], 95% CI, P = 0.26). Heterogeneity was detected statistically (Cochran's Q = 27.65; degree of freedom (DF) = 2; P = 0.00001; I_2 = 95%). A sensitivity test aimed at detecting the effect of publication bias by using the fixed model instead of the random model altered the result with the difference now significantly in favour of the IPC group (pooled standard mean difference = –0.30 [-0.51, -0.09], 95% CI, P = 0.005).

2.4.6 DVT/PE Related Mortality

Four studies reported no deaths caused by DVT/PE during the time of the study in either group [22, 23, 28, 29] and four other studies did not report on mortality rates in relation to DVT/PE in included patients [24-27]. Only one study reported deaths related to development of a PE complication; with statistically comparable rates as 2/60 patients died from a PE complication in the IPC group compared to 4/60 in the control group (P = 0.08) [21].

Other secondary outcomes reported by the studies included for review included complications/adverse events, compliance and IPC device comfort. Four of the included studies reported on complications and adverse events such as infection, bleeding, bruising, oozing, soft-tissue problems, and gastrointestinal problems (Supplemental Table 2.3) [21, 22, 24, 27]. Both Kurtoglu and Pitto reported fewer complications in the IPC group compared to the LMWH group, with Pitto reporting significantly less bruising, oozing, and bleeding from the wound in the IPC group ($p < 0.05$ for all) [21, 22]. In contrast, Gelfer reported a greater number of adverse events in the IPC group (76 vs. 68 events) compared to the LMWH group [24]. Chin reported no statistically significant difference in bleeding complications between groups, with no other adverse events reported in any group [27]. Compliance was also an outcome reported by three studies included for review [23, 26, 28]. All three studies reported on compliance with the IPC device, with Colwell also reporting on

compliance with the use of LMWH (Supplemental Table 2.3) [28]. These studies report varying rates of compliance, with Silbersack reporting continuous usage on day 1 post-op, with between 6 and 8 hours per day thereafter [23], and Colwell reporting a mean of 20 hours per day [28]. Edwards reported higher rates of compliance for those who were negative for DVT development compared to those who were positive for DVT development [26]. Eisele also reported on comfort with the IPC device, reporting a mean comfort score of 7.6 out of 10 [25].

2.5 Discussion

The importance of DVT prophylaxis arises from the increased risk of developing a fatal PE in those patients. DVT is thought to affect 1% to 2% of all hospitalised patients [37], and it can be recognised by the development of a localised swelling and tenderness in the calf area, although often it will have an asymptomatic course. Even though most DVTs start and remain confined to the calf muscles with the majority resolving spontaneously, the risk of proximal propagation and development of PEs increases according to the severity of the initiating pro-thrombotic stimulus [38]. Around 10% of PEs carry a risk of immediate death, whereas death can occur late in another 5% of all PEs [38]. Furthermore, the risk of recurrent VTE is higher in patients with DVT and silent PE, when compared to patients with DVT and no PE [39]. Also, about 50% of patients after an acute episode of DVT will have ultrasonographic features that are difficult to differentiate from the original findings of DVT; whereas only 20% to 30% of patients with symptoms suggestive of recurrent DVT will actually have the disease, making the diagnosis of recurrent DVT very challenging [37]. This is important, as the risk of case-fatality from a recurrent VTE with a PE complication is reported to be at 4% to 9% [40].

In a study by Arabi et al (2013), the use of pneumatic compression lead to a reduced incident rate of VTE in critically ill patients when compared to graduated compression stockings. Of the 798 included in their study, the overall rate of VTE was 7.1%; with 4.8% in the IPC group, 10% in the graduated compression stockings group ($P = 0.04$), a finding that was not altered by the type of chemoprophylactic agent used, trauma involved or type of surgery performed [41].

In another study, Colwell et al (2014) assessed the efficacy of an IPC device – with or without aspirin - in the reduction of symptomatic VTE rates in patients undergoing hip and knee arthroplasty, 28/3090 (0.92%) of the patients developed VTE; this was comparable to risk reduction reported with the use of warfarin, dabigatran, enoxaparin and rivaroxaban in other studies they included in their comparisons with a margin of 1.0%. Only rivaroxaban in knee arthroplasty procedures had a better risk reduction rate out of this margin by 0.06% [42].

Hardwick et al (2011) aimed to evaluate the difference between an IPC device and the use of a LMWH in the prevention of VTE in patients admitted electively for THA surgery and showed that major bleeding occurred in 11 patients, all in the LMWH group (6%), making the use of IPC in those patients significantly superior in terms of reducing the need for postoperative blood transfusion; however, VTE occurred at similar rates in the two groups - 5.1% in the IPC group vs. 5.3% in the LMWH group [43].

Lacut et al (2005) studied the adequacy of IPC devices in the prevention of DVT in 151 patients with acute intracerebral bleeding compared to the use of GCS alone; they found that 4.7% in the IPC group developed DVT compared to 15.9% in the GCS group (relative risk 0.29; 95% CI; P = 0.03) [44]. Thus, the use of IPC in this cohort provides superior risk reduction for developing VTE over GCS, while simultaneously reducing the risk of the disastrous complications that can result from the use of a more traditional chemoprophylactic agent, such as a LMWH, in particular the risk of mortality and strokes.

Stannard et al (2006) looked at the difference between IPC of the foot combined with enoxaparin (group A) against enoxaparin alone (group B) in the prevention of DVT following trauma. In group A, 9/103 patients developed DVT compared to 13/97 in group B; this difference was not found to be statistically significant. However, 2/103 in group A and 11/97 in group B developed large (> 2 cm) or occlusive DVTs (P = 0.025). Furthermore, 2 patients in group B were diagnosed with PEs while none occurred in group A. Those who developed DVT required more blood transfusions (mean = 7.4 units) compared to others (mean = 3.9) [45].

A systematic review of combined IPC and pharmacological agents versus single modalities in the prevention of VTE in high risk patients by Kakkos et al (2009) found that the use of both IPC and chemoprophylaxis significantly reduced the incidence of PE (from about 3% to 1%; odds ratio (OR) 0.39, 95% CI: 0.25 - 0.63) and DVT (from about 4% to 1%; OR 0.43, 95% CI: 0.24 - 0.76) when compared to

compression alone. [46] Similarly, the combined use of both IPC and chemoprophylaxis resulted in better outcomes for DVT (from 4.21% to 0.65%; OR 0.16, 95% CI: 0.07 - 0.34) when compared to chemoprophylaxis alone. The combination of compression and chemoprophylaxis was superior in reducing the incidence of both DVT and PE when compared to the combination of compression and aspirin, however this difference was not statistically significant [46].

We identified nine papers – all RCTs – which compared the use of an IPC device – with or without any additional pharmacological agents – to the more traditional method of chemoprophylaxis by means of a LMWH – mostly Enoxaparin – in surgical patients; with orthopaedic THA/TKA being the most common procedures. Those studies had a combined total of 3,347 patients – 1,680 in the IPC group and 1,667 controls – with similar age groups.

The main outcome measures of this review are the development of DVT and/or PE. The rate of developing DVT was reported in all nine studies; we found that DVT significantly occurred in more patients in the control group (89/1,667) compared to the IPC group (38/1,680) ($P = 0.04$). A sensitivity test by using the fixed effects model did not change this finding ($P = 0.00001$). Another sensitivity test by adding the data extracted from a study that could not be included in the systematic review due to the lack of clearly identified groups also showed the difference between the groups to favour the use of IPC devices in the prevention of DVT ($P = 0.01$).

A sensitivity test including studies which randomised cases to receive IPC alone, without additional chemoprophylaxis, showed no significant difference in the rate of DVT between IPC and control groups. A further sensitivity test to assess if observed differences were related to pharmacological protocol differences and not necessarily related to IPC by including data from seven studies using only LMWH showed the difference between groups to slightly favour the IPC group, however, the difference was non-significant.

The risk of PE in the review was reported in eight studies [21-24, 26-29]; however, five studies had zero events in both arms [22-24, 27, 29] and therefore a pooled estimate could only be generated from three studies [21, 26, 28] with 5/400 occurring in the IPC group compared to 7/392 in the controls; the difference was not significant (P = 0.56).

The number of patients who required blood transfusion was reported in three studies 158/450 in the IPC group compared to 187/442 in the other group; this difference showed a statistically significant association between using IPC and limiting the need for blood transfusion (P = 0.02; Figure 2.5) [26-28]. However, the amount of blood transfusion one needed did not differ significantly between the two groups (P = 0.26) in the three studies that reported on the number of blood units per patient group [21-23].

The only study that reported any DVT/PE related mortality did not show any significant difference between the use of IPC vs. pharmacological agents (P = 0.08) [21].

2.5.1 Limitations

The main limitation to this review was the lack of blinding in all included RCTs; there is an increased likelihood of differential treatment or assessment of outcomes in the absence of blinding among groups. However, it is not difficult to see how blinding can be difficult considering the questions at hand; also the invention of devices that can mimic IPC devices would prove expensive if not impossible. Another limiting factor was the heterogeneous nature of both the intervention and control groups pooled in the meta-analysis. Some studies combined the use of IPC with pharmacological treatment, whereas in other studies, cases within the intervention group only had IPC for DVT prevention. We tried to stratify our results by performing separate sensitivity analysis by pooling the data from studies in which cases did not receive additional chemoprophylaxis with compression. Also, the controls were randomised to receive different forms of chemoprophylaxis; furthermore, there was a lack of a universal dose even when using the same agent. The duration of follow-up and hospital stay were also different among the included

studies. Finally, the radiological test performed to detect DVT also varied, as well as the timing of that test (Table 2.2).

2.5.2 Conclusion

A combination of both IPC and chemoprophylaxis appears to be the best approach. Improved rates of DVT incidence in patients undergoing major orthopaedic or neurosurgical procedures were not associated with the use of IPC devices alone, with IPC neither inferior nor superior to chemoprophylaxis. The difference in terms of the risk of developing PE was not significant. IPC resulted in significantly decreased requirements for blood transfusion, both as absolute number of patients or amount of blood transfusion. Studies were not powered enough to make conclusions regarding VTE-related mortality. Limitations currently exist in both the study design and outcome reporting of trials investigating the use of IPC as a DVT prophylaxis in major orthopaedic or neurosurgical patients. As such, the authors conclude that large, randomised multi-centre trials comparing the use of IPC or chemoprophylaxis alone to a combination of both treatments are needed to elucidate the true efficacy of IPC in DVT prevention. The type, dose, and frequency of chemoprophylaxis used will also need to be investigated. Furthermore, improved reporting is required whereby the type of IPC, duration of use (hours per day and total days), in addition to the type, dose, and frequency of the chemoprophylaxis protocol and the number of both symptomatic and asymptomatic DVT/PE, and death from VTE events is clearly reported.

2.6 References

[1] White, R., "The Epidemiology of Venous Thromboembolism," *Circulation,* vol. 107, no. 23 suppl 1, pp. I-4-I-8, June 17, 2003 2003.

[2] Epley, D., "Pulmonary emboli risk reduction," *J Vasc Nurs,* vol. 18, no. 2, pp. 61-8; quiz 69-70, Jun 2000.

[3] Urbankova, J., Quiroz, R., Kucher, N., and Goldhaber, S., "Intermittent pneumatic compression and deep vein thrombosis prevention. A meta-analysis in postoperative patients," *Thromb Haemost,* vol. 94, no. 6, pp. 1181-5, Dec 2005.

[4] Colwell, C. J., Kwong, L., Turpie, A., and Davidson, B., "Flexibility in administration of fondaparinux for prevention of symptomatic venous thromboembolism in orthopaedic surgery," *J Arthroplasty,* vol. 21, no. 1, pp. 36-45, Jan 2006.

[5] Turpie, A., Bauer, K., Caprini, J., Comp, P., Gent, M., and Muntz, J., "Fondaparinux combined with intermittent pneumatic compression vs. intermittent pneumatic compression alone for prevention of venous thromboembolism after abdominal surgery: a randomized, double-blind comparison," *J Thromb Haemost,* vol. 5, no. 9, pp. 1854-61, Sep 2007.

[6] Hull, R., Yusen, R., and Bergqvist, D., "State-of-the-art review: Assessing the safety profiles of new anticoagulants for major orthopedic surgery thromboprophylaxis," *Clin Appl Thromb Hemost,* vol. 15, no. 4, pp. 377-88, Jul-Aug 2009.

[7] Kurtz, S., Ong, K., Lau, E., Mowat, F., and Halpern, M., "Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030," *J Bone Joint Surg Am,* vol. 89, no. 4, pp. 780-5, Apr 2007.

[8] Cushner, F., Agnelli, G., FitzGerald, G., and Warwick, D., "Complications and functional outcomes after total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY)," *Am J Orthop (Belle Mead NJ),* vol. 39, no. 9 Suppl, pp. 22-8, Sep 2010.

[9] Iorio, A. and Agnelli, G., "Low-molecular-weight and unfractionated heparin for prevention of venous thromboembolism in neurosurgery: a meta-analysis," *Arch Intern Med,* vol. 160, no. 15, pp. 2327-32, Aug 14-28 2000.

[10] Carman, T., Kanner, A., Barnett, G., and Deitcher, S., "Prevention of thromboembolism after neurosurgery for brain and spinal tumors," *South Med J,* vol. 96, no. 1, pp. 17-22, Jan 2003.

[11] Gnanalingham, K. and Holland, J., "Attitudes to the use of prophylaxis for thrombo-embolism in neurosurgical patients," *J Clin Neurosci,* vol. 10, no. 4, pp. 467-9, Jul 2003.

[12] Agnelli, G., "Prevention of venous thromboembolism in surgical patients," *Circulation,* vol. 110, no. 24 Suppl 1, pp. IV4-12, Dec 14 2004.

[13] Danish, S., Burnett, M., Ong, J., Sonnad, S., Maloney-Wilensky, E., and Stein, S., "Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis," *Neurosurgery,* vol. 56, no. 6, pp. 1286-92; discussion 1292-4, Jun 2005.

[14] Morris, R. and Woodcock, J., "Evidence-based compression: prevention of stasis and deep vein thrombosis," *Ann Surg,* vol. 239, no. 2, pp. 162-71, Feb 2004.

[15] Tarnay, T., Rohr, P., Davidson, A., Stevenson, M., Byars, E., and Hopkins, G., "Pneumatic calf compression, fibrinolysis, and the prevention of deep venous thrombosis," *Surgery,* vol. 88, no. 4, pp. 489-96, Oct 1980.

[16] Salzman, E. *et al.,* "Effect of optimization of hemodynamics on fibrinolytic activity and antithrombotic efficacy of external pneumatic calf compression," *Ann Surg,* vol. 206, no. 5, pp. 636-41, Nov 1987.

[17] Jacobs, D., Piotrowski, J., Hoppensteadt, D., Salvator, A., and Fareed, J., "Hemodynamic and fibrinolytic consequences of intermittent pneumatic compression: preliminary results," *J Trauma,* vol. 40, no. 5, pp. 710-16; discussion 716-7, May 1996.

[18] Comerota, A. *et al.,* "The fibrinolytic effects of intermittent pneumatic compression: mechanism of enhanced fibrinolysis," *Ann Surg,* vol. 226, no. 3, pp. 306-13; discussion 313-4, Sep 1997.

[19] Chouhan, V., Comerota, A., Sun, L., Harada, R., Gaughan, J., and Rao, A., "Inhibition of tissue factor pathway during intermittent pneumatic compression: A possible mechanism for antithrombotic effect," *Arterioscler Thromb Vasc Biol,* vol. 19, no. 11, pp. 2812-7, Nov 1999.

[20] Liberati, A. *et al.,* "The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions:

explanation and elaboration," *J Clin Epidemiol,* vol. 62, no. 10, pp. e1-34, Oct 2009.

[21] Kurtoglu, M. *et al.*, "Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin," *World J Surg,* vol. 28, no. 8, pp. 807-11, Aug 2004.

[22] Pitto, R., Hamer, H., Heiss-Dunlop, W., and Kuehle, J., "Mechanical prophylaxis of deep-vein thrombosis after total hip replacement a randomised clinical trial," *J Bone Joint Surg Br,* vol. 86, no. 5, pp. 639-42, Jul 2004.

[23] Silbersack, Y., Taute, B., Hein, W., and Podhaisky, H., "Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression," *J Bone Joint Surg Br,* vol. 86, no. 6, pp. 809-12, Aug 2004.

[24] Gelfer, Y., Tavor, H., Oron, A., Peer, A., Halperin, N., and Robinson, D., "Deep vein thrombosis prevention in joint arthroplasties: continuous enhanced circulation therapy vs low molecular weight heparin," *J Arthroplasty,* vol. 21, no. 2, pp. 206-14, Feb 2006.

[25] Eisele, R., Kinzl, L., and Koelsch, T., "Rapid-inflation intermittent pneumatic compression for prevention of deep venous thrombosis," *J Bone Joint Surg Am,* vol. 89, no. 5, pp. 1050-6, May 2007.

[26] Edwards, J., Pulido, P., Ezzet, K., Copp, S., Walker, R., and Colwell, C. J., "Portable compression device and low-molecular-weight heparin compared with low-molecular-weight heparin for thromboprophylaxis after total joint arthroplasty," *J Arthroplasty,* vol. 23, no. 8, pp. 1122-7, Dec 2008.

[27] Chin, P., Amin, M., Yang, K., Yeo, S., and Lo, N., "Thromboembolic prophylaxis for total knee arthroplasty in Asian patients: a randomised controlled trial," *J Orthop Surg (Hong Kong),* vol. 17, no. 1, pp. 1-5, Apr 2009.

[28] Colwell, C. J. *et al.*, "Thrombosis prevention after total hip arthroplasty: a prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin," *J Bone Joint Surg Am,* vol. 92, no. 3, pp. 527-35, Mar 2010.

[29] Windisch, C., Kolb, W., Kolb, K., Grutzner, P., Venbrocks, R., and Anders, J., "Pneumatic compression with foot pumps facilitates early postoperative

mobilisation in total knee arthroplasty," *Int Orthop,* vol. 35, no. 7, pp. 995-1000, Jul 2011.

[30] Downs, S. and Black, N., "The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions," *J Epidemiol Community Health,* vol. 52, no. 6, pp. 377-84, Jun 1998.

[31] The Nordic Cochrane Centre TCc. Review Manager (RevMan) [Computer Program]. Version 5.2. 2012.

[32] DerSimonian, R. and Laird, N., "Evaluating the effect of coaching on SAT scores: a meta-analysis," *Harvard Educational Review,* vol. 53, pp. 1-15, 1983.

[33] Sterne, J., Egger, M., and Moher, D., "Chapter 10: Addressing reporting biases," in *Cochrane Handbook for Systematic Reviews of Intervention,* J. Higgins and S. Green, Eds. Version 5.1.0 (updated 2011).

[34] Yusuf, S., Peto, R., Lewis, J., Collins, R., and Sleight, P., "Beta blockade during and after myocardial infarction: an overview of the randomized trials," *Prog Cardiovasc Dis,* vol. 27, no. 5, pp. 335-71, Mar-Apr 1985.

[35] Higgins, J. and Green, S., "Cochrane Handbook for Systematic Reviews of Interventions". *The Cochrane Collaboration,* 2011.

[36] Sobieraj-Teague, M. *et al.,* "Randomized controlled trial of a new portable calf compression device (Venowave) for prevention of venous thrombosis in high-risk neurosurgical patients," *J Thromb Haemost,* vol. 10, no. 2, pp. 229-35, Feb 2012.

[37] Line, B., "Pathophysiology and diagnosis of deep venous thrombosis," *Semin Nucl Med,* vol. 31, no. 2, pp. 90-101, Apr 2001.

[38] Kearon, C., "Natural history of venous thromboembolism," *Circulation,* vol. 107, no. 23 Suppl 1, pp. I22-30, Jun 17 2003.

[39] Jimenez, D., Diaz, G., Marin, E., Vidal, R., Sueiro, A., and Yusen, R., "The risk of recurrent venous thromboembolism in patients with unprovoked symptomatic deep vein thrombosis and asymptomatic pulmonary embolism," *Thromb Haemost,* vol. 95, no. 3, pp. 562-6, Mar 2006.

[40] Douketis, J., Gu, C., Schulman, S., Ghirarduzzi, A., Pengo, V., and Prandoni, P., "The risk for fatal pulmonary embolism after discontinuing anticoagulant

therapy for venous thromboembolism," *Ann Intern Med,* vol. 147, no. 11, pp. 766-74, Dec 4 2007.

[41] Arabi, Y. *et al.*, "Use of intermittent pneumatic compression and not graduated compression stockings is associated with lower incident VTE in critically ill patients: a multiple propensity scores adjusted analysis," *Chest,* vol. 144, no. 1, pp. 152-9, Jul 2013.

[42] Colwell, C. J. *et al.*, "A mobile compression device for thrombosis prevention in hip and knee arthroplasty," *J Bone Joint Surg Am,* vol. 96, no. 3, pp. 177-83, Feb 5 2014.

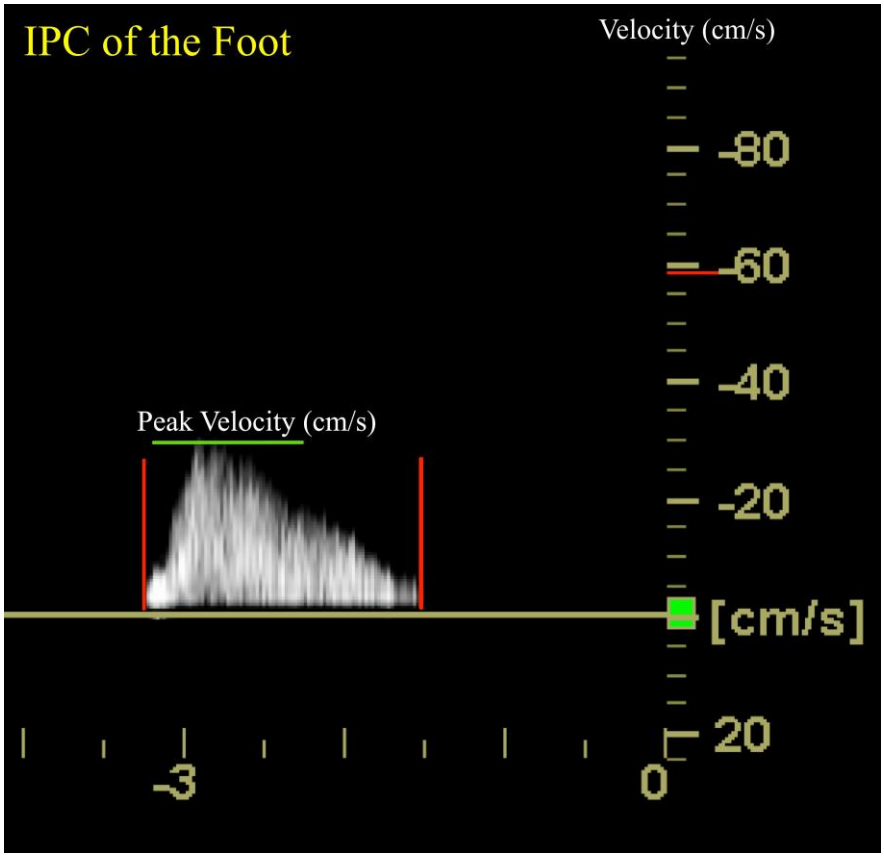
[43] Hardwick, M., Pulido, P., and Colwell, C. J., "A mobile compression device compared with low-molecular-weight heparin for prevention of venous thromboembolism in total hip arthroplasty," *Orthop Nurs,* vol. 30, no. 5, pp. 312-6, Sep-Oct 2011.

[44] Lacut, K. *et al.*, "Prevention of venous thrombosis in patients with acute intracerebral hemorrhage," *Neurology,* vol. 65, no. 6, pp. 865-9, Sep 27 2005.

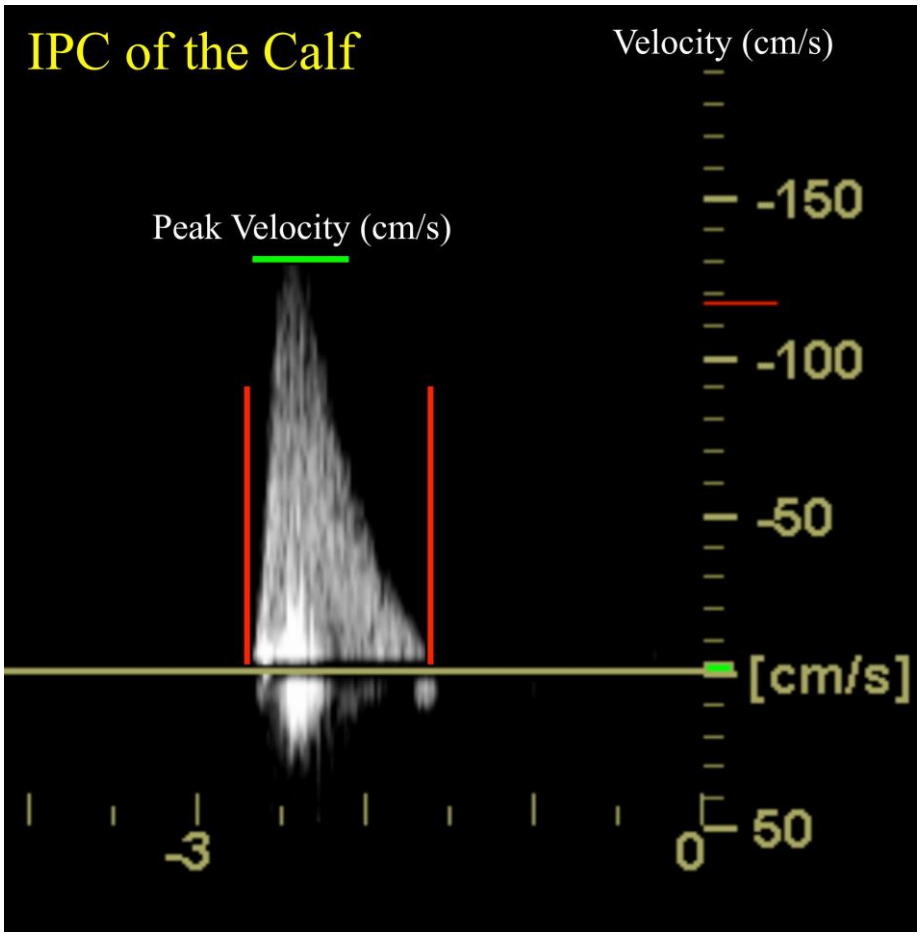
[45] Stannard, J. *et al.*, "Prophylaxis against deep-vein thrombosis following trauma: a prospective, randomized comparison of mechanical and pharmacologic prophylaxis," *J Bone Joint Surg Am,* vol. 88, no. 2, pp. 261-6, Feb 2006.

[46] Kakkos, S., Caprini, J., Geroulakos, G., Nicolaides, A., Stansby, G., and Reddy, D., "Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thrombo-embolism in high-risk patients," *Eur J Vasc Endovasc Surg,* vol. 37, no. 3, pp. 364-5, Mar 2009.

2.7 Supplemental Figures and Tables



Supplemental Figure 2.6 IPC of the foot. The vertical lines outline venous blood flow in the popliteal vein due to a 3 s compression by an AV Impulse System foot cuff. Peak velocity (cm/s) is indicated by the horizontal line. The application of the cuff to the foot results in a moderate increase in peak velocity from baseline blood flow with a recordable peak flow until the next compression and peak (not shown in this image).



Supplemental Figure 2.7 IPC of the calf. The vertical lines outline venous blood flow in the popliteal vein due to a 3 s compression by an AV Impulse System calf cuff. Peak velocity (cm/s) is indicated by the horizontal line. The application of the cuff to the calf results in a much greater increase in peak velocity from baseline blood flow than is seen with compression of the foot. As the peaks are so high, there is generally no recordable blood flow seen between peaks. The increase in peak velocity will vary with both the position of the cuffs and the compression device used.

Supplemental Table 2.3 Quality Assessment for Risk of Bias

Number	Question	Kurtoglu 2004	Pitto 2004	Silbersack 2004	Gelfer 2006	Eisele 2007	Edwards 2008	Chin 2009	Colwell 2010	Windisch 2010
1	Hypothesis/ objective clear?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Main outcomes clearly described in introduction or methods?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	Are patients' characteristics clearly described?	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No
4	Are interventions clearly described?	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
5	Are confounders equally distributed?	UTD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6	Are the main findings clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7	Are estimates or variability provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
8	Are important adverse events reported?	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
9	Are the characteristics of those lost to follow up described?	No	No	Yes	Yes	No	No	No	No	No
10	Are specific p values reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11	Were potentially eligible subjects representative of the population?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
12	Were participating subjects representative of the population?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
13	Were staff, places and facilities representative of the treatment most patients receive?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14	Was an attempt made to blind subjects to the intervention they received?	No	No	No	No	No	No	No	No	No

15	Was an attempt made to blind main outcome assessors?	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes
16	If any results reflect data dredging, is this clear?	No	No	No	No	No	No	No	No	No
17	Do analyses adjust for length of follow up differences?	No	No	No	No	No	No	No	No	No
18	Were appropriate statistical analyses used?	Yes	Yes	UTD	Yes	UTD	Yes	Yes	Yes	Yes
19	Was compliance with the intervention reliable?	UTD	Yes	Yes	UTD	Yes	Yes	UTD	Yes	UTD
20	Were the main outcome measures valid and reliable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
21	Were study groups recruited from the same population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
22	Were subjects recruited over similar time periods?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
23	Were study subjects randomised to intervention groups?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
24	Was treatment assignment concealed?	No	Yes	No	Yes	No	No	No	No	No
25	Was there adequate adjustment for confounders in the analysis?	UTD	Yes	UTD	Yes	UTD	Yes	UTD	Yes	UTD
26	Were losses of patients to follow-up taken into account?	No	No	No	No	No	No	No	No	No
27	Was an appropriate sample size calculation carried out?	No	Yes	Yes	Yes	UTD	Yes	UTD	Yes	No
	Number of "Yes" results	14	22	19	22	15	19	15	21	16

UTD = unable to determine

Chapter 3

Comparative Lower Limb Haemodynamics Using Neuromuscular Electrical Stimulation (NMES) versus Intermittent Pneumatic Compression (IPC)

Published Reference:

Broderick BJ, O'Connell S, Moloney S, O'Halloran K, Sheehan J, Quondamatteo F, Quinlan LR, ÓLaighin G. Comparative lower limb hemodynamics using neuromuscular electrical stimulation (NMES) versus intermittent pneumatic compression (IPC). *Physiological Measurement.* 2014;35(9):1849-59.

Background

One of the complications associated with orthopaedic surgery is that of venous stasis, which can lead to the development of deep vein thrombosis (DVT), a pathological blood clot that can disrupt and impede recovery following surgery. Intermittent pneumatic compression (IPC) and neuromuscular electrical stimulation (NMES) are two methods of venous stasis prevention. As reported in Chapter 2, IPC is currently used post-surgery to prevent DVT development. However, the true efficacy of IPC remains unknown and results of the systematic review and meta-analysis report that large randomised multi-centre trials are needed to elucidate its true benefit. While the results of the nine studies included for review and meta-analysis suggest that use of an IPC device for venous stasis and DVT prevention is neither superior nor inferior to use of chemoprophylaxis, there were limitations encountered when carrying out the systematic review and meta-analysis. These limitations comprised of inconsistencies with the use of IPC, both the type and duration of use; inconsistencies with the use of chemoprophylaxis, both the agent and dosage utilised; and inconsistencies in the reporting of outcomes. As it stands, results of the meta- analysis suggest that a combined approach of IPC and chemoprophylaxis is of most benefit to high-risk surgical patients.

NMES is an alternative mechanical method to IPC. While NMES has been reported to prevent venous stasis, and may be a useful technology both during and following surgery, its use is not widespread. NMES is an evolving technology that can be utilised to elicit a muscular contraction in order to increase venous haemodynamics. It aims to mimic a voluntary muscle contraction to lead to compression of the veins both in and surrounding the targeted muscle or group of muscles. As NMES aims to provide a muscular contraction akin to a voluntary physiological contraction, it may be of greater benefit than the external compression applied with the use of IPC and may reduce the need for chemoprophylaxis.

An aim of this thesis is to investigate the use of NMES as part of a post-operative care regime in orthopaedic patients by preventing venous stasis and with this in mind, the aim of this study was to investigate and compare the use of NMES and IPC with regard to preventing venous stasis. The outcome of interest was that of lower limb venous haemodyanmics, namely measures of ejected volume, peak velocity and time averaged mean velocity.

Contribution to work

Study design: Barry J Broderick.

Data collection:

- Subject consent: Sandra O'Connell, Shelly Moloney, Kevin O'Halloran.
- Subject testing: Sandra O'Connell, Shelly Moloney, Kevin O'Halloran.

Data Analysis: Sandra O'Connell.

Interpretation of results: Sandra O'Connell, Leo R Quinlan, Gearoid ÓLaighin.

Drafting of manuscript: Sandra O'Connell.

Critical review of manuscript: Sandra O'Connell, Barry J Broderick, Leo R Quinlan, Gearoid ÓLaighin.

3.1 Abstract

Background: Deep Vein Thrombosis (DVT) is a life threatening condition and a serious concern among hospitalised patients, with death occurring in approximately 6% of cases. Intermittent pneumatic compression (IPC) is commonly used for DVT prevention, however suffers from low compliance and issues of usability and portability. Neuromuscular electrical stimulation (NMES) has been shown to improve lower limb haemodynamics but direct comparison with IPC in terms of haemodynamics is rare but very important to determine the potential effectiveness of NMES in DVT prevention.

Methods and Results: Lower limb IPC were compared to calf NMES, in 30 healthy volunteers (18-23 years). Each intervention was carried out on each leg, blood flow through the popliteal vein was measured using Doppler ultrasound. All interventions produced significantly greater haemodynamic responses compared to control. Calf- IPC and NMES produced significant increases in peak venous velocity, with NMES producing the greatest ejected volume at 23.22ml from a baseline of 2.52ml ($p < 0.001$ vs. control).

Conclusion: Improving lower limb haemodynamics is vital in preventing DVT. NMES resulted in larger ejected volumes compared to IPC (3 times greater than foot- IPC and 1.7 times greater than calf-IPC) and more effectively empties the veins and soleal sinuses. This is an important finding as DVT occurs predominantly in the soleal sinuses. NMES is silent and portable and thus does not suffer many of the issues associated with IPC. This work supports the potential widespread application of NMES in hospital and home settings where the risk of DVT formation is high.

3.2 Introduction

Prevention of Deep Vein Thrombosis (DVT) in postoperative and other medical settings primarily involves the use of anticoagulants, Graduated Compression Stockings (GCS) and/or Intermittent Pneumatic Compression (IPC) [1]. Each of these methods has associated issues with contraindications to use and poor levels of compliance by the patient population while in use in the clinic and laterally at home. The ideal prophylaxis should promote good haemodynamics, be portable, have good usability characteristics and thus sustain high levels of compliance. An intervention that will combine all of these factors will ultimately reduce DVT incidence.

Neuromuscular Electrical Stimulation (NMES) is a potential alternative method that may compete favourably with existing methods haemodynamically, in user-friendliness and ultimately in patient compliance [2-4]. NMES like IPC is a technological intervention that results in the movement of blood out of the lower limb during the active cycle of the device.

Current standard therapy employs IPC, which involves the use of a cycle of compression and relaxation of pumped air in an inflatable chamber placed around the limb. Its main objective is to mechanically squeeze blood from the underlying veins. The blood is displaced proximally, assuming competent venous valve function. IPC is an effective method used as part of surgical practice to assist blood flow following surgery and prevent or reduce complications such as DVT [5-8]. IPC has also been used in the prevention of DVT in non-surgical patients, such as those with stroke or cancer, as well as in the treatment of oedema, lymphoedema and chronic arterial disease [9-12]. However, despite its widespread use there are significant patient compliance issues with IPC and thus its full effectiveness is often not achieved, as patients do not adhere to recommended use for the required amount of time despite the increased risk of DVT [1, 13, 14]. Patients report cuffs are difficult to put on, uncomfortable to wear, the device is not portable and it is noisy to the point that patients stop the therapy. This is particularly true in an orthopaedic ward setting where often multiple devices are in use at once.

The haemodynamic properties of IPC, such as peak venous velocity, volume of blood expelled and blood flow duration, are easily measured using Doppler ultrasound. Both the site of blood flow measurement and the part of the limb compressed are important in assessing the effectiveness of any intervention. Blood flow velocity depends on vein diameter and it is clear that the venous compartment of the foot holds a smaller volume of blood than that of the calf or thigh. Consequently, foot compression has been shown to produce more modest results when compared to calf and thigh compression [15-17]. IPC devices can have single or multiple chambers, which can compress sequentially and in a proximal direction starting from the ankle. These chambers can encompass the whole limb or different parts of the limb separately or in combination [18]. Duration of compression/relaxation cycle, applied pressures and overall cycle times vary with device manufacturer and is further modified by personal choice of the attending physician. However, in all cases the goal of compression is to give a significant increase in venous blood flow which subsequently returns to baseline between pulses [19].

However, as IPC does not activate the skeletal muscle pump in the calf, it has been suggested that blood is pushed past the soleal sinuses, leaving the blood in the soleal sinuses stagnant [19, 20]. As a result, compression may not be adequate to induce complete emptying of blood from the lower limb venous system. Thus while IPC, when used correctly, reduces DVT risk there is room for improvement in its haemodynamic performance aside from the well-documented compliance issues. Complications with IPC are rare but serious and include compartment syndrome, common peroneal nerve palsy due to nerve damage caused by the intermittent compression and skin ulceration [21-23]. Thus there is a gap in the post-surgical arsenal available to prevent DVT and reduce swelling. For any intervention to fill this gap the most important element will be that it performs at least as well as IPC in terms of haemodynamic performance. Following establishing its bona fides at this fundamental physiological level, issues of ease of use, portability and compliance will come into focus.

Surface neuromuscular electrical stimulation is emerging as an alternative method of assisting venous return following surgery. NMES is used to generate a physiological contraction of muscles by delivering a series of controlled electrical pulses via skin surface electrodes placed over the motor points of the targeted muscle. For example, NMES applied to the calf muscle artificially activates the calf muscle pump and results in ejection of blood from the venous compartment [24]. This calf muscle activation produces venous flow similar to that of a voluntary muscle contraction, with relaxation of the muscle allowing the vessels to refill. NMES has been shown to improve venous return [2, 25, 26]. Research into stimulation waveform configurations and shapes, advanced skin surface electrodes and electrode placement has improved the performance of NMES whilst maintaining patient comfort [4, 27, 28]. NMES is delivered through a portable, noiseless device that does not require clinical expertise to operate, making it an attractive method to be used in the home. Furthermore, removal of electrodes is not necessary for patient ambulation as stimulation can be paused during use. As this device has the potential to be worn while a patient is either immobile, standing or walking, it would be suitable for use both during the early stage of immobilisation following surgery and throughout the recovery/rehabilitation period in the home, therefore bridging the gap between the hospital and home settings.

In this paper, we directly compare the haemodynamic performance of NMES-induced contractions of the calf muscle pump with IPC of the foot and calf separately on a pulse-by-pulse basis. This paper is the first direct comparison of NMES versus a clinic standard IPC device in terms of haemodynamic performance and an important step in establishing the potential of NMES as a DVT prophylaxis.

3.3 Methods

3.3.1 Subjects

Thirty healthy subjects (21 male and 9 female) mean age of 21 ± 1.08, weight (kg) 75.26 ± 13.88, height (m) 1.78 ± 0.10, BMI (kg/m^2) 23.54 ± 3.04 and with no history of cardiovascular problems were recruited for this study. Ethical approval was obtained from the Research Ethics Committee, NUI Galway and all subjects provided written, informed consent.

3.3.2 Study Protocol

Lower limb haemodynamic performance was the primary outcome of this study. Four interventions of five-minute duration were applied to each subject: control (rest), foot- IPC, calf-IPC and calf-NMES. The order of each intervention and the leg on which it began was randomised before the study began. To ensure that baseline equilibrium venous flow was reached, a rest period of three minutes was allowed between each intervention and at the beginning of the study. Each intervention was carried out for five minutes; no measurements were taken in the first minute. No order effect was observed in the data collected.

3.3.3 IPC Protocol

Intermittent pneumatic compression (IPC) was applied using the Novamedix AV Impulse System Model 6000 (Covidien, Mansfield, MA, USA). This device is designed to allow for compression to be applied to the foot or calf separately. Inflation pads were placed on the subject's foot and calf separately and connected to the IPC device. Once the pads were positioned correctly the device was programmed to deliver compression pulses (one pulse is defined as 130mmHg for 1 second) every 20 seconds, over a period of 5 minutes. Compression of the foot and calf were performed separately.

3.3.4 NMES Protocol

A custom-built, two-channel muscle stimulator (Duo-STIM, Bioelectronics Research Cluster, NUI Galway) was used to deliver NMES to the calf muscles. Two self- adhesive 5cm x 5cm PALS surface electrodes (Ultrastim, Axelgaard Manufacturing Co., Ltd., CA, USA) were placed over the motor points of the soleus muscles of both legs (Figure 3.1). To ensure correct electrode placement and to ensure that the subject was comfortable with the sensation of the electrical stimulation, a series of test pulses were applied initially at a very low intensity. The stimulus intensity was gradually increased until a contraction of the calf muscle was observed. Correct electrode placement was confirmed by either a visible tightening of the soleus muscle or a slight plantar flexion. Once the subject reached the maximum comfortable stimulation intensity this intensity was set and used for the remainder of the NMES protocol. The stimulation intensity voltage across all participants had a median and interquartile range of 32V (25.6; 38.4).

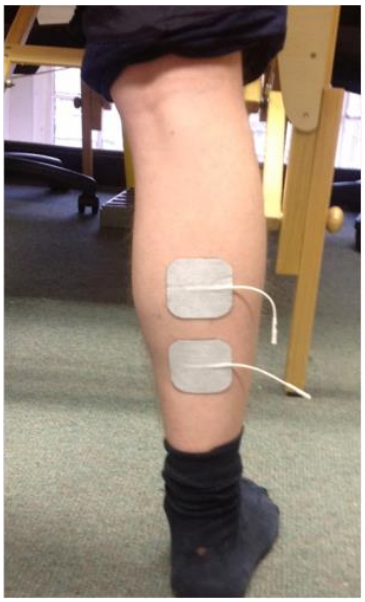


Figure 3.1 Position of the self-adhesive 5 cm x 5 cm PALS skin surface electrodes placed over the motor points of the soleus muscle.

The Duo-STIM was set to a total cycle time of 22 seconds (one pulse is defined by an active contraction time of 1s) with an OFF time of 20 seconds, repeated over 5 minutes. This time profile was selected to match the timing of the Novamedix AV Impulse System Model 6000. The stimulator was programmed to provide a pulse frequency of 36Hz and a balanced biphasic waveform with a pulse width of 350μs. A comfortable calf muscle contraction was produced using a Ramp-Up Time of 0.5s, a contraction time of 1s and a Ramp-Down Time of 0.5s. The stimulation parameters were selected to provide an effective contraction while maximising subject comfort and were chosen based on previous work using NMES [29]. The electrical stimulation was applied to one leg at a time in accordance with the randomisation of the interventions.

3.3.5 Haemodynamic Measurement

Subjects' were positioned in a semi recumbent position and lower limb haemodynamics assessed with a Duplex Doppler ultrasound using a 4-8 MHz linear transducer (LOGIQ e; GE Medical Systems). To ensure the validity and precision of the Doppler ultrasound operator, a reliability analysis was performed using Cronbach's alpha, which was found to be 0.952.

All blood flow measurements were taken at the popliteal vein to reflect venous outflow from the deep veins of the lower leg. No measurement was taken during the first minute of the 5-minute intervention. Blood flow was sampled 3 times for rigor over the remaining 4 minutes and the mean of the three measurements used for analysis. Popliteal vein diameter (cm, Figure 3.2A) and Peak venous velocity (cm/s, Figure 3.2B, line 3) were recorded from the Doppler waveform. The blood flow response to the intervention (Control, NMES, Calf-IPC, Foot-IPC) is clearly identifiable. The blood flow waveform response to intervention is selected for analysis on the Doppler instrument as indicated by vertical callipers positioned at the start and end of the waveform indicated by lines 1 and 2 in Figure 3.2B. The Doppler unit's in-built software calculates time averaged mean velocity (TAMEAN) (cm/s) and volume flow (mL/min) between the vertical callipers. Volume flow represents the cross-sectional area of the popliteal vein (cm^2) X mean velocity (cm/s).

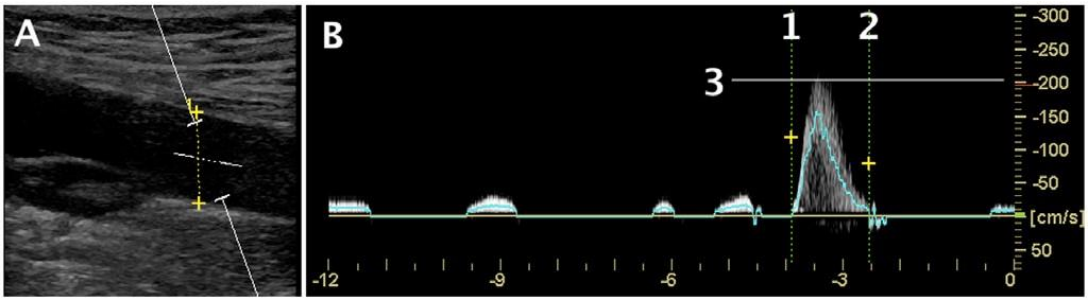


Figure 3.2 Representative Doppler ultrasound capture window used for blood flow analysis. A. Representative screen shot from Duplex Doppler ultrasound measuring popliteal vein diameter. **B.** Representative screen shot from Duplex Doppler ultrasound showing blood flow waveform in response to NMES stimulation. For haemodynamic analysis each waveform produced in response to the intervention is analysed by positioning callipers appropriately. Peak venous velocity (cm/s, line 3), time averaged mean velocity (TAMEAN (cm/s), mean flow between lines 1 and 2) and volume flow (mL/min, volume flow between lines 1 and 2). The X-axis reflects time in seconds.

Ejected volume measures the volume of blood displaced through the popliteal vein during a single pulse of the intervention and was calculated offline using Equation 3.1:

[Equation 3.1]

Ejected Volume (mL) = Volume Flow (mL/min) X Duration of single Intervention pulse (min)

The duration of a single intervention pulse represents the time for one pulse of the intervention (NMES or IPC, stimulation or compression respectively) as defined under IPC and NMES protocols above. For the control intervention the Duration of Intervention pulse was taken as 1 second.

3.3.6 Statistical Analysis

As this study followed a repeated measures design, the data were fitted to a multivariate repeated measures model. A multivariate repeated measures analysis was used to identify any differences between each intervention in terms of blood flow. The Greenhouse-Geisser correction was used to correct any violations to the assumption of sphericity. All statistical analyses were carried out using SPSS (SPSS for Windows, version 22, IBM Corporation).

3.4 Results

Measurements of peak venous velocity, TAMEAN and ejected volume are summarised in Table 3.1. Peak venous velocity, TAMEAN and ejected volume improved significantly with all interventions ($p < 0.001$ vs. control). There is evidence of an overall intervention effect and gender effect on lower limb haemodynamics ($p < 0.001$ for both factors). Gender was found to have a significant effect on peak venous velocity ($p = 0.003$) and TAMEAN ($p = 0.042$), with females having a greater peak venous velocities and TAMEAN. The interaction between intervention and gender was found to have a significant effect on TAMEAN ($p = 0.023$).

Table 3.1 Median and (Interquartile Range) of Ejected Volume (EV), Peak Venous Velocity (PV) and Time Averaged Mean (TAMEAN) in Subgroups of Features. *P* Value using Bonferroni Correction

Feature	EV (ml)	*P*	PV (cm/s)	*P*	TAMEAN (cm/s)	*P*
GENDER Male Female	 9.9(4; 17) 7.0(2; 12)	 P=0.065	 73.3(19; 115) 88.0(23; 130)	 P=0.003	 15.7(6; 22) 17.5(6; 25)	 P=0.042
INTERVENTION Control Foot-IPC Calf-IPC NMES	 2.1(2; 3) 7.2(5; 10) 12.3(9; 15) 19.8(15; 31)	 P<0.001* P<0.001* P<0.001*	 10.8(9; 13) 50.5(35; 67) 125.6(110;146) 108.8(87; 131)	 P<0.001* P<0.001* P<0.001*	 3.6(3; 5) 11.5(8; 15) 21.8(19; 27) 22.2(17; 28)	 P<0.001* P<0.001* P<0.001*

Both calf-IPC and calf-NMES resulted in a significantly greater peak venous velocity (Figure 3.3) and TAMEAN (Figure 3.4) when compared to foot-IPC ($p < 0.001$). There was no significant difference observed between calf-IPC and NMES for either peak venous velocity or TAMEAN ($p = 0.283$ and $p = 1.000$ respectively).

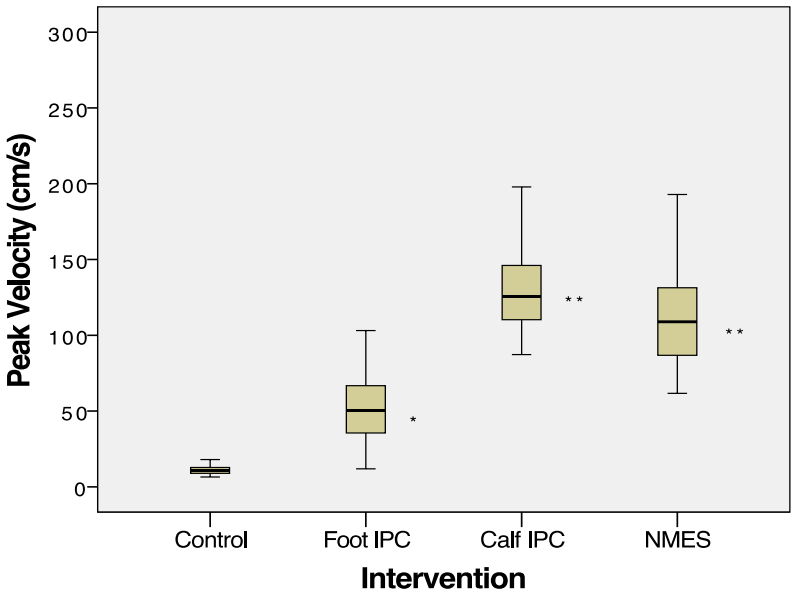


Figure 3.3 Effect of intervention on the peak venous velocity (cm/s). Both NMES and calf-IPC produced similar increases in peak venous velocity, which were significantly greater than both foot-IPC and control. *$p < 0.001$ vs. control, **$p < 0.001$ vs. foot-IPC.

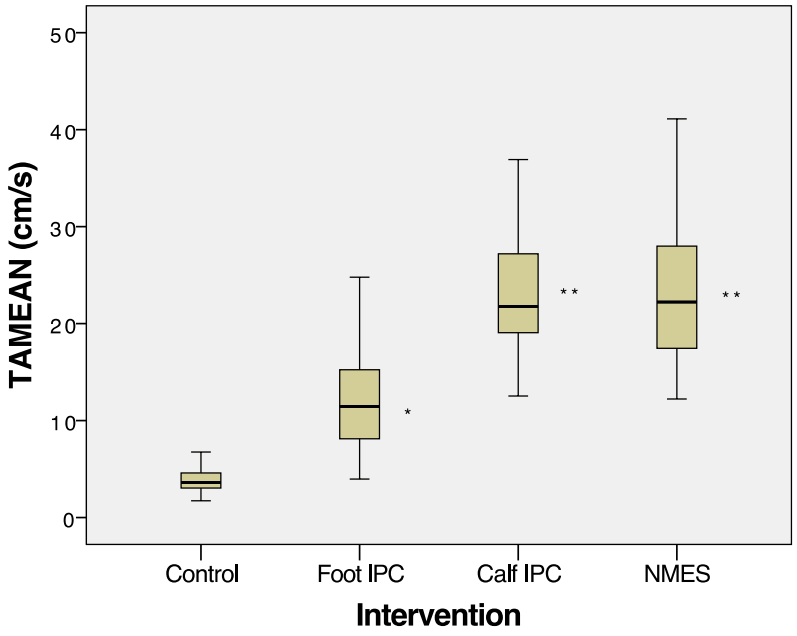


Figure 3.4 Effect of intervention on TAMEAN (cm/s). Both NMES and calf-IPC produced similar increases in TAMEAN, which were significantly greater than both foot-IPC and control. *$p < 0.001$ vs. control, **$p < 0.001$ vs. foot-IPC.

Significantly, NMES produced the largest increase in ejected volume 19.81ml (15.4- 30.81), which was 1.7 times that of calf-IPC (Figure 3.5).

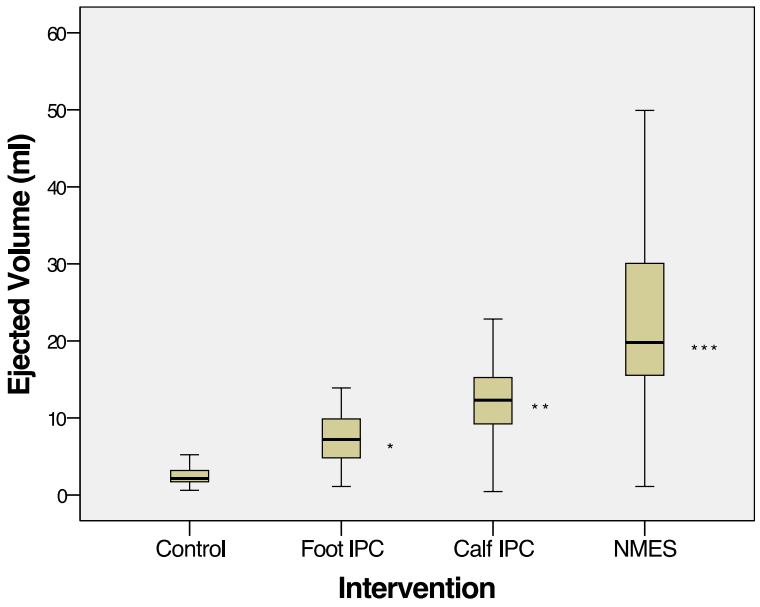


Figure 3.5 Effect of intervention on the ejected volume (ml). NMES produced the greatest ejected volume compared to all other interventions. *p < 0.001 vs. control, **p < 0.001 vs. foot-IPC, ***p < 0.001 vs. calf-IPC.

3.5 Discussion

In this paper, for the first time, we have demonstrated enhanced lower limb haemodynamics using NMES compared to IPC. In matched device active/silent protocols NMES was as effective as IPC in terms of peak velocity and TAMEAN and out-performed both foot-IPC and calf-IPC in terms of ejected volume. In the clinical arena this is a very significant finding as the greater the ejected volume, the less blood is left in stasis in the veins and soleal sinuses and therefore it is less likely for a DVT to form. This data is supported by a number of other studies, which have found ejected volumes due to NMES to be significantly higher than baseline [2, 29, 30].

The main technologic intervention in common use for DVT prevention is IPC, but IPC suffers from low compliance and thus there is a need for viable alternatives. IPC compresses the limb externally, leading eventually to the compression of the underlying muscles, the superficial veins and finally the deep veins. This action does not mimic a normal physiological process. Unlike IPC, NMES produces a physiological muscle contraction similar to that observed during normal walking, resulting in the large increase in ejected volume that was observed. Additionally, at the end of the NMES-elicited contraction, we were able to observe in some cases that the Doppler recording of blood flow fell to zero, whereas following the IPC cycle, Doppler blood flow returned to the non-zero baseline level. This suggests that NMES more completely empties the venous compartments than IPC, which is a critical element in DVT prevention. More data and further study is required to support this observation. However, this observation was also made by Faghri et al. [19] and Laverick et al. [20] as being a feature of NMES-elicited venous return.

The aim of both IPC and NMES in the prevention of DVT is to prevent venous stasis. Peak venous velocity is a measurement commonly used to assess the effectiveness of DVT prophylaxis methods in preventing venous stasis. In this study, all interventions were found to significantly increase peak venous velocity from baseline resting values.

These results are in contrast to Izumi et al [31] and Czyryn et al [3] who found NMES produced greater peak venous velocities than IPC. However, these differences may be accounted for by differences in muscles stimulated and different stimulation parameters used in these studies. Izumi et al stimulated the tibialis anterior muscle as opposed to the soleus muscle and used a square wave pulse 500μs in duration at a rate of 50 Hz, whereas in this study we employed a balanced biphasic waveform with a pulse width of 350μs and a rate of 36 Hz. These parameters were chosen as our previous work found them to optimise both muscle contraction and patient comfort [27]. Izumi et al also used a compression of 40mmHg on the calf as opposed to the 130mmHg used in our study [31].

These parameters may account for the differences observed in peak venous velocities. Czyryn et al applied NMES to the foot using a biphasic symmetrical square wave 300ms in duration and at a rate of 50Hz and they applied IPC to the foot at a pressure of 130mmHg for a 3 second duration [3]. The different stimulation parameters used in this study, coupled with both the stimulation and compression being applied to the foot as opposed to the calf, may account for the differences observed. Although foot-IPC does improve lower limb haemodynamics, it does so to a lesser degree than calf-IPC or NMES applied to the calf. While it is important to increase venous velocity in reducing venous stasis, it is important to do so to a safe level. An excessive increase in venous velocity could possibly damage the blood vessel endothelium and lead to thrombus formation or potentially dislodge a clot already present in the deep veins or soleal sinuses. Consequently, other factors, such as the ejected volume, need to be considered when assessing the effectiveness of DVT prophylaxis methods.

The current study was carried out in young (18-23 years), healthy participants. There was a gender difference in the responses measured with females having a lower ejected volume and higher TAMEAN, which is likely to result from anatomical size difference in the gender groups with males generally having a larger calf musculature. However, the population most at risk for DVT development would be an older age group, many with pre-existing health problems.

As DVT is most likely to occur following surgery, especially orthopaedic surgery [32-37], where prolonged bed rest and immobilisation are common, a follow-on study should be carried out in this patient population. Further study is required to establish the longer-term effects of NMES and to evaluate the use of NMES over a full recovery/rehabilitation period until the patient is mobile as there is still a high risk of DVT development up to 5 weeks post-surgery [38, 39]. Furthermore, to strengthen the data presented here studies should examine an older population cohort and assess effects of NMES on enhancing fibrinolytic activity.

However, significantly in this study we have shown that NMES is equal to IPC in terms of peak velocity and TAMEAN and outperforms IPC in terms of ejected venous volume. Our results suggest that NMES is a superior method of improving lower limb haemodynamics and supports the viable use of NMES as a DVT prophylaxis method. This significant validation of the haemodynamic performance of NMES make it a viable alternative to IPC in the clinical and home setting. Furthermore, NMES does not suffer the negative aspects of IPC use, NMES is silent, portable and has very favourable usability characteristics, which would support a high rate of compliance.

3.6 References

[1] MacLellan, D. and Fletcher, J., "Mechanical compression in the prophylaxis of venous thromboembolism," *ANZ J Surg*, vol. 77, no. 6, pp. 418-23, Jun 2007.

[2] Broderick, B., O'Briain, D., Breen, P., Kearns, S., and ÓLaighin, G., "A pilot evaluation of a neuromuscular electrical stimulation (NMES) based methodology for the prevention of venous stasis during bed rest," *Med Eng Phys*, vol. 32, no. 4, pp. 349-55, May 2010.

[3] Czyrny, J., Kaplan, R., Wilding, G., Purdy, C., and Hirsh, J., "Electrical foot stimulation: a potential new method of deep venous thrombosis prophylaxis," *Vascular*, vol. 18, no. 1, pp. 20-7, Jan-Feb 2010.

[4] Broderick, B., Kennedy, C., Breen, P., Kearns, S., and ÓLaighin, G., "Patient tolerance of neuromuscular electrical stimulation (NMES) in the presence of orthopaedic implants," *Med Eng Phys*, vol. 33, no. 1, pp. 56-61, Jan 2011.

[5] Vanek, V., "Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves," *Am Surg*, vol. 64, no. 11, pp. 1050-8, Nov 1998.

[6] Tamir, L., Hendel, D., Neyman, C., Eshkenazi, A. U., Ben-Zvi, Y., and Zomer, R., "Sequential foot compression reduces lower limb swelling and pain after total knee arthroplasty," *J Arthroplasty*, vol. 14, no. 3, pp. 333-8, Apr 1999.

[7] Fujisawa, M., Naito, M., Asayama, I., Kambe, T., and Koga, K., "Effect of calf-thigh intermittent pneumatic compression device after total hip arthroplasty: comparative analysis with plantar compression on the effectiveness of reducing thrombogenesis and leg swelling," *J Orthop Sci*, vol. 8, no. 6, pp. 807-11, 2003.

[8] Morris, R. J. and Woodcock, J. P., "Evidence-based compression: prevention of stasis and deep vein thrombosis," *Ann Surg*, vol. 239, no. 2, pp. 162-71, Feb 2004.

[9] Morris, R., "Intermittent pneumatic compression - systems and applications,"
J Med Eng Technol, vol. 32, no. 3, pp. 179-88, May-Jun 2008.

[10] Vanscheidt, W., Ukat, A., and Partsch, H., "Dose-response of compression therapy for chronic venous edema--higher pressures are associated with greater volume reduction: two randomized clinical studies," *J Vasc Surg,* vol. 49, no. 2, pp. 395-402, 402 e1, Feb 2009.

[11] Chang, C. and Cormier, J., "Lymphedema interventions: exercise, surgery, and compression devices," *Semin Oncol Nurs,* vol. 29, no. 1, pp. 28-40, Feb 2013.

[12] Dennis, M., Sandercock, P., Reid, J., Graham, C., Forbes, J., and Murray, G., "Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial," *Lancet,* vol. 382, no. 9891, pp. 516- 24, Aug 10 2013.

[13] Geerts, W. H. *et al.*, "Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy," *Chest,* vol. 126, no. 3 Suppl, pp. 338S-400S, Sep 2004.

[14] Bockheim, H. M., McAllen, K. J., Baker, R., and Barletta, J. F., "Mechanical prophylaxis to prevent venous thromboembolism in surgical patients: a prospective trial evaluating compliance,"*J Crit Care,* vol. 24, no. 2, pp. 192-6, Jun 2009.

[15] Ricci, M., Fisk, P., Knight, S., and Case, T., "Hemodynamic evaluation of foot venous compression devices," *J Vasc Surg,* vol. 26, no. 5, pp. 803-8, Nov 1997.

[16] Delis, K., Slimani, G., Hafez, H., and Nicolaides, A., "Enhancing venous outflow in the lower limb with intermittent pneumatic compression. A comparative haemodynamic analysis on the effect of foot vs. calf vs. foot and calf compression," *Eur J Vasc Endovasc Surg,* vol. 19, no. 3, pp. 250-60, Mar 2000.

[17] Whitelaw, G., Oladipo, O., Shah, B., DeMuth, K., Coffman, J., and Segal, D., "Evaluation of intermittent pneumatic compression devices," *Orthopedics,* vol. 24, no. 3, pp. 257-61, Mar 2001.

[18] Morris, R. J. and Woodcock, J. P., "Intermittent pneumatic compression or graduated compression stockings for deep vein thrombosis prophylaxis? A systematic review of direct clinical comparisons," *Ann Surg,* vol. 251, no. 3, pp. 393-6, Mar 2010.

[19] Faghri, P., Meerdervort, H. V., Glaser, R., and Figoni, S., "Electrical stimulation-induced contraction to reduce blood stasis during arthroplasty," *IEEE Trans Rehabil Eng,* vol. 5, no. 1, pp. 62-9, Mar 1997.

[20] Laverick, M., McGivern, R., Crone, M., and Mollan, R., "A comparison of the effects of electrical calf muscle stimulation and the venous foot pump on venous blood flow in the lower leg," *Phlebologie,* vol. 5, pp. 285-290, 1990.

[21] Werbel, G. and Shybut, G., "Acute compartment syndrome caused by a malfunctioning pneumatic-compression boot. A case report," *J Bone Joint Surg Am,* vol. 68, no. 9, pp. 1445-6, Dec 1986.

[22] Pittman, G., "Peroneal nerve palsy following sequential pneumatic compression," *JAMA,* vol. 261, no. 15, pp. 2201-2, Apr 21 1989.

[23] Strup, S., Gudziak, M., Mulholland, S., and Gomella, L., "The effect of intermittent pneumatic compression devices on intraoperative blood loss during radical prostatectomy and radical cystectomy," *J Urol,* vol. 150, no. 4, pp. 1176-8, Oct 1993.

[24] Lyons, G., Leane, G., and Grace, P., "The effect of electrical stimulation of the calf muscle and compression stocking on venous blood flow velocity," *Eur J Vasc Endovasc Surg,* vol. 23, no. 6, pp. 564-6, Jun 2002.

[25] Clarke-Moloney, M., Lyons, G., Breen, P., Burke, P., and Grace, P., "Haemodynamic study examining the response of venous blood flow to electrical stimulation of the gastrocnemius muscle in patients with chronic venous disease," *Eur J Vasc Endovasc Surg,* vol. 31, no. 3, pp. 300-5, Mar 2006.

[26] Broderick, B., Breathnach, O., Condon, F., Masterson, E., and ÓLaighin, G., "Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty," *J Orthop Surg Res,* vol. 8, pp. 3-10, 2013.

[27] Lyons, G., Leane, G., Clarke-Moloney, M., O'Brien, J., and Grace, P., "An investigation of the effect of electrode size and electrode location on comfort during stimulation of the gastrocnemius muscle," *Med Eng Phys,* vol. 26, no. 10, pp. 873-8, Dec 2004.

[28] Breen, P., Corley, G., O'Keeffe, D., Conway, R., and ÓLaighin, G., "A programmable and portable NMES device for drop foot correction and blood flow assist applications," *Med Eng Phys,* vol. 31, no. 3, pp. 400-8, Apr 2009.

[29] Breen, P., Galvin, O., Quondamatteo, F., Grace, P., and ÓLaighin, G., "Comparison of single- and two-channel neuromuscular electrical stimulation sites for enhancing venous return," *IEEE Trans Neural Syst Rehabil Eng,* vol. 20, no. 3, pp. 389-94, May 2012.

[30] Corley, G., Breen, P., Birlea, S., Serrador, J., Grace, P., and ÓLaighin, G., "Hemodynamic effects of habituation to a week-long program of neuromuscular electrical stimulation," *Med Eng Phys,* vol. 34, no. 4, pp. 459- 65, May 2012.

[31] Izumi, M., Ikeuchi, M., Mitani, T., Taniguchi, S., and Tani, T., "Prevention of venous stasis in the lower limb by transcutaneous electrical nerve stimulation," *Eur J Vasc Endovasc Surg,* vol. 39, no. 5, pp. 642-5, May 2010.

[32] Hull, R. *et al.,* "A comparison of subcutaneous low-molecular-weight heparin with warfarin sodium for prophylaxis against deep-vein thrombosis after hip or knee implantation," *N Engl J Med,* vol. 329, no. 19, pp. 1370-6, Nov 4 1993.

[33] Eriksson, B., Kalebo, P., Ekman, S., Lindbratt, S., Kerry, R., and Close, P., "Direct thrombin inhibition with Rec-hirudin CGP 39393 as prophylaxis of thromboembolic complications after total hip replacement," *Thromb Haemost,* vol. 72, no. 2, pp. 227-31, Aug 1994.

[34] Bergqvist, D., "Prolonged prophylaxis in postoperative medicine," *Semin Thromb Hemost,* vol. 23, no. 2, pp. 149-54, 1997.

[35] Francis, C. *et al.,* "Prevention of deep-vein thrombosis after total hip arthroplasty. Comparison of warfarin and dalteparin," *J Bone Joint Surg Am,* vol. 79, no. 9, pp. 1365-72, Sep 1997.

[36] Robinson, K. *et al.,* "Accuracy of screening compression ultrasonography and clinical examination for the diagnosis of deep vein thrombosis after total hip or knee arthroplasty," *Can J Surg,* vol. 41, no. 5, pp. 368-73, Oct 1998.

[37] Schindler, O. and Dalziel, R., "Post-thrombotic syndrome after total hip or knee arthroplasty: incidence in patients with asymptomatic deep venous thrombosis," *J Orthop Surg (Hong Kong)*, vol. 13, no. 2, pp. 113-9, Aug 2005.

[38] Johnson, R., Green, J., and Charnley, J., "Pulmonary embolism and its prophylaxis following the Charnley total hip replacement," *Clin Orthop Relat Res*, no. 127, pp. 123-32, 1977.

[39] Huber, O., Bounameaux, H., Borst, F., and Rohner, A., "Postoperative pulmonary embolism after hospital discharge. An underestimated risk," *Arch Surg*, vol. 127, no. 3, pp. 310-3, Mar 1992.

Chapter 4

These Shoes are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps

Published Reference:

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Background

Chapters 2 and 3 have focused upon the clinical complication of venous stasis and DVT following TKA. While the mechanical method of IPC is commonly utilised post-surgery for venous stasis and DVT prevention, results of Chapter 2 have highlighted the lack of clarity with regard to its true effectiveness. Chapter 3 was carried out to assess the use of NMES as a method of recovery with regard to preventing venous stasis. NMES was compared to IPC in healthy participants, showing promising haemodynamic results, increasing both velocities and volumes to a greater degree than IPC.

Further to assessing its effects on venous stasis prevention, this thesis aims to assess the use of NMES as a method of enhancing functional recovery through outcomes of physical activity levels, knee range of motion and lower limb swelling. These measures play a major role in functional recovery post- TKA, with improvements in physical activity an important goal for many patients following surgery. When the measurement of physical activity is utilised as an indicator of functional recovery, its accurate quantification is of the utmost importance. As such, an aim within this thesis was to investigate the sensitivity and specificity of a number of activity monitors that have the potential to be utilised by TKA patients post-surgery as a method of monitoring physical activity levels.

Commercial activity monitors with a screen and/or a smartphone application may be of great benefit to patients following TKA-surgery. These monitors allow access to real time physical activity data that would allow a patient to easily track their functional recovery progression. Visualisation of physical activity levels would encourage improvements in physical activity and provide motivation for achieving the level of activity required to improve functional health following surgery.

A commonly utilised output from activity monitors is that of step count. Step count is an easy-to-understand output with regard to quantifying physical activity in any population and is often utilised when aiming to improve physical activity levels.

Indeed, a daily step count of 10,000 steps is widely recognised as the recommended number of steps required per day to attain adequate physical activity levels and achieve health benefits. When carrying out 10,000 steps per day, it is easy to imagine that a number of different factors come into play, such as surface type, footwear type, walking speed, activity intensity etc. It is important to consider the effects these factors may have on the accuracy of activity monitors, especially when utilised as an intervention to improve physical activity levels and functional health, such as following TKA.

In these circumstances, both the sensitivity and specificity of activity monitors come into question. While it is necessary for the activity monitors to be sensitive, i.e. detect and register a step when a step is taken, it is also of importance that they be specific, i.e. disregard non-stepping movements. Focusing first on activity monitor sensitivity, the aim of Chapter 4 was to carry out a comprehensive evaluation on the step detection sensitivity of a number of physical activity monitors that have the potential to be utilised by TKA patients post-surgery while walking over different surfaces and in different types of footwear when aiming to achieve the recommended daily goal of 10,000 steps.

Contribution to work

Study design: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

Data collection:

- Subject consent: Sandra O'Connell, Lisa Kelly, Elaine Murphy, Sorcha Beirne, Niall Burke, Orlaith Kilgannon.
- Subject testing: Sandra O'Connell, Lisa Kelly, Elaine Murphy, Sorcha Beirne, Niall Burke, Orlaith Kilgannon.

Data Analysis: Sandra O'Connell.

Interpretation of results: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

Drafting of manuscript: Sandra O'Connell.

Critical review of manuscript: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

4.1 Abstract

Introduction: Physical activity is a vitally important part of a healthy lifestyle, and is of major benefit to both physical and mental health. A daily step count of 10,000 steps is recommended globally to achieve an appropriate level of physical activity. Accurate quantification of physical activity during conditions reflecting those needed to achieve the recommended daily step count of 10,000 steps is essential. As such, we aimed to assess four commercial activity monitors for their sensitivity/accuracy in a prescribed walking route that reflects a range of surfaces that would typically be used to achieve the recommended daily step count, in two types of footwear expected to be used throughout the day when aiming to achieve the recommended daily step count, and in a timeframe required to do so.

Methods: Four commercial activity monitors were worn simultaneously by participants (n= 15) during a prescribed walking route reflective of surfaces typically encountered while achieving the daily recommended 10,000 steps. Activity monitors tested were the Garmin Vivofit ™, New Lifestyles' NL-2000 ™ pedometer, Withings Smart Activity Monitor Tracker (Pulse O_2) ™, and Fitbit One ™.

Results: All activity monitors tested were accurate in their step detection over the variety of different surfaces tested (natural lawn grass, gravel, ceramic tile, tarmacadam/asphalt, linoleum), when wearing both running shoes and hard-soled dress shoes.

Conclusion: All activity monitors tested were accurate in their step detection sensitivity and are valid monitors for physical activity quantification over the variety of different surfaces tested, when wearing both running shoes and hard-soled dress shoes, and over a timeframe necessary for accumulating the recommended daily step count of 10,000 steps. However, it is important to consider the accuracy of activity monitors, particularly when physical activity in the form of stepping activities is prescribed as an intervention in the treatment or prevention of a disease state.

4.2 Introduction

Physical activity is an essential part of a healthy lifestyle, playing an important role in improving and maintaining both physical and mental health [1-4]. Indeed, lack of physical activity has been recognised as the fourth leading risk factor for global mortality, associated with 6% of deaths worldwide [5]. Since the benefits of physical activity have been recognised globally, governments internationally have highlighted to their citizens the need to be physically active on a regular basis. In 1996, the US Surgeon General recommended that as part of a healthy lifestyle, people of all ages should partake in at least 30 minutes of moderate-intensity physical activity, such as brisk walking, on a daily basis [6]. The 2008 'Physical Activity Guidelines for Americans' from the Centers for Disease Control (CDC) recommended that adults need 2 hours and 30 minutes of moderate intensity aerobic physical activity, for example brisk walking, per week [7]. These two recommendations correspond closely with the 2010 WHO recommendation that adults should do at least 150 minutes of moderate intensity aerobic physical activity throughout the week [5].

An important consideration in assisting persons to change their physical activity behaviour and to adhere to these public health recommendations is providing them with the ability to easily quantify the extent of physical activity completed in a given day. The development of commercial pedometers in the late 1960s provided a convenient, low cost method of quantifying one form of physical activity, namely walking. These devices provided straightforward feedback to the user of the quantity of physical activity completed, specifically their step count. A series of pedometer-based studies, from 2004 to 2011, evaluated the relationship between step count and adherence to physical activity guidelines and reported that less than 7,500 steps per day represented sedentary or "low-active" behaviour [8, 9] and taking 10,000 steps per day was consistent with a physical activity level associated with person who is "active" [8, 10, 11]. Furthermore, a study carried out in an overweight population from the Lower Mississippi Delta of the U.S.A. reported a step count of 9,154 steps per day to equate to 30 minutes of moderate-to-vigorous physical activity. The authors concluded that, in this population, a step count of 8,300 to 9,100 steps a day

should be accumulated in order to achieve recommended physical activity guidelines [12].

As part of their physical activity guidelines, the WHO states that physical activity in adults includes recreational or leisure-time physical activity, occupational (i.e. work), household chores, transportation (e.g. walking or cycling), play, games, planned exercise or sports in the context of daily, family, and community activities [5]. Thus the recommended "quantity" of physical activity of 10,000 steps being proposed internationally would only typically be achieved through a combination of these activities and under the varied circumstances associated with these activities. In other words, the recommended step count of 10,000 steps would typically be achieved, not only through a specific programme of exercise, but also through a combination of activities in the home, in the work place, and while getting to and from work. These activities would typically involve the person walking on a wide variety of surfaces from footpaths, indoor floors with varied surface types, and outdoor natural walking surfaces such as grass pathways. Indeed, one group have examined the effect of walking surface on step count sensitivity/accuracy of a pedometer and found surface type significantly affected step count [13]. Additionally, a number of physical activity device manufacturers websites state that surface type can affect step count sensitivity/accuracy of their devices [14, 15].

Furthermore, the range of activities conducted in achieving the recommended step count of 10,000 steps would also typically involve the person changing their footwear from more formal "dress" shoes in the workplace to more comfortable runner-type shoes in the home and while exercising. Therefore, a physical activity monitor being used to quantify adherence to the recommended daily step count must be able to deal with: (i) a variety of walking surfaces, (ii) different footwear, and (iii) extended periods of walking, where the accumulated number of steps is in the order of 10,000 steps. These three variables have the potential to affect step count detection accuracy. Thus, it is the view of the authors that activity monitor testing must involve: (i) walking on different surfaces that reflect the range of surfaces that will typically be encountered to achieve the daily step count goal, (ii) walking with different footwear that reflects the different types of footwear expected to be used throughout the day, and (iii) walking for periods of time that properly reflect the time

required to achieve the recommended daily step count. In fact, a review of the literature highlights that these considerations have not been widely adopted in a wide range of studies where the sensitivity of activity monitors has been assessed [16-21]. Often, the types of surfaces and types of footwear tested are either not reported or not taken into consideration during testing. Furthermore, the timeframe of testing is often far less than would be required to achieve the recommended daily step count of 10,000 steps. For example, timeframes of between 11 and 25 minutes have previously been utilised and would be completely insufficient for accumulating 10,000 steps [16-20].

In this paper we aimed to assess four commercial activity monitors: the Withings Smart Activity Monitor Tracker (Pulse O_2) ^{TM}, the NL-2000 pedometer ^{TM}, the Garmin Vivofit ^{TM}, and the Fitbit One ^{TM}. We aimed to assess the step detection sensitivity of each activity monitor, i.e. the ability of the activity monitors to detect and count an actual step as a step, over a prescribed walking route that reflects a range of surfaces that would typically be used to achieve the recommended daily step count and in a timeframe required to do so. In addition, we also aimed to investigate two different types of footwear typically used throughout the day when aiming to achieve the recommended daily step count of 10,000 steps.

4.3 Methods

4.3.1 Participants

Fifteen healthy participants (8 female, 7 male) took part in this study, with a mean age of 21.1 ± 1.1 years. Males had a mean BMI of 23.60 ± 2.70kg/m^2 while females had a mean BMI of 21.88 ± 1.81kg/m^2. None of the participants had any history of cardiovascular disease or neurological disorders. Ethics committee approval was obtained from the Galway University Hospitals Research Ethics Committee, and all participants provided written, informed consent.

4.3.2 Study Protocol

All 15 participants completed a prescribed walking route. The activity monitors tested in this study were the Withings Smart Activity Monitor Tracker (Pulse O_2) ™ (Withings, Issy-les-Moulineaux, France), NL-2000 pedometer ™ (New Lifestyles, Missouri, USA), Garmin Vivofit ™ (Garmin, Kansas, USA), and Fitbit One ™ (Fitbit, San Francisco, USA) (See Table 4.1). The NL-2000 pedometer ™ was chosen as this device is a popular pedometer shown to be accurate in step detection. The Withings Smart Activity Monitor Tracker (Pulse O_2) ™, Garmin Vivofit ™ and Fitbit One ™ monitors were chosen based upon their popularity and reasonable price range.

All activity monitors were put in place at the manufacturer's recommended body location (Figure 4.1) by the investigators as per the manufacturers' instructions. All four activity monitors were worn simultaneously on each participant for the duration of testing. The Garmin Vivofit ™ was worn on the non-dominant wrist, with the NL-2000 ™ and Withings Smart Activity Monitor Tracker (Pulse O_2) ™ worn on opposite sides of the waist. The Fitbit ™ activity monitor was clipped onto clothing at the level of the chest. Participants were video recorded throughout the study with a hand-held camcorder. The true step count was extracted manually from the recorded video in real time and was then compared to the step count registered by each activity monitor.

Additionally, the ActivPAL micro ™ (PAL Technologies Ltd., Glasgow, UK) was worn by each participant as a reference device for measuring the overall total step count for the prescribed walking route. The ActivPAL ™ was attached to the thigh

using Tegaderm transparent dressing (3M Health Care, Minnesota, USA). The ActivPAL micro™ device was chosen as a reference device in this study as it is one of the most widely utilised activity monitors in physical activity research. The ActivPAL ™ has been utilised extensively across all age groups and in both healthy and patient groups.

Table 4.1 Details of the Different Activity Monitors Tested

Activity Monitor	Specifications	Outputs	Interface	Location of Attachment	Validation Studies
ActivPAL micro™	*Sensor:* 3-axis accelerometer. *Recording/ battery life:* 10+ days	Step count; time sitting/lying, standing, stepping; number of transitions from standing to sitting; energy expenditure	Need to connect to PC to download and view data	Anterior aspect of the thigh	Ryan et al., 2006 [22]; Godfrey et al., 2007 [23]; Maddocks et al., 2008 [24]; Grant et al., 2008 [25]; Busse et al., 2009 [26]; Harrington et al., 2011 [27]; Storm et al., 2015 [19]
Withings Smart Activity Monitor Tracker (Pulse O_2)™	*Sensor:* 3-axis accelerometer; optoelectronics sensor. *Recording/ battery life:* 2 weeks	Step count; distance; elevation; calories; sleep cycle; heart rate & blood O_2	Screen and smart phone application	On the wrist (detachable wristband); clipped on at the hip (detachable clip); in a pocket	Ferguson et al., 2015 [28]; Storm et al., 2015 [19]
Fitbit One™	*Sensor:* 3-axis accelerometer; altimeter. *Recording/ battery life:* 10-14 days	Step count; distance; elevation; calories; sleep cycle	Screen and smart phone application	Clipped on at hip or chest level; in a pocket; in a wristband (at night)	Ferguson et al., 2015 [28]; Storm et al., 2015 [19]; Klassen et al., 2015 [29]; Simpson et al., 2015 [30]; Diaz et al., 2015 [31]; Lee et al., 2014 [32]; Tackas et al., 2014 [20]
Garmin Vivofit™	*Sensor:* 3-axis accelerometer. *Recording/ battery life:*	Step count; distance; calories; sleep cycle; heart rate; sitting,	Screen and smart phone application	Wristband	

	24/7 recording; more than one year battery life	standing			
NL-2000 pedometer™	*Sensor:* piezoelectric strain gauge. *Recording/ battery life:* 7 day automatic memory; removable 3V lithium battery	Step count; elevation; calories	Screen	Clipped on at the hip level	Crouter et al., 2003 [33]; Schneider et al. 2003 [34]; Schneider et al., 2004 [35]; Grant et al., 2008 [25]

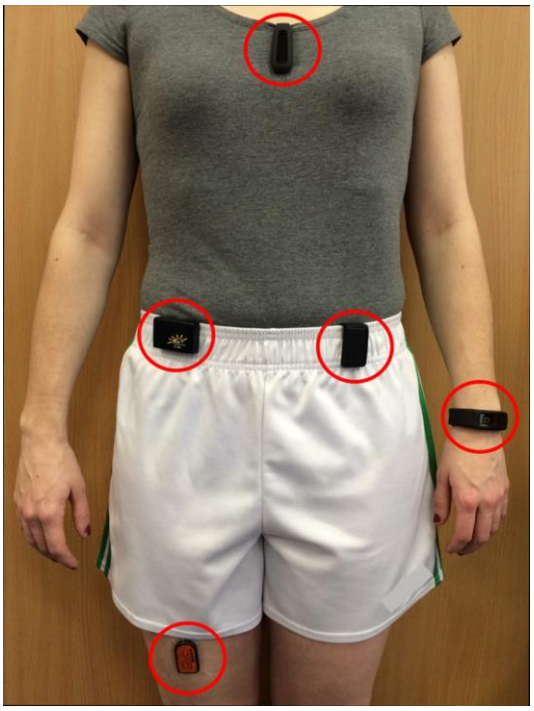

Figure 4.1 Position of the activity monitors. The ActivPAL micro ™ activity monitor on the thigh (right), the NL-2000 ™ pedometer on the waist (right), the Garmin Vivofit ™ on the wrist (left), the Withings Smart Activity Monitor Tracker (Pulse O_2) ™ on the waist (left), the Fitbit One ™ activity monitor on the chest.

Participants completed a prescribed flat walking route consisting of five different walking surfaces: linoleum (800m), natural lawn grass (900m), gravel (990m), ceramic tile (400m) and tarmacadam/asphalt (880m). In addition, the prescribed walking route included stair walking (49 steps up and 49 steps down, step height 16cm) and ramp walking (240m up and 240m down at an incline of 4.05%) (Figure 4.2).

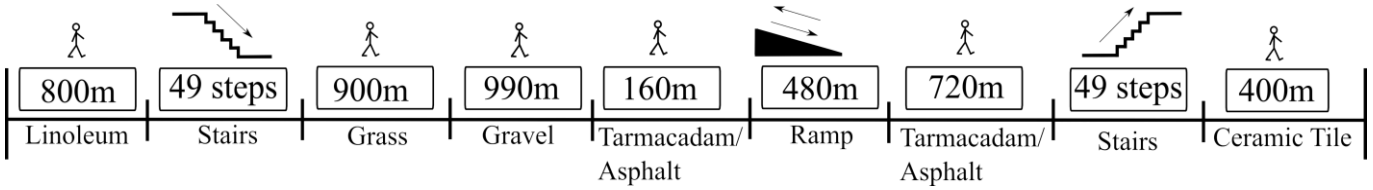

Figure 4.2 Prescribed walking route. Breakdown of surfaces and distances throughout the walking route.

Each participant completed the walking route twice: the first time wearing standard running shoes, the second time wearing hard-soled dress shoes. At all times the participants were asked to walk at their normal walking pace, in other words, self-selected walking speed.

4.3.3 Inter-device Reliability

There were between three and five of each device type used during testing. Prior to testing, each unit of each device type was tested over a 400m flat walk of uniform ceramic tile surface while wearing hard-soled shoes. One investigator wore each unit of a device type simultaneously for the 400m walk. The step counts on each unit of that device type were then compared. There was found to be no difference in step counts between the Fitbit ™ units. The largest difference between the units of the remaining activity monitors was 0.19% for the NL-2000 ™ units, 1.55% for the ActivPAL ™ units, and 13.67% for the Garmin ™ units. For the Garmin units, any step counts outside of ±2 SD of the observed count were excluded from analysis.

4.3.4 Statistical Analysis

All statistical analyses were carried out using SPSS (SPSS for Mac, version 20, IBM Corporation). Sample size was chosen by selecting a type I error rate (α) of 5%, a power ($1 - \beta$) of 0.80, a sampling ratio of 1 ($\kappa = n_A / n_B$), and a standard deviation of 250 steps (2.5% of the recommended daily step count of 10,000 steps). The Shapiro-Wilk test was used to analyse normality of data. Data were then fitted to a repeated measures model as this study followed a repeated measures design. Repeated-measures analysis of variance and post-hoc follow-up were used to detect differences in step count between the true step count extracted manually from the video recordings and the step count registered by each activity monitor and to detect step count detection errors associated with each surface type during the walking route. The Greenhouse-Geisser correction was used to correct any violations of the assumption of sphericity. The mean absolute percentage error (MAPE) was calculated for each activity monitor using equation 4.1 with N the number of steps as extracted from video analysis and $\tilde{N}$ the number of steps as recorded from each activity monitor.

[Equation 4.1] $$MAPE = [(\tilde{N} - N)/N] * 100$$

There is no standard for acceptable error in step detection in activity monitors, but we have chosen to select a 5% error zone as being acceptable. Bland-Altman plots were plotted to examine the agreement in step count between the observed step count and the step count recorded on the individual activity monitors. An unpaired t-test was carried out to assess any differences in step count between participants classed as 'fast' and 'medium to slow' speed walkers.

4.4 Results

Step counts obtained from video analysis are referred to as the observed step count and were compared to output counts from each activity monitor. Surface type did not affect step count detection on the four activity monitors tested. The mean step counts for the four activity monitors tested over each section of the walking route are given in Table 4.2. There was no statistically significant difference in activity monitor detected step count vs. the observed step count for the Withings Smart Activity Monitor Tracker (Pulse O_2) ™, NL-2000 pedometer ™, Garmin Vivofit ™, or Fitbit One ™ activity monitors on the linoleum ($P = 0.106$), gravel ($P = 0.131$), natural lawn grass ($P = 0.195$), tarmacadam/asphalt ($P = 0.286$), or ceramic tile ($P = 0.457$) surfaces. There was also no statistically significant difference in activity monitor detected step count versus the observed count for the Withings Smart Activity Monitor Tracker (Pulse O_2) ™, NL-2000 pedometer ™, Garmin Vivofit ™, and Fitbit One ™ activity monitors on the ramp section of the walking route ($P= 0.591$). Stairs walking did not affect step count, with no statistically significant difference in activity monitor detected step count vs. the observed step count for any activity monitor ($P > 0.05$ for all). Over the entire walking route, independent of surface type, there was no statistically significant difference in step count between the observed count and the four activity monitors tested ($P > 0.05$; Figure 4.3).

Table 4.2 Mean Step Counts Observed and Registered on the Four Activity Monitors Tested over the Different Surface Types of the Walking Route

	Observed Step Count	Withings ™	Garmin ™	NL-2000 ™	Fitbit ™	P Value
Natural Lawn Grass	1937 ± 166	1945 ± 190	1921 ± 156	1888 ± 222	1928 ± 169	0.195
Gravel	2422 ± 158	2408 ± 143	2359 ± 150	2388 ± 251	2424 ± 159	0.131
Linoleum	1979 ± 182	1982 ± 193	1987 ± 175	1922 ± 268	1984 ± 191	0.106
Tarmacadam/ Asphalt	2234 ± 234	2186 ± 251	2185 ± 235	2214 ± 239	2210 ± 303	0.286
Ceramic Tile	469 ± 31	455 ± 50	465 ± 21	436 ± 108	473 ± 41	0.457
Ramp	954 ± 63	965 ± 97	951 ± 78	952 ± 87	959 ± 83	0.591
Stairs Up	111 ± 9	112 ± 8	114 ± 10	102 ± 19	110 ± 11	0.083
Stairs Down	117 ± 4	111 ± 14	115 ± 11	113 ± 9	118 ± 23	0.129
Total Step Count	10950 ± 1209	10866 ± 1246	10950 ± 1364	10695 ± 1281	10875 ± 1236	0.213

There was no statistically significant difference in step count between the observed step count and the step count registered on each activity monitor over the different surfaces tested. Figures represent mean ± SD.

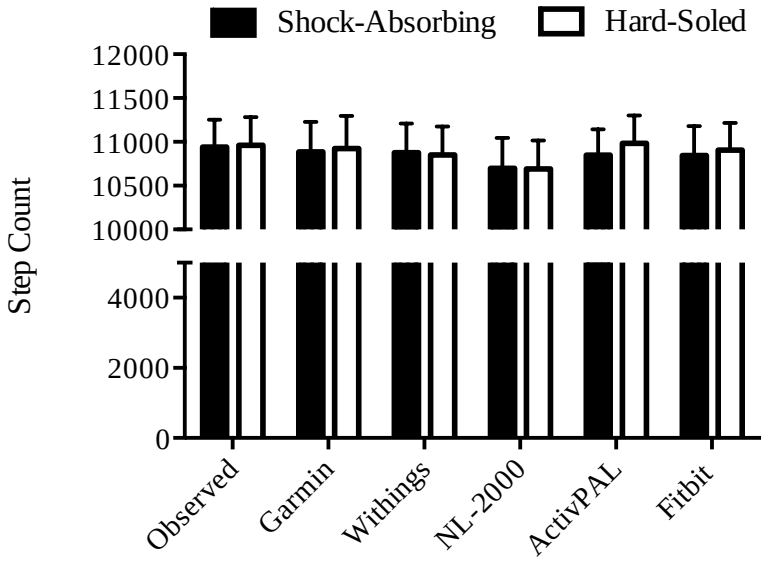

Figure 4.3 Overall walking route step count. Independent of surface type, there was no statistically significant difference in step count versus the observed step count or versus the ActivPAL ™ activity monitor. All data represent mean ± SEM.

There was also no statistically significant difference in step count between the step count on the ActivPAL ™ reference device and the Withings Smart Activity Monitor Tracker (Pulse O_2) ™, NL-2000 pedometer ™, Garmin Vivofit ™, or Fitbit One ™ activity monitors ($P > 0.05$ for all). There was no statistically significant difference in step count when the devices were compared to each other on any surface type or overall, independent of surface type ($P > 0.05$ for all). Mean absolute percentage errors for each of the four activity monitors are given in Table 4.3. Over the prescribed walking route, eight mean absolute percentage errors were found to be outside of our selected 5% error zone. The Withings Smart Activity Monitor Tracker (Pulse O_2) ™ had a step count error for stair walking only, with errors on descending stairs of 6.64% and on ascending stairs of 5.93%. The Garmin ™ had step count errors on the ceramic tile of 5.43%, on ascending stairs of 11.33% and on descending stairs of 6.48%. The NL-2000 pedometer ™ step count error on ceramic tile was 7.66% and on ascending stairs of 8.65%. The Fitbit ™ had step count error on descending stairs of 6.03%.

All other mean absolute percentage errors remained within the 5% error zone. The absolute percentage error range is also in Table 4.3. Although there was no significant difference in the step counts observed versus the step counts detected by the activity monitors, these values show the variation in the percentage error for the activity monitors (Table 4.3). For example, when walking down stairs, the Fitbit One ™ activity monitor had a mean absolute percentage error of 6.03% and a mean absolute percentage error range of -16.36% to 99.16%.

When all values lying ± 2SD from the mean observed step count were removed, only two mean absolute percentage errors were found to be outside the 5% error zone (Table 4.4). These were both for the Garmin ™ device, with error on ascending stairs of 6.59% and on descending stairs of 5.03%.

Table 4.3 Mean Absolute Percentage Error (MAPE) and Error Range for the Four Activity Monitors Tested Irrespective of Footwear Type

	Withings ™		Garmin ™		NL-2000 ™		Fitbit ™	
	MAPE	Error Range	MAPE	Error Range	MAPE	Error Range	MAPE	Error Range
Natural Lawn Grass	1.70	-6.34 to 15.96	3.99	-16.41 to 14.09	3.68	-25.95 to 7.41	1.24	-11.99 to 2.99
Gravel	1.81	-17.89 to 9.01	4.55	-16.29 to 11.67	2.83	-42.59 to 8.96	0.69	-1.68 to 4.70
Linoleum	1.32	-6.51 to 5.61	3.15	-9.54 to 7.65	4.17	-49.13 to 5.16	1.34	-7.78 to 7.20
Tarmacadam/ Asphalt	2.40	-23.58 to 3.05	4.66	-33.67 to 3.57	1.28	-6.84 to 3.13	3.26	-37.59 to 19.04
Ceramic Tile	3.20	-22.20 to 0.22	**5.43**	-16.89 to 13.23	**7.66**	-63.43 to 0.00	1.06	-1.04 to 7.02
Ramp	3.52	-29.69 to 22.53	4.10	-13.98 to 16.13	3.08	-13.76 to 22.00	2.18	-15.76 to 24.55
Stairs Up	**6.64**	-22.94 to 79.41	**11.33**	-14.29 to 80.88	**8.65**	- 47.71 to 2.86	2.93	-20.69 to 8.62
Stairs Down	**5.93**	-47.46 to 2.61	**6.48**	-10.53 to 5.58	4.43	-25.62 to 5.45	**6.03**	-16.36 to 99.16
Total Step Count	1.36	-9.55 to 3.42	4.61	-21.73 to 9.46	2.82	-18.61 to 3.13	1.44	-8.01 to 3.89

Eight mean absolute percentage errors were found to be outside of our selected 5% error zone (in bold): the Withings Smart Activity Monitor Tracker (Pulse O_2) ™ step count error on the stairs down and stairs up sections, the Garmin ™ step count error on the ceramic tile and stairs up and stairs down sections, NL-2000 pedometer ™ step count error on the ceramic tile and stairs up sections, and the Fitbit ™ step count error on the stairs down section of the walking route. The error range shows the variation in percentage error for each activity monitor over each surface type.

Table 4.4 Mean Absolute Percentage Error (MAPE) and Error Range for the Four Activity Monitors Tested: All Values ± 2SD from the Mean Observed Step Count Excluded

	Withings ™		Garmin ™		NL-2000 ™		Fitbit ™	
	MAPE	Error Range	MAPE	Error Range	MAPE	Error Range	MAPE	Error Range
Natural Lawn Grass	1.21	-6.34 to 7.47	2.18	-14.31 to 5.19	2.23	-14.40 to 7.41	1.24	-11.99 to 2.99
Gravel	1.25	-5.88 to 9.01	2.75	-10.06 to 11.67	1.46	-7.17 to 8.96	0.69	-1.68 to 4.70
Linoleum	1.32	-6.51 to 5.61	3.15	-9.54 to 7.65	2.02	-8.07 to 5.16	1.34	-7.78 to 7.20
Tarmacadam/ Asphalt	1.67	-6.91 to 3.05	3.10	-14.45 to 3.57	1.28	-6.84 to 3.13	2.07	-8.33 to 19.04
Ceramic Tile	0.82	-1.46 to 0.22	1.36	-0.64 to 6.41	0.69	-1.60 to 0	1.06	-1.04 to 7.02
Ramp	1.91	-4.04 to 10.99	2.96	-13.98 to 7.28	2.43	-13.76 to 6.99	0.90	-4.36 to 4.11
Stairs Up	3.46	-13.04 to 14.02	**6.59**	-14.29 to 16.22	2.65	-8.04 to 2.86	2.32	-9.09 to 8.62
Stairs Down	2.20	-7.29 to 2.61	**5.03**	-7.27 to 5.88	1.91	-6.25 to 5.45	2.10	-7.14 to 1.65
Total Step Count	1.36	-9.55 to 3.42	4.58	-21.73 to 9.46	2.82	-18.61 to 3.13	1.44	-8.01 to 3.89

With all values lying ± 2SD from the mean observed step count removed, only two mean absolute percentage errors were found to be outside of our selected 5% error zone (in bold): both for the Garmin ™ device, on the stairs up and stairs down sections. The error range shows the variation in percentage error for each activity monitor over each surface type.

Bland-Altman plots for the number of steps showed average ± limits of agreement underestimation of 84±238, 44±735, 75±235, 35±232, and 254±488 for the Withings ™, Garmin ™, Fitbit ™, ActivPAL ™, and NL-2000 ™ activity monitors respectively (Figure 4.4).

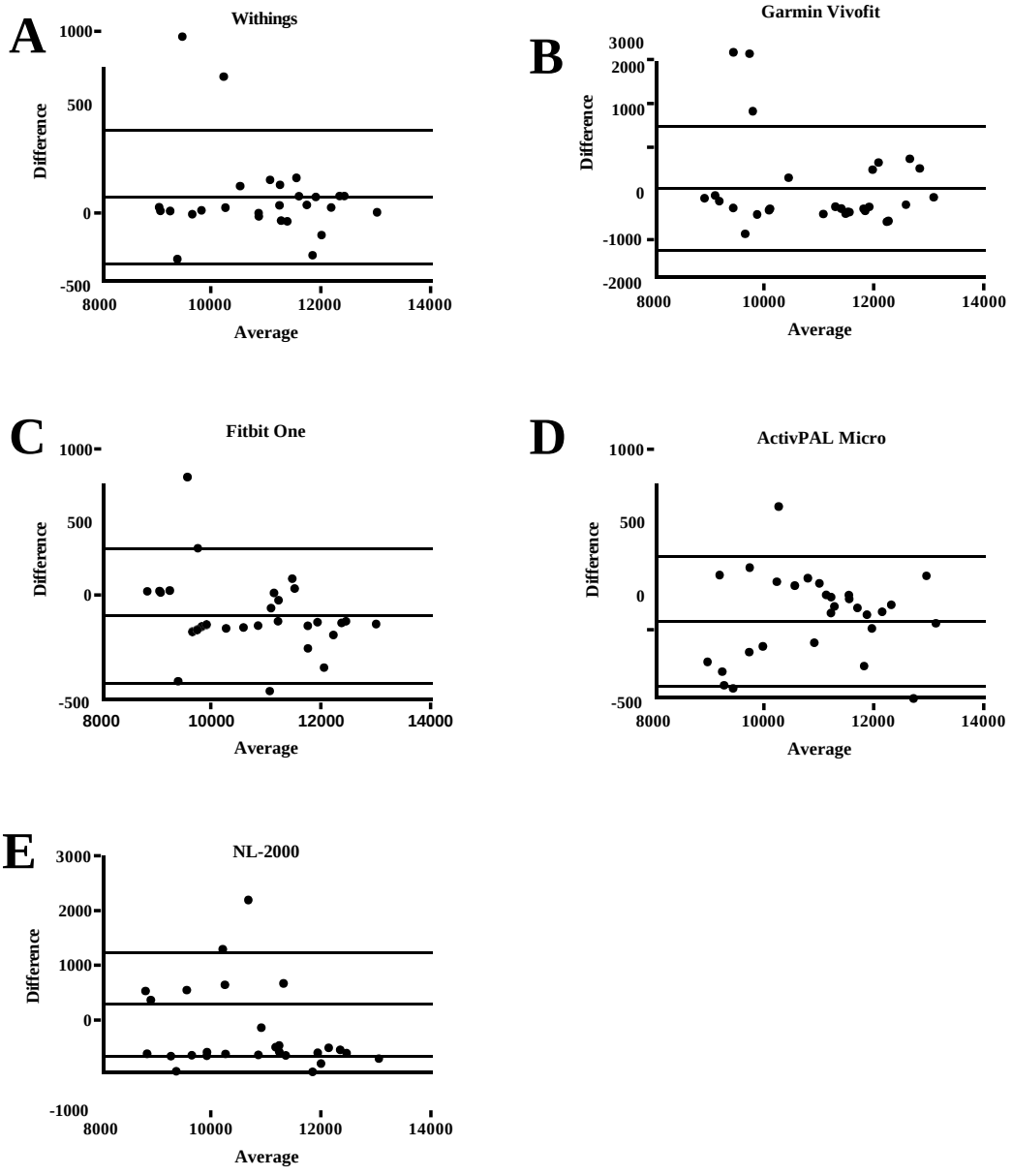

Figure 4.4 Bland Altman plots for step counts of the A. Withings ™, B. Garmin ™, C. Fitbit ™, D. ActivPAL ™, and E. NL-2000 ™ activity monitors. The solid line represents the mean step count difference between the step count observed from the video recordings and each activity monitor for the overall step count. The dashed lines indicate mean ± limits of agreement (1.96*SD).

Footwear type did not affect step detection of any activity monitor; there was no statistically significant difference in step count between the observed count and any activity monitor ($P > 0.05$ for all).

Participants took a median time of 4 hours and 4 minutes to complete the entire walking route. Seven participants were classed as being walkers of a ‘fast’ speed as they completed the walking route in a time of between 2 hours and 6 minutes and 3 hours and 2 minutes, a gap of 1 hour and 2 minutes from the median walking time. Eight participants were classed as being walkers of a ‘medium to slow’ speed as they completed the walking route in a time between the median time (4 hours and 4 minutes) and 4 hours and 38 minutes. There was a statistically significant difference in step count between the ‘medium to slow’ speed walkers and ‘fast’ speed walkers, with the ‘medium to slow’ speed walkers taking a greater number of steps ($P = 0.002$). Additionally, the mean walking speed for the ‘fast’ walkers was 0.84m/s compared to 0.74m/s for the ‘medium to slow’ speed walkers, a statistically significant difference ($P = 0.031$).

4.5 Discussion

This study assessed four commercial activity monitors: the Withings Smart Activity Monitor Tracker (Pulse O_2) ™, NL-2000 pedometer ™, Garmin Vivofit ™, and Fitbit One ™ for their step count detection accuracy over a prescribed walking route that reflected a range of surfaces that would typically be encountered to achieve the recommended daily step count and in a timeframe required to do so. In addition, we investigated two different types of footwear typically used throughout the day when aiming to achieve the recommended daily step count of 10,000 steps.

As stated by the WHO, physical activity includes a variety of activities, such as recreational or leisure-time physical activity, occupational (i.e. work), household chores, and transportation (e.g. walking or cycling) [5]. As such, the recommended daily step count of 10,000 steps would typically be achieved over a variety of different surfaces. Taking this into consideration, we tested a prescribed walking route consisting of various surfaces that would be encountered on a daily basis, namely linoleum, natural lawn grass, gravel, tarmacadam/asphalt, and ceramic tile surfaces. All activity monitors were found to be accurate in step detection, irrespective of surface type. This is an important finding as step count is one of the main parameters utilised in physical activity quantification. It is vital that persons changing their behaviour to adhere to public health physical activity recommendations can be confident in the sensitivity of the activity monitors they are employing to achieve their physical activity goals and reach the recommended daily step count of 10,000 steps. Additionally, our results correspond with those obtained by Brown et al when they investigated the accuracy of the *ActiPed* ™ activity monitor over two different surface types, namely grass and concrete. Participants walked 1,010m on grass and 1,070m on concrete, with the authors finding the *ActiPed* ™ to be accurate in step count detection regardless of surface type [36].

When considering step counts, as opposed to surface type, participants in our study exceeded the recommended daily step count of 10,000 steps, taking an average of 10,950 steps to complete the prescribed walking route. Over the course of the entire walking route, independent of surface type, all activity monitors were found to be

sensitive in their step detection accuracy, on both flat surfaces and stairs walking. Indeed, it is important to consider the effect of stairs walking, which is an activity of daily living and part of the normal daily step count goal for many adults. We observed similar results to those obtained by Storm et al, who investigated the sensitivity of both the ActivPAL ™ and Movemonitor ™ activity monitors during stairs walking at a self-selected walking speed, finding both activity monitors to be accurate in step detection [19]. Accuracy is an important factor to consider when the quantification of physical activity is paramount, such as when physical activity may be prescribed as an intervention in the treatment or prevention of a disease state. Sensitivity in this case is the probability that a step will be detected when a step is actually performed and a measure of all true positives (TP; i.e. a step was performed and it was detected) divided by the true positive (TP) plus the false negatives (FN; i.e. a step was performed but not detected). Due to the nature of the data output from the activity monitors, calculating FN is not possible thus we presented the MAPE as a valid measure of accuracy.

When we investigated the effect of two different types of footwear: running shoes and hard-soled dress shoes, on the sensitivity of the activity monitors, we found no effect on step detection sensitivity. To the best of our knowledge, this is the first study to assess the effects of footwear on the step detection sensitivity of activity monitors and is an important and positive finding, as activities carried out to achieve the recommended step count of 10,000 will most likely be done in various different types of footwear. However, we only investigated two different types of footwear. It would also be of interest to investigate other types of footwear that would often be worn on a daily basis when accumulating the recommended daily step count of 10,000 steps. Examples include slippers, flip-flops, high-heeled shoes, and hiking boots. These different types of footwear differ in terms of their sole type, degree of foot contact with the ground/floor, and the way in which they are worn, i.e. loose fitting or tight fitting on the foot, all of which may play a role in the step detection sensitivity of activity monitors.

The authors do recognise that limitations exist with our study, namely we have tested the accuracy of four commercial activity monitors but have not evaluated their specificity. For example, it is also of vital importance to validate activity monitors

during a variety of activities of daily living that do not involve direct stepping, such as driving, cycling, and swimming. Furthermore, acceleration signals recorded by activity monitors can differ depending on the location of attachment [37]. Thus, the attachment location for each activity monitor is important to consider. In this study, we assessed each activity monitor in only one location. However, we specifically chose attachment locations for each activity monitor that was specified by the manufacturers.

Additionally, it is important to consider walking speed when evaluating the sensitivity of activity monitors. Slow walking speeds, for example, have been shown to reduce the sensitivity of some activity monitors [18, 27, 38-40]. In this study, we evaluated different distributions of walking speeds within the normal walking self-selected walking speeds and found a greater speed and lesser number of steps in the 'fast' speed walkers. However, evaluation on a range of specific walking speeds, such as on a treadmill, would be of benefit to further elucidate the effect of walking speed on activity monitor step detection sensitivity.

4.5.1 Conclusions

Our study provides a comprehensive evaluation of four commercial activity monitors when (i) walking on different surfaces that reflect the range of surfaces that will typically be used to achieve the daily step count goal, (ii) walking with different footwear that reflects the different types of footwear expected to be used throughout the day, and (iii) walking for periods of time that properly reflect the time required to achieve the recommended daily step count. All activity monitors tested were accurate in their step detection sensitivity and are valid monitors for physical activity quantification over the variety of different flat surfaces tested and when stairs and ramp walking, when wearing both running shoes and hard-soled dress shoes, and over a timeframe necessary for accumulating the recommended daily step count of 10,000 steps. It is important to consider accuracy for activity monitors, particularly when physical activity in the form of stepping activities is prescribed as an intervention in the treatment or prevention of a disease state. All aspects of daily physical activity that go towards achieving the daily recommended step count of 10,000 steps are necessary to consider in accurate physical activity quantification.

4.6 References

[1] Karmisholt, K. and Gotzsche, P., "Physical activity for secondary prevention of disease. Systematic reviews of randomised clinical trials," *Dan Med Bull,* vol. 52, no. 2, pp. 90-4, May 2005.

[2] Penedo, F. and Dahn, J., "Exercise and well-being: a review of mental and physical health benefits associated with physical activity," *Curr Opin Psychiatry,* vol. 18, no. 2, pp. 189-93, Mar 2005.

[3] Nunan, D., Mahtani, K., Roberts, N., and Heneghan, C., "Physical activity for the prevention and treatment of major chronic disease: an overview of systematic reviews," *Syst Rev,* vol. 2, p. 56, 2013.

[4] Young, D. *et al.*, "Effects of physical activity and sedentary time on the risk of heart failure," *Circ Heart Fail,* vol. 7, no. 1, pp. 21-7, Jan 2014.

[5] World Health Organization. Global Recommendations on Physical Activity for Health. 2010. Available from: http://whqlibdoc.who.int/publications/2010/9789241599979_eng.pdf?ua=1

[6] U.S. Department of Health and Human Services. Physical activity and health: a report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996. Available from: http://www.cdc.gov/nccdphp/sgr/chapcon.htm

[7] Centers for Disease Control. "2008 Physical Activity Guidelines for Americans." U.S. Department of Health and Human Services. Available from: http://www.health.gov/paguidelines/guidelines/summary.aspx

[8] Tudor-Locke, C. and Bassett, D. R., Jr., "How many steps/day are enough? Preliminary pedometer indices for public health," *Sports Med,* vol. 34, no. 1, pp. 1-8, 2004.

[9] Tudor-Locke, C., Leonardi, C., Johnson, W. D., Katzmarzyk, P. T., and Church, T. S., "Accelerometer steps/day translation of moderate-to-vigorous activity," *Prev Med,* vol. 53, no. 1-2, pp. 31-3, Jul-Aug 2011.

[10] Kang, M., Marshall, S. J., Barreira, T. V., and Lee, J. O., "Effect of pedometer-based physical activity interventions: a meta-analysis," *Res Q Exerc Sport,* vol. 80, no. 3, pp. 648-55, Sep 2009.

[11] Tudor-Locke, C., Hatano, Y., Pangrazi, R. P., and Kang, M., "Revisiting "how many steps are enough?" *Med Sci Sports Exerc,* vol. 40, no. 7 Suppl, pp. S537-43, Jul 2008.

[12] Harrington, D. M. *et al.*, "Step-based translation of physical activity guidelines in the Lower Mississippi Delta," *Appl Physiol Nutr Metab,* vol. 36, no. 4, pp. 583-5, Aug 2011.

[13] Leicht, A. S. and Crowther, R. G., "Pedometer accuracy during walking over different surfaces," *Med Sci Sports Exerc,* vol. 39, no. 10, pp. 1847-50, Oct 2007.

[14] Fitbit [Internet]. "How does my tracker count steps?" Available from: https://help.fitbit.com/articles/en_US/Help_article/How-does-my-tracker-count-steps

[15] New Lifestyles [Internet]. "NL-2000 pedometer User's Guide. Available from: http://www.thepedometercompany.com/instructions.html

[16] Dahlgren, G., Carlsson, D., Moorhead, A., Hager-Ross, C., and McDonough, S. M., "Test-retest reliability of step counts with the ActivPAL device in common daily activities," *Gait Posture,* vol. 32, no. 3, pp. 386-90, Jul 2010.

[17] Dondzila, C. J., Swartz, A. M., Miller, N. E., Lenz, E. K., and Strath, S. J., "Accuracy of uploadable pedometers in laboratory, overground, and free-living conditions in young and older adults," *Int J Behav Nutr Phys Act,* vol. 9, p. 143, 2012.

[18] Giannakidou, D. M. *et al.*, "The validity of two Omron pedometers during treadmill walking is speed dependent," *Eur J Appl Physiol,* vol. 112, no. 1, pp. 49-57, Jan 2012.

[19] Storm, F. A., Heller, B. W., and Mazza, C., "Step detection and activity recognition accuracy of seven physical activity monitors," *PLoS One,* vol. 10, no. 3, p. e0118723, 2015.

[20] Takacs, J., Pollock, C. L., Guenther, J. R., Bahar, M., Napier, C., and Hunt, M. A., "Validation of the Fitbit One activity monitor device during treadmill walking," *J Sci Med Sport,* vol. 17, no. 5, pp. 496-500, Sep 2014.

[21] Taraldsen, K. *et al.*, "Evaluation of a body-worn sensor system to measure physical activity in older people with impaired function," *Phys Ther,* vol. 91, no. 2, pp. 277-85, Feb 2011.

[22] Ryan, C. G., Grant, P. M., Tigbe, W. W., and Granat, M. H., "The validity and reliability of a novel activity monitor as a measure of walking," *Br J Sports Med,* vol. 40, no. 9, pp. 779-84, Sep 2006.

[23] Godfrey, A., Culhane, K. M., and Lyons, G. M., "Comparison of the performance of the activPAL Professional physical activity logger to a discrete accelerometer-based activity monitor," *Med Eng Phys,* vol. 29, no. 8, pp. 930-4, Oct 2007.

[24] Maddocks, M., Petrou, A., Skipper, L., and Wilcock, A., "Validity of three accelerometers during treadmill walking and motor vehicle travel," *Br J Sports Med,* vol. 44, no. 8, pp. 606-8, Jun 2010.

[25] Grant, P. M., Dall, P. M., Mitchell, S. L., and Granat, M. H., "Activity-monitor accuracy in measuring step number and cadence in community-dwelling older adults," *J Aging Phys Act,* vol. 16, no. 2, pp. 201-14, Apr 2008.

[26] Busse, M. E., van Deursen, R. W., and Wiles, C. M., "Real-life step and activity measurement: reliability and validity," *J Med Eng Technol,* vol. 33, no. 1, pp. 33-41, 2009.

[27] Harrington, D. M., Welk, G. J., and Donnelly, A. E., "Validation of MET estimates and step measurement using the ActivPAL physical activity logger," *J Sports Sci,* vol. 29, no. 6, pp. 627-33, Mar 2011.

[28] Ferguson, T., Rowlands, A. V., Olds, T., and Maher, C., "The validity of consumer-level, activity monitors in healthy adults worn in free-living conditions: a cross-sectional study," *Int J Behav Nutr Phys Act,* vol. 12, p. 42, 2015.

[29] Klassen, T. D. *et al.,* ""Stepping Up" Activity Poststroke: Ankle-Positioned Accelerometer Can Accurately Record Steps During Slow Walking," *Phys Ther,* Aug 6 2015.

[30] Simpson, L. A. *et al.,* "Capturing step counts at slow walking speeds in older adults: Comparison of ankle and waist placement of measuring device," *J Rehabil Med,* Jul 15 2015.

[31] Diaz, K. M. *et al.,* "Fitbit(R): An accurate and reliable device for wireless physical activity tracking," *Int J Cardiol,* vol. 185, pp. 138-40, Apr 15 2015.

[32] Lee, J. M., Kim, Y., and Welk, G. J., "Validity of consumer-based physical activity monitors," *Med Sci Sports Exerc*, vol. 46, no. 9, pp. 1840-8, Sep 2014.

[33] Crouter, S. E., Schneider, P. L., Karabulut, M., and Bassett, D. R., Jr., "Validity of 10 electronic pedometers for measuring steps, distance, and energy cost," *Med Sci Sports Exerc*, vol. 35, no. 8, pp. 1455-60, Aug 2003.

[34] Schneider, P. L., Crouter, S. E., Lukajic, O., and Bassett, D. R., Jr., "Accuracy and reliability of 10 pedometers for measuring steps over a 400-m walk," *Med Sci Sports Exerc*, vol. 35, no. 10, pp. 1779-84, Oct 2003.

[35] Schneider, P. L., Crouter, S., and Bassett, D. R., "Pedometer measures of free-living physical activity: comparison of 13 models," *Med Sci Sports Exerc*, vol. 36, no. 2, pp. 331-5, Feb 2004.

[36] Brown, D. K., Grimwade, D., Martinez-Bussion, D., Taylor, M. J., and Gladwell, V. F., "The validity of the ActiPed for physical activity monitoring," *Int J Sports Med*, vol. 34, no. 5, pp. 431-7, May 2013.

[37] Murphy, S. L., "Review of physical activity measurement using accelerometers in older adults: considerations for research design and conduct," *Prev Med*, vol. 48, no. 2, pp. 108-14, Feb 2009.

[38] Cyarto, E. V., Myers, A., and Tudor-Locke, C., "Pedometer accuracy in nursing home and community-dwelling older adults," *Med Sci Sports Exerc*, vol. 36, no. 2, pp. 205-9, Feb 2004.

[39] Johnson, M., Meltz, K., Hart, K., Schmudlach, M., Clarkson, L., and Borman, K., "Validity of the Actical activity monitor for assessing steps and energy expenditure during walking," *J Sports Sci*, vol. 33, no. 8, pp. 769-76, 2015.

[40] Stansfield, B., Hajarnis, M., and Sudarshan, R., "Characteristics of very slow stepping in healthy adults and validity of the activPAL3 activity monitor in detecting these steps," *Med Eng Phys*, vol. 37, no. 1, pp. 42-7, Jan 2015.

Chapter 5

When a Step is not a Step!
Specificity Analysis of Five Physical Activity Monitors

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Background

Physical activity is an important aspect of a healthy lifestyle and valuable outcome following lower limb orthopaedic surgery as a measure of functional recovery. The accurate quantification of physical activity is of the utmost importance, especially when prescribed as an intervention for improving functional recovery and in the treatment or prevention of a disease state, such as following TKA. When utilising activity monitors to quantify physical activity levels post-TKA, both the sensitivity and specificity of the monitors come into question. Chapter 4 was carried out to comprehensively assess the sensitivity of a number of commercial activity monitors that have the potential to be utilised by TKA patients. The monitors tested, the Garmin Vivofit™, Withings™, Fitbit™, NL-2000™ and ActivPAL™ activity monitors, were evaluated over different surface types and utilising different footwear types while achieving the recommended daily step count of 10,000 steps. Under these conditions, all monitors tested were found to be sensitive in their step detection and could be considered as potential monitors for physical activity quantification in TKA patients post-surgery.

While this is a very promising finding, before choosing an activity monitor to accurately quantify physical activity levels in TKA patients, it is also essential to evaluate their specificity, i.e. their ability to distinguish stepping from non-stepping activities and to disregard non- stepping movements. Continuing on from the work carried out in Chapter 4, the aim of Chapter 5 was to focus on specificity and further evaluate a number of physical activity monitors during a range of non-stepping physical activities.

Contribution to work

Study design: Sandra O'Connell, Gearoid ÓLaighin, Leo Quinlan.

Data collection:

- Subject consent: Sandra O'Connell.
- Subject testing: Sandra O'Connell.

Data Analysis: Sandra O'Connell.

Interpretation of results: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

Drafting of manuscript: Sandra O'Connell.

Critical review of manuscript: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

5.1 Abstract

Introduction: Physical activity is an essential aspect of a healthy lifestyle for both physical and mental health states. As step count is one of the most utilised measures for quantifying physical activity it is important that activity-monitoring devices be both sensitive and specific in recording actual steps taken and disregard non-stepping body movements. The objective of this study was to assess the specificity of five activity monitors during a variety of prescribed non-stepping activities.
Methods: Participants wore five activity monitors simultaneously for a variety of prescribed activities including deskwork, taking an elevator, taking a bus journey, automobile driving, washing and drying dishes; functional reaching task; indoor cycling; outdoor cycling; and indoor rowing. Each task was carried out for either a specific duration of time or over a specific distance. Activity monitors tested were the ActivPAL micro™, NL-2000™ pedometer, Withings Smart Activity Monitor Tracker (Pulse O_2)™, Fitbit One™ and Jawbone UP™. Participants were video-recorded while carrying out the prescribed activities and the false positive step count registered on each activity monitor was obtained and compared to the video.
Results: All activity monitors registered a significant number of false positive steps per minute during one or more of the prescribed activities. The Withings™ activity monitor performed best, registering a significant number of false positive steps per minute during the outdoor cycling activity only ($P = 0.025$). The Jawbone™ registered a significant number of false positive steps during the functional reaching task and while washing and drying dishes, which involved arm and hand movement ($P < 0.01$ for both). The ActivPAL™ registered a significant number of false positive steps during the cycling exercises ($P < 0.001$ for both).
Conclusion: As a number of false positive steps were registered on the activity monitors during the non-stepping activities, the authors conclude that non-stepping physical activities can result in the false detection of steps. This can negatively affect the quantification of physical activity with regard to step count as an output. The Withings™ activity monitor performed best with regard to specificity during the activities of daily living tested.

5.2 Introduction

The benefits to general health of physical activity are universally recognised [1-3]. Clear guidelines have been published by the US Surgeon General (1996), the Centers for Disease Control (CDC, 2008) and the World Health Organization (WHO, 2010). To maximise the health benefits of physical activity for the general population, these guidelines recommend that activities, such as brisk walking, be carried out daily [4-6]. An essential part of achieving a behavioural change in promoting physical activity is the capacity to easily monitor goal setting. The use of physical activity monitors has exploded in the last 5 years, both in the consumer market and increasingly as tools for clinical settings [7-9]. The most commonly utilised output parameter from these monitors is the cumulative step count over a day, week and beyond. In line with the WHO recommendations, many individuals aim to improve on their physical activity levels by reaching a personal goal or the recommended goal of 10,000 steps per day [4-6]. Utilising an easily quantifiable output such as step count supports a person in achieving physical activity goals and maintaining a healthy lifestyle [10, 11]. Cumulative logging of step count can become a key factor in the promotion and maintenance of physical activity levels and mental wellbeing. As persons become increasingly dependent on the activity monitor to unobtrusively record their activity level, the question of the device's sensitivity and specificity to the reported output becomes an increasingly important one.

We have previously examined the step count sensitivity of a number of physical activity-monitoring devices during walking over a variety of surface types while achieving the recommended daily step goal of 10,000 steps. We found all devices tested to be sensitive in step detection, with a mean absolute percentage error ranging from 1.36% to 4.61% for the four activity monitors tested [12]. However, while this is a very important factor to consider in assessing the performance of an activity monitor, it is equally critical that the activity-monitors are not just sensitive but also specific in their capacity to monitor actual steps performed. The ideal activity monitor should only record a step when a step is actually taken, while disregarding non-stepping body movements.

The literature is sparse when reporting on the specificity of physical activity monitors examined. Chen et al (2016) investigated three consumer wristband activity monitors; Fitbit Flex, Garmin Vivofit and Jawbone UP during a range of normal daily activities, including playing a tablet computer game, folding laundry, pushing a stroller and carrying a bag [13]. They reported substantial false step detection events during the task of folding laundry and reported the accuracy under each activity to range widely both between monitors and activities performed [13]. In a similar study, Sellers et al (2016) investigated the ActivPAL3 monitor during a range of activities of daily living [14]. These activities included hanging laundry out to dry, putting on a duvet cover and pillowcase, cleaning a framed picture, writing a letter/list and vacuuming. The authors reported step detection sensitivity of 76.1% for young people but only 40.4% for older adults during normal activities of daily living. While they reported the ActivPAL3 to accurately detect 'purposeful stepping', the detection of smaller stepping movements during the activities of daily living was reported as being poor [14]. These studies reveal a significant degree of variability in the step detection specificity during activities that are not solely purposeful stepping activities like walking. Normal activities of daily living include a range of stepping and non-stepping activities and also range from low to high levels of intensity. As step count is now a pervasive and easily understandable measure of physical activity it is essential that monitors be both sensitive and specific in their measures.

The aim of this paper is to assess five activity monitors in healthy adults: the Jawbone UP™, Withings Smart Activity Monitor Tracker (Pulse O_2) ™, NL-2000 pedometer™, ActivPAL micro™ and Fitbit One™ for their step detection specificity over a range of different physical activities that mimic typical activities of daily living of various intensity levels.

5.3 Methods

5.3.1 Participants

A pool of 37 participants (12 male) took part in the study involving the performance of 9 prescribed activities which may trigger false detection of stepping: (i) deskwork, (ii) taking an elevator, (iii) taking a bus journey, (iv) driving an automobile, (v) washing and drying dishes, (vi) functional reaching task, (vii) indoor cycling, (viii) outdoor cycling and (iv) indoor rowing. Participants had a mean age of 39 ± 13.87 years and a mean body mass index (BMI) of 25 ± 3.79 kg/m^2. A random sample of ten participants carried out each activity. The mean ages and BMIs of the ten participants that carried out each activity are given in Table 5.1. None of the participants had any history of cardiovascular disease or neurological disorders. Ethics committee approval (reference number CA-1069) was obtained from the Galway University Hospitals Research Ethics Committee for this study and all participants provided written, informed consent.

Table 5.1 Demographic Details for the Ten Participants that Carried out Each Specificity Activity

Specificity Activity	Gender	Age (years)	Weight (kg)	BMI (kg/m^2)
Deskwork	6 female; 4 male	33 ± 11.15	71.28 ± 14.07	24.62 ± 3.96
Elevator	9 female; 1 male	35 ± 14.11	68.40 ± 12.08	24.41 ± 3.98
Bus journey	8 female; 2 male	38 ± 13.91	65.90 ± 13.93	24.09 ± 5.08
Automobile driving	7 female; 3 male	43 ± 14.98	71.06 ± 12.79	25.10 ± 4.88
Washing and drying dishes	9 female; 1 male	32 ± 12.5	63.90 ± 8.52	23.25 ± 3.43
Functional reaching task	9 female; 1 male	32 ± 12.63	66.40 ± 9.25	24.05 ± 3.39
Indoor cycling	9 female; 1 male	32 ± 12.63	64.10 ± 10.72	23.22 ± 3.42
Outdoor cycling	8 female; 2 male	29 ± 8.68	65.56 ± 10.13	23.92 ± 3.08
Indoor Rowing	7 female; 3 male	48 ± 10.61	71.28 ± 13.55	23.86 ± 3.11

All values represent mean ± SD. BMI = Body Mass Index; SD = Standard Deviation.

5.3.2 Study Protocol

All activity monitors were positioned as per manufacturer's recommended body locations (Figure 5.1). Tegaderm transparent dressing (3M Health Care, Minnesota, USA) was used to affix the ActivPAL ™ to the mid-anterior aspect of the thigh, with the Jawbone UP ™ worn on the wrist, the Withings Smart Activity Monitor Tracker (Pulse O_2) ™ and NL-2000 pedometer ™ worn on opposite hips and the Fitbit One™ clipped on at the level of the chest.

Figure 5.1 Positioning of each activity monitor. The ActivPAL™ is worn on the right thigh, the NL-2000™ on the left hip, the Withings™ on the right hip, the Jawbone™ on the right wrist and the Fitbit™ at the level of the chest.

The ActivPAL micro™ device was chosen for use in this study as it is one of the most widely utilised research-grade activity monitors in physical activity research. The ActivPAL ™ has been utilised extensively across all age groups and in both healthy and patient groups. The NL-2000 pedometer ™ was chosen as this device is a popular pedometer shown to be accurate in step detection. The Withings Smart Activity Monitor Tracker (Pulse O_2) ™, Jawbone UP ™ and Fitbit One ™ monitors were chosen based upon their popularity and reasonable price range.

Participants wore the activity monitors simultaneously for the duration of each test condition. For the NL-2000™, Withings™ and Fitbit™ monitors the recorded step count was obtained directly from the device screen interface. To extract the step count data from the Jawbone™, it was synced to a smartphone via Bluetooth and step count was obtained from the Jawbone™ smartphone application. To extract the step count data from the ActivPAL™, it was manually connected to a PC and the data downloaded using the ActivPAL™ software program, which outputs the step count data.

To ensure the step count was accurate for the activity only, and not contaminated by activity just before or after the prescribed activity, specific procedures were put in place for each monitor. For the NL-2000™, Withings™ and Fitbit™ monitors, the step counts displayed on the device interfaces were noted immediately before and immediately after each activity. For the Jawbone™, it was synced both immediately before and immediately after each individual activity. The ActivPAL™ device was programmed before each individual activity, a procedure that cleared all previous data. Additionally, to prevent capturing data pre- or post-activity, all participants were instructed to be/stand still before commencing the activity and to be/stand still once the activity was completed. Participants were also video-recorded with a hand-held camcorder during each activity excepting automobile driving and the bus journey when participants were seated for the duration of testing. The timing for each activity, excepting the automobile driving and bus journey, was started at the same time as the video began recording. The step count obtained from each activity monitor was compared to the step count obtained from the recorded video.

5.3.3 Prescribed Activities

Nine typical activities of daily living were prescribed and preformed in a controlled and monitored way. Activities were grouped into three classes, as passive non- stepping activities (deskwork, elevator, bus journey, automobile driving), moderate non-stepping activities (washing and drying dishes, functional reaching task) or active non-stepping activities (indoor cycling, outdoor cycling, indoor rowing).

5.3.3.1. Deskwork

Participants sat at a desk doing deskwork for 40 minutes. The majority of this time was spent typing.

5.3.3.2. Elevator

Participants took an elevator ride, up 3 floors and down 3 floors, three times.

5.3.3.3. Bus Journey

Participants took a 3km round trip bus journey while sitting in the middle of the bus. The bus route travelled through a university campus, which featured speed ramps at various intervals.

5.3.3.4. Automobile Driving

Participants drove a manual gear car for a total of ~ 50km. The driving route consisted of driving on a local road (~ 2km, driving in a built-up area), urban road (~ 5km, city centre driving), driving on a category A road (~ 6km, national primary road), driving on a category B road (~ 14km, regional road), driving on a category C road (~ 8km, rural country road) and driving on a motorway (~ 15km).

5.3.3.5. Washing and Drying Dishes

Participants were instructed to wash dishes at a sink while standing still, without taking any steps. Ten pieces of Tupperware were scrubbed three times on the inside and three times on the outside using a dish-washing brush held in the dominant hand. The items were then dried with three strokes on the outside and three strokes on the inside using a dishcloth. This process was repeated continuously for a total of ten minutes.

5.3.3.6. Functional Reaching Task

Participants stacked 10 books taking them individually from the floor and stacking them on a shelf just above eye level. An adjustable shelf was used and adjusted based on the height of each participant to be just above his or her eye level. All participants had a similar reach effort when carrying out this task. When all books were stacked the procedure was reversed and the books were individually returned to the floor. This action was repeated continuously for ten minutes.

5.3.3.7. Indoor Cycling

Participants cycled on a Kettler Cycle Ergometer (Heinz Kettler GmbH & Co., Germany) for a total of 2km at a speed of 15-20km/h set at a comfortable intensity.

5.3.3.8. Outdoor Cycling

Participants cycled a pedal bike at a self-selected easy pace for a total of 2km over a tarmacadam surface at a comfortable intensity.

5.3.3.9. Indoor Rowing

Participants rowed 2km at a low resistance setting at a stroke rate of 20-25 strokes/minute on a Concept 2 rower (Concept2, Inc. Morrisville, Vermont, US).

5.3.4 Statistical Analysis

All statistical analyses were carried out using SPSS (SPSS for Mac, version 22, IBM Corporation). A negative binomial regression analysis was used to model the step count data with follow-up simple comparison (least significant difference) used to detect differences between the reference category (video recordings) and the false positive steps registered by each activity monitor. A false positive (FP) was taken as a step registered by the monitors when no step was actually taken. The video recordings were used as the criterion measure. As a result of the nature of the study, a high number of 0 steps were observed during some activities. In these cases, specifically deskwork and elevator ride, comparisons were made descriptively.

5.4 Results

All monitors tested recorded steps when no steps actually took place (false positives) to a greater or lesser extent depending on the activity being performed. With the exception of the Jawbone™ device, all other monitors generated most false positives during active non-stepping activities (Figure 5.2). The Jawbone™ registered its greatest number of false positives during moderate non-stepping activities.

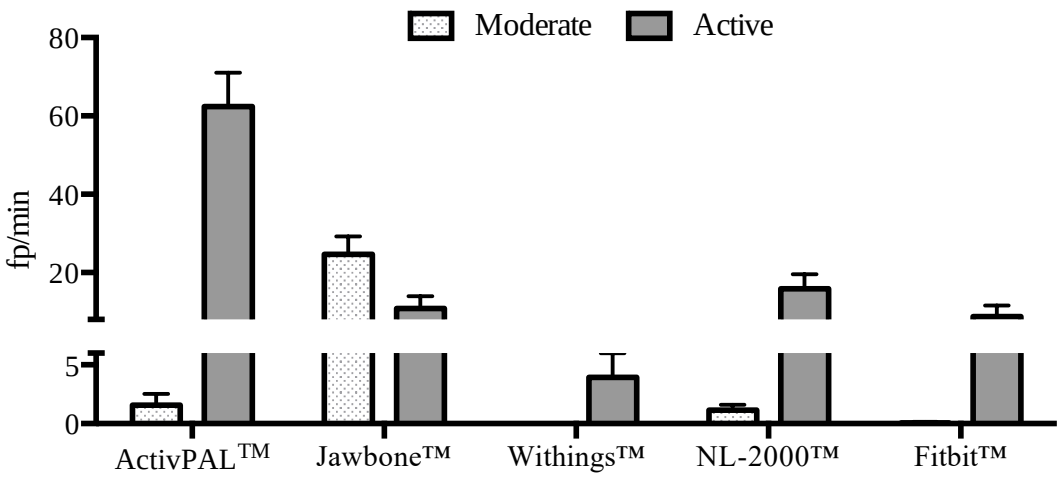

Figure 5.2 Overall specificity (fp/min) of activity monitors during the moderate and active non-stepping activities. Fp/min = false positives per minute. N = 10/activity. Data represents mean ± SEM.

5.4.1 ActivPAL™ Activity Monitor

The ActivPAL™ activity monitor was found to be specific for step detection during all but one of the passive and moderate non-stepping activities (Figures 5.3 and 5.4). For the functional reaching task the ActivPAL™ registered a non-significant number of false positives. The ActivPAL™ correctly (no false positives registered), did not record any steps during the other activities: deskwork, taking an elevator ride, taking a bus journey, automobile driving or washing and drying dishes (Table 5.2). This was also true during the active non-stepping activity of indoor rowing, whereby the ActivPAL™ correctly did not register any false positives. However, the ActivPAL™ was found to be less specific for step detection during the cycling activities. The ActivPAL™ registered 97±12 fp/min during the indoor cycling activity and 90±26 fp/min during the outdoor cycling activity (Figure 5.5).

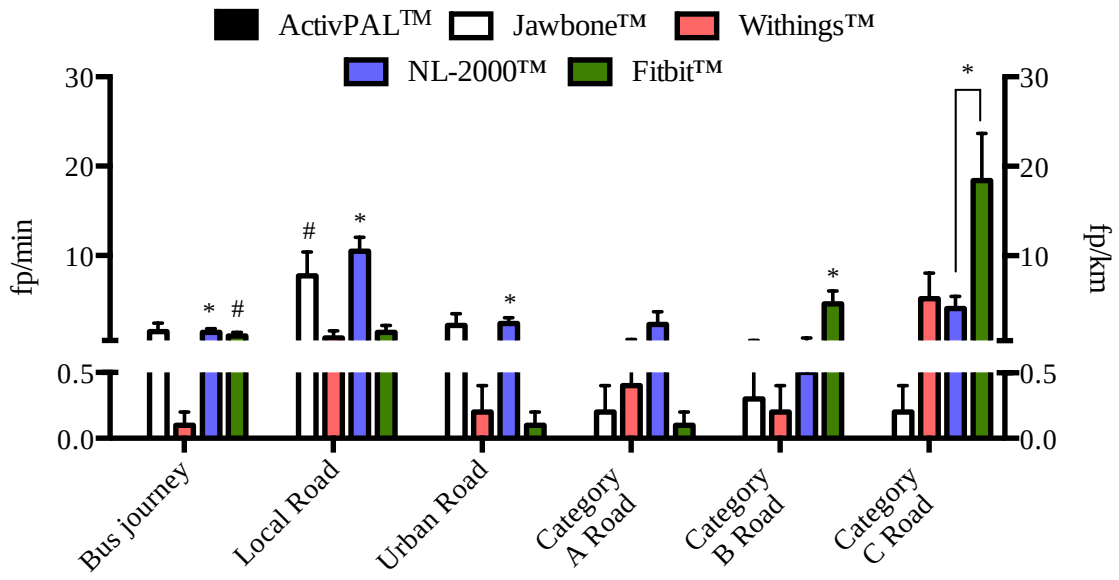

Figure 5.3 Specificity of each activity monitor during the passive non-stepping activities. Data for deskwork, taking an elevator and automobile driving on a motorway have been excluded due to the high number of zero false positives correctly recorded by the devices during these activities. The mean false positives detected during the bus journey are expressed as false positives detected per minute as represented by the left y-axis. The mean false positives detected during the driving activity are expressed as false positives detected per kilometre driven as represented by the right y-axis. * $P \leq 0.001$ vs. zero false positives, # $P < 0.05$ vs. zero false positives. N = 10/activity. Data represents mean ± SEM.

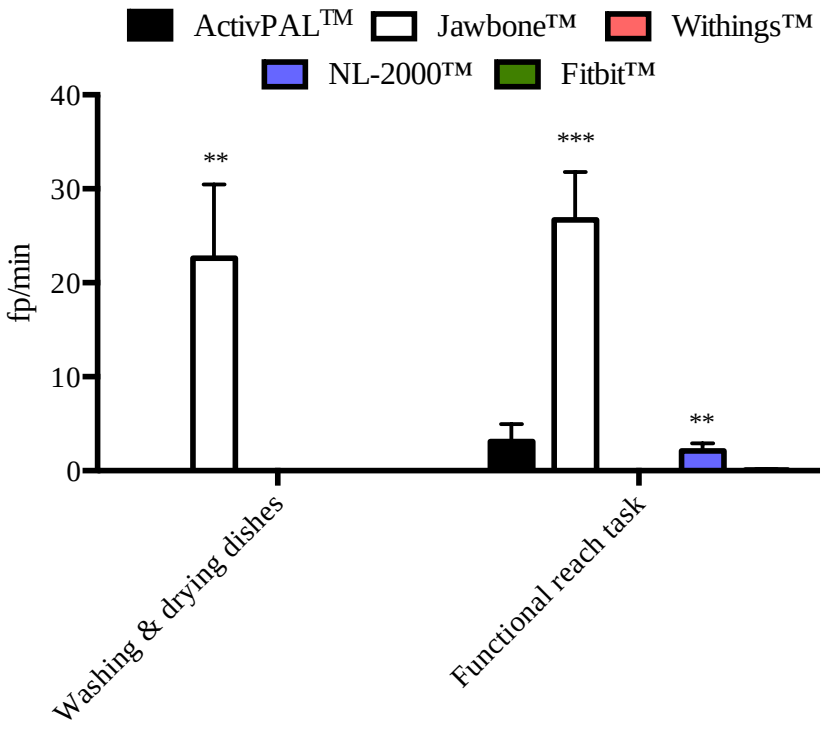

Figure 5.4 Specificity (fp/min) of each activity monitor during the moderate non-stepping activities. While the ActivPAL™ registered a number of fp/min during the functional reaching task, this was found to be non-significant. *** $P < 0.001$ vs. video recording (zero fp/min), ** $P < 0.01$ vs. video recording (zero fp/min). N = 10/activity. Data represents mean ± SEM.

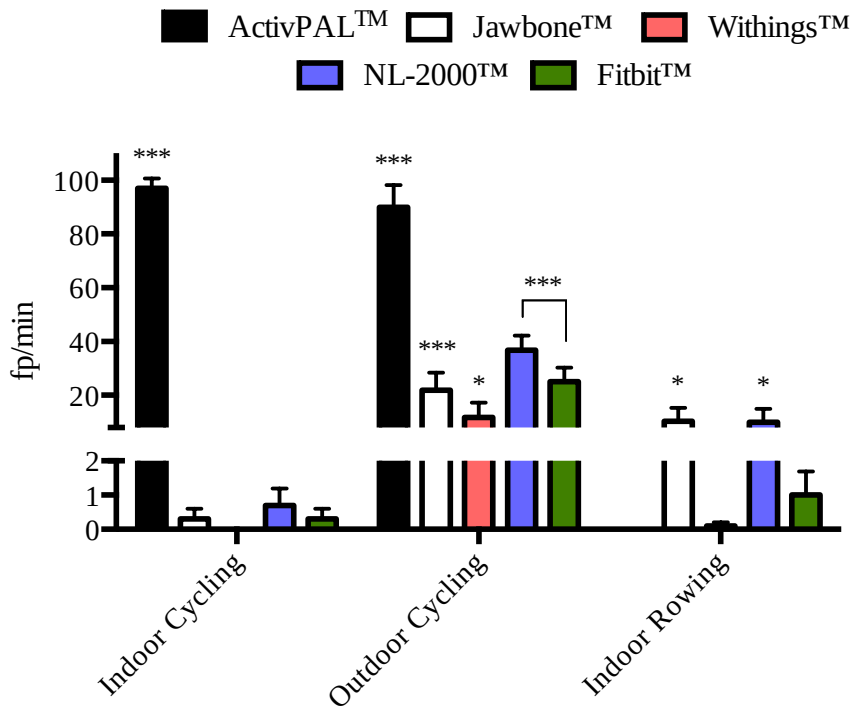

Figure 5.5 Specificity (fp/min) of each activity monitor during the active non-stepping activities. *** P < 0.001 vs. video recording (zero fp/min), * P < 0.05 vs. video recording (zero fp/min). N = 10/activity. Data represents mean ± SEM.

5.4.2 Jawbone™ Activity Monitor

The Jawbone™ activity monitor was found to be specific during the majority of the passive non-stepping activities aside from driving on a local road with the Jawbone™ registering on average 8±8 fp/km. No statistically significant number of fp/km or fp/min was registered on any other road type or during the remaining passive non-stepping activities of deskwork, taking an elevator ride or taking a bus journey (Table 5.2). The Jawbone™ was found to be less specific during the moderate non-stepping activities where 23±25 fp/min were registered while washing and drying dishes and 27±16 fp/min during the functional reaching task (Figure 5.4). Similar results were observed during the active non-stepping activities of outdoor cycling (22±21 fp/min) and indoor rowing (10±16 fp/min) but not during indoor cycling (Figure 5.5).

5.4.3 Withings™ Activity Monitor

Similar to the ActivPAL™ activity monitor, the Withings™ monitor was found to be specific during all passive and moderate non-stepping activities (Figures 5.3 and 5.4). Although a small number of fp/min were registered for a small number of participants during the automobile driving activity, these values did not reach statistical significance (Table 5.2). The Withings™ was also found to be specific during the active non-stepping activities of indoor cycling and indoor rowing, whereby the participants were active, but on a static exercise machine. The Withings™ correctly did not register any steps during these activities. However, this was not true during outdoor cycling. Cycling outside over a standard tarmacadam road surface on a pedal bicycle resulted in the Withings™ registering a significant number of false positives, averaging 12±17 fp/min (Figure 5.5).

5.4.4 NL-2000™ Activity Monitor

While the NL-2000™ activity monitor was found to be specific during the passive non-stepping activities of deskwork and taking an elevator ride, the same results were not observed during the bus journey or while automobile driving. A significant number of false positives were registered during the bus journey and on certain road types during automobile driving. The NL-2000™ registered 10±5 fp/km while driving on a local road, 3±2 fp/km driving on an urban road and 4±4 fp/km driving on a category C road, all of which were statistically significant (Figure 5.3). A number of fp/km were also registered on the NL-2000™ while driving on the category A and B roads but these values did not reach statistical significance (Table 5.2). The NL-2000™ was found to be specific while washing and drying dishes but not during the functional reaching task, where 2±3 fp/min were registered (Figure 5.4). While the NL-2000™ registered very few fp/min during the indoor cycling activity, a significant number of fp/min were registered during the outdoor cycling and indoor rowing activities. An average of 37±17 fp/min were registered during outdoor cycling, with an average of 10±16 fp/min registered during indoor rowing (Figure 5.5).

5.4.5 Fitbit™ Activity Monitor

Similar to the other monitors examined, the Fitbit™ monitor was found to be specific during the deskwork and elevator ride activities, correctly registering zero false positives during these activities (Table 5.2). However, similar to the NL-2000™ monitor, the Fitbit™ registered a significant number of false positives during the bus journey and on certain road types during automobile driving (Figure 5.3). During the automobile driving activity, the Fitbit™ registered 5±5 fp/km while driving on a category B road and 18±17 fp/km while driving on a category C road. However, the Fitbit™ was found to be specific during the moderate non-stepping activities of washing and drying dishes and during the functional reaching task, correctly registering zero false positives (Figure 5.4). This was also observed during the active activities of indoor cycling and indoor rowing, but for a small number of participants where a non-significant number of false positives were registered for each activity. However, the Fitbit™ was found to register false positives during outdoor cycling, registering a significant average of 25±17 fp/min during this activity (Figure 5.5).

Table 5.2 Mean False Positives per Minute for all Activity Monitors During the Non-Stepping Prescribed Activities

	ActivPAL™		**Jawbone™**		**Withings™**		**NL-2000™**		**Fitbit™**	
	FP ± SD	P Value	FP ± SD	P Value	FP ± SD	P Value	FP ± SD	P Value	FP ± SD	P Value
Desk work (min)	0	—	0	—	0	—	0	—	0	—
3rd floor elevator (min)	0	—	1 ± 2	—	0	—	0	—	0	—
Bus journey (min)	0	—	2 ± 3	0.090	0	0.292	1 ± 1	**0.001**	1 ± 1	**0.012**
Automobile driving: Local road (km)	0	—	8 ± 8	**0.002**	1 ± 2	0.292	10 ± 5	< **0.001**	1 ± 3	0.062
Automobile driving: Urban road (km)	0	—	2 ± 4	0.080	0 ± 1	0.292	3 ± 2	< **0.001**	0	0.292
Automobile driving Category A road (km)	0	—	0	0.292	0 ± 1	0.057	2 ± 4	0.088	0	0.292
Automobile driving: Category B road (km)	0	—	0 ± 1	0.138	0 ± 1	0.292	1 ± 1	0.086	5 ± 5	**0.001**
Automobile driving: Category C road (km)	0	—	0 ± 1	0.292	5 ± 9	0.052	4 ± 4	**0.001**	18 ± 17	< **0.001**
Automobile driving: Motorway (km)	0	—	0	—	0	—	0	—	0	—
Washing and drying dishes (min)	0	—	23 ± 25	**0.002**	0	—	0	—	0	—

Functional reaching task (min)	3 ± 6	0.064	27 ± 16	< **0.001**	0	—	2 ± 3	**0.006**	0	0.292
Indoor cycling (min)	97 ± 12	< **0.001**	0 ± 1	0.495	0	0.136	1 ± 2	0.136	0 ± 1	0.057
Outdoor cycling (min)	90 ± 26	< **0.001**	22 ± 21	< **0.001**	12 ± 17	**0.025**	37 ± 17	< **0.001**	25 ± 17	< **0.001**
Indoor rowing (min)	0	—	10 ± 16	**0.032**	0	0.292	10 ± 16	**0.033**	1 ± 2	0.123

All false positive values represent mean ± SD. The mean false positives detected during the driving activities have been adjusted to reflect the false positives detected per kilometre driven. This is to allow for direct comparison between the step counts detected on each road type. All other false positive values represent the false positives detected per minute of each activity. Significant values are highlighted in bold. '—' indicates no p value obtained. FP = False Positives; SD = Standard Deviation. N = 10/activity.

5.5 Discussion

This study assessed five activity monitors: the Jawbone UP™, Withings Smart Activity Monitor Tracker (Pulse O_2) ™, NL-2000 pedometer™, ActivPAL micro™ and Fitbit One™ for their specificity for step detection during a series of non-stepping activities, representing examples of typical activities of normal daily living.

While there are many possible outputs from most activity monitors, such as time spent active, distance moved and calories burned, step count remains one of the most popular and translatable outputs in use today. Many research studies and consumer electronic articles have focused on step count as an output for measuring physical activity [11, 15, 16]. Many national and international health organisations have provided recommendations on step count goals in line with improving population health. The current recognised recommendation is 10,000 steps per day, which is a convenient method of physical activity quantification for the general public to comprehend. As many activities of daily living involve both stepping and non-stepping movements, it is important that activity monitors are both sensitive and specific in their detection of their primary output, i.e. actual steps taken. Previously, we have shown a number of physical activity monitors to be sensitive in step detection when actively walking over a variety of surfaces and in different types of footwear, while reaching the recommended daily 10,000 step goal [12]. However, our previous work focused on the performance of the activity monitors during purposeful stepping only. A critical question for activity monitors is, are steps recorded when no steps are actually taken? Considering this issue, in our current study we tested the specificity of activity monitors in distinguishing stepping from non-stepping movements during a number of prescribed activities typical of activities of daily living. It is important to gain an understanding of the true specificity of activity-monitoring devices in situations reflective of normal everyday activities.

In this paper we report on specificity as the number of false positives registered per minute for each activity. Our results demonstrate that, when grouped by activity type, the majority of the activity monitors tested were least specific during active non-stepping activities, which involved indoor cycling, outdoor cycling and indoor

rowing. As these activities involve a significant amount of non-stepping body movements, and considering the typical movements involved in these activities, it is not entirely surprising that a number of false positive were registered specifically during these activities. It is interesting to note however, that during the indoor activities on a static rowing or cycling ergometer, there was less variation in the false positive count compared to outdoor cycling. During outdoor cycling, all activity monitors registered a significant number of false positives.

While the ActivPAL™ monitor was found to be specific during passive and moderate non-stepping activities, a significant number of false positives were registered during the active cycling activities. This is likely due to the continuous changing of the leg position from the horizontal to the vertical plane and thus the location of the ActivPAL™ on the anterior aspect of the thigh has a role to play in these results. In a similar manner, the Jawbone™ activity monitor registered the greatest number of false positives during the moderate non-stepping activities of washing and drying dishes and the functional reaching task. This may reflect the fact that the Jawbone™ is worn on the wrist. Both moderate non-stepping activities performed focused on upper body movement involving both the arms and hands, which mostly likely played a role in the significant number of false positives registered by the Jawbone™.

Additionally, the Jawbone™ registered a significant number of false positives during automobile driving on a local road. The local road, through a built-up area, consisted of a number of speed bumps and required regular gear changes. As the Jawbone™ recommended wearing location is the non-dominant wrist, the majority of participants wore the Jawbone™ on the left wrist throughout this study, which is the hand involved in gear changing in the manual car used in this work. This, at least in part, may explain why the Jawbone™ registered a significant number of false positives during this section of automobile driving. It could be interesting to assess different placements of the Jawbone™ while driving. The Jawbone™ was not the only activity monitor found to register a significant number of false positives during automobile driving however. The NL-2000™ registered a significant number of false positives on a local road, an urban road and a category C road, while the Fitbit™ also registered a significant number of false positives on a category C road in addition to

on a category B road. These monitors also registered a significant number of false positives during the bus journey. As the NL-2000^{TM} monitor was worn at the waist and on the left had side of the body in this study, which is the clutching side in a manual car, this may have affected the false positives recorded. The Fitbit^{TM} however, was worn at the level of the chest, and as with the bus journey, it is likely that surface type, i.e. the bumpiness of the road, played a role in the false positives observed in that case.

These findings are relevant to all users of physical activity monitors from the typical sedentary user to the most active of users. The sensitivity and specificity of these devices are important considerations for both the general public interested in tracking step count for personal achievement, but also special populations tracking activity as part of a lifestyle prescription. Increasingly, wearable activity monitors are part of a suite of tools employed in tackling conditions such as obesity, COPD and type-2 diabetes. In these instances, the activity monitors play a critical role in monitoring progress towards improving physical activity levels and goal setting as part of behavioural change lifestyle interventions.

By way of example we can take four individuals representing a spread of activity levels from sedentary (taxi driver), low active (office worker), somewhat active (school teacher) to highly active (student football player). Based on these classifications individuals would be expected to achieve less than 5000 steps, 6250 steps, 8750 steps or greater than 12500 steps per day on average respectively [11]. The possible effect of false positives generated by each monitor on daily step count is presented in Table 5.3.

Table 5.3 Estimated False Positives Generated Daily Based on Conservative Estimates of Time Spent on Sample Activities for Different Categories of Potential Activity Monitor Users Over a Typical 12-hour Day

	Taxi Driver (5000 steps/day)					**Office Worker (6250 steps/day)**					**School Teacher (8750 steps/day)**					**Student Football Player (12000 steps/day)**				
	T/D	AM 1	AM 2	AM 3	AM 4	T/D	AM 1	AM 2	AM 3	AM 4	T/D	AM 1	AM 2	AM 3	AM 4	T/D	AM 1	AM 2	AM 3	AM 4
Deskwork (min)	-	-	-	-	-	360	0	0	0	0	120	0	0	0	0	120	0	0	0	0
3rd floor elevator (min)	-	-	-	-	-	15	15	0	0	0	5	5	0	0	0	-	-	-	-	-
Bus journey (min)	-	-	-	-	-	60	120	0	60	60	-	-	-	-	-	60	120	0	60	60
Driving: Local road (km)	40	320	40	400	40	-	-	-	-	-	10	80	10	100	10	-	-	-	-	-
Driving: Urban road (km)	35	70	0	105	0	-	-	-	-	-	10	20	0	30	0	-	-	-	-	-

Driving: Category A Road (km)	-	-	-	-	-	-	-	-	-	-	5	0	0	10	0	-	-	-	-	-
Driving: Category B Road (km)	-	-	-	-	-	-	-	-	-	-	5	0	0	5	25	10	0	0	10	50
Driving: Category C Road (km)	-	-	-	-	-	30	0	150	120	540	5	0	25	20	90	10	0	50	40	180
Driving: Motorway (km)	-	-	-	-	-	-	-	-	-	-	10	0	0	0	0	-	-	-	-	-
Washing and drying dishes (min)	20	460	0	0	0	20	460	0	0	0	20	460	0	0	0	20	460	0	0	0
Functional reaching task (min)	15	405	0	30	0	30	810	0	60	0	20	540	0	40	0	60	1620	0	120	0
Total (false positives)		1255	40	535	40		1405	150	240	600		1105	35	205	125		2200	50	230	290
% of the average daily step count that is false		25.1	0.8	10.7	0.8		22.5	2.4	3.8	9.6		12.6	0.4	2.3	1.4		18.3	0.4	1.9	2.4

Values for the automobile driving activity are expressed as the number of false positives detected per kilometre driven. Values for all other activities are expressed as the number of false positives detected per minute. The ActivPAL^{TM} monitor has been excluded from this table, as it correctly did not register any false positives during the included sample activities. T/D = Time in minutes/Distance in kilometres; AM = Activity Monitor. AM 1 = Jawbone^{TM}; AM 2 = Withings^{TM}; AM 3 = NL-2000^{TM}; AM 4 = Fitbit^{TM}.

As is evident from Table 5.3, across a spectrum of users from sedentary to highly active, all monitors have the capacity to contribute false positives to daily step counts. A recent survey published by the National Transport Authority of Ireland reported that taxi drivers drive a minimum of 4 and a maximum of 5 hours per day. Within this timeframe taxi drivers drive up to 14.9 kilometres per hiring cycle, with hiring cycles lasting anywhere up to 59 minutes [17]. Based on our conservative estimates in Table 5.3, the Jawbone™ and NL-2000™ can generate false positives accounting for up to 25.1% and 10.7% of the daily average of 5000 steps for a sedentary Taxi driver [11]. Had the Taxi driver been using a Withings™ or Fitbit™ device in our example then the false positives could be significantly less.

In a typical day in the life of an office worker, washing and drying dishes, carrying out several hours of deskwork, stacking books, taking the elevator several times throughout the day, taking a bus and short car journey to and from work is not uncommon. Again, based on our estimates, the Jawbone™ monitor can generate false positives accounting for up to 22.5% of the daily average of 6250 steps for a low active office worker. Using a Withings™, NL2000™ or Fitbit™ could have resulted in a much lower contribution of false positives at 2.4, 3.8 and 9.6 % of the daily average respectively. A similar pattern is apparent for a typical active user such as a schoolteacher, while a highly active user such as a student football player could equally be exposed to the accumulation of false positive step counts.

While a typical day in the life of the average activity monitor user will be highly variable and could consist of many different stepping and non-stepping activities, in this paper we have highlighted the effect of some normal activities of daily living on step count. Our data, and when considered for typical users in Table 5.3, serve to highlight the potential for false positive steps to be registered during a normal day consisting of some passive, moderate and active non-stepping activities. In a similar study carried out by Stackpool et al participants wore the Nike Fuelband, Fitbit Ultra, Jawbone UP and NL-2000i pedometer when utilising an elliptical cross-trainer and carrying out agility exercises in a gymnasium, including agility ladder drills (seven different moves), 10 basketball free throws and a basketball half-court lay-up drill for one minute [18]. The authors reported inaccuracies in the activity monitors during the agility tests, with all monitors excepting the Jawbone UP significantly

underestimating steps [18]. The Nike Fuelband was found to underestimate steps by 34%, the Fitbit Ultra by 20% and the NL-2000i by 17%. During the elliptical exercise the only significant difference lay with the NL-2000i, which underestimated steps by 6% [18]. Although these monitors underestimated step counts during these activities and our results highlight the potential for the registering of false positive steps, both studies highlight the variability that can occur during physical activities that are not specifically stepping activities.

Overall, this data is important to consider when utilising activity monitors in both the research and clinical domains whether using research grade or off-the-shelf consumer-based tracking tools. While the ActivPAL^{TM} is a research-grade activity monitor and the other activity monitors tested here are consumer-grade monitors, the specificity was observed to vary for all monitors during one or more non-stepping activity. However, all activities in this study are classed as physical activity and go towards maintaining a healthy and active lifestyle. Accurate translation of the activity carried out during these non-stepping activities into step count could be of interest. Clearly it is important to consider non-stepping activities when wearing physical activity monitors to accurately quantify overall physical activity levels. It is evident from our data that typical non-stepping activities, likely to be carried out in everyday life, result in the recording of steps when none are taken. As mentioned above, these factors are especially important to consider in situations whereby physical activity is prescribed as an intervention in the prevention or treatment of chronic disease, where accurate physical activity quantification is of the utmost importance.

5.5.1 Conclusions

This study provides the first comprehensive specificity evaluation of five activity monitors during a variety of prescribed physical activities involving non-stepping body movements. From our results, we can conclude that false positive steps are detected and registered during a range of non-stepping activities, affecting the quantification of physical activity with regard to step count as the primary output. The range and impact of the false positives detected will differ depending on the activities carried out and the activity monitors utilised, with the results highlighting the specificity variability that can exist during a range of non-stepping physical

activities. The Withings^{TM} monitor performed best across all non-stepping activities, registering a significant number of fp/min only during the outdoor cycling activity. The specificity of an activity monitor needs to be considered carefully when choosing an activity monitor to accurately quantify the variety of physical activities that can be carried out on any typical day.

5.6 References

[1] Penedo, F. J. and Dahn, J. R., "Exercise and well-being: a review of mental and physical health benefits associated with physical activity," *Curr Opin Psychiatry,* vol. 18, no. 2, pp. 189-93, Mar 2005.

[2] Pedersen, B. K. and Saltin, B., "Evidence for prescribing exercise as therapy in chronic disease," *Scand J Med Sci Sports,* vol. 16 Suppl 1, pp. 3-63, Feb 2006.

[3] Warburton, D. E., Nicol, C. W., and Bredin, S. S., "Health benefits of physical activity: the evidence," *CMAJ,* vol. 174, no. 6, pp. 801-9, Mar 14 2006.

[4] U.S. Department of Health and Human Services. Physical activity and health: a report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996. [Internet]. Available from: http://www.cdc.gov/nccdphp/sgr/chapcon.htm

[5] Centers for Disease Control. "2008 Physical Activity Guidelines for Americans." U.S. Department of Health and Human Services. [Internet]. Available from: http://www.health.gov/paguidelines/guidelines/summary.aspx

[6] World Health Organization. Global Recommendations on Physical Activity for Health. 2010. [Internet]. Available from: http://whqlibdoc.who.int/publications/2010/9789241599979_eng.pdf?ua=1

[7] Colbert, L. H., Matthews, C. E., Havighurst, T. C., Kim, K., and Schoeller, D. A., "Comparative validity of physical activity measures in older adults," *Med Sci Sports Exerc,* vol. 43, no. 5, pp. 867-76, May 2011.

[8] Van Remoortel, H. *et al.,* "Validity of activity monitors in health and chronic disease: a systematic review," *Int J Behav Nutr Phys Act,* vol. 9, p. 84, 2012.

[9] White, L., Volfson, Z., Faulkner, G., and Arbour-Nicitopoulos, K., "Reliability and Validity of Physical Activity Instruments Used in Children and Youth With Physical Disabilities: A Systematic Review," *Pediatr Exerc Sci,* vol. 28, no. 2, pp. 240-63, May 2016.

[10] Tudor-Locke, C., Ainsworth, B. E., Whitt, M. C., Thompson, R. W., Addy, C. L., and Jones, D. A., "The relationship between pedometer-determined ambulatory activity and body composition variables," *Int J Obes Relat Metab Disord,* vol. 25, no. 11, pp. 1571-8, Nov 2001.

[11] Tudor-Locke, C. and Bassett, D. R., Jr., "How many steps/day are enough? Preliminary pedometer indices for public health," *Sports Med,* vol. 34, no. 1, pp. 1-8, 2004.

[12] O'Connell S, G ÓLaighin, Kelly L, Murphy E, Beirne S, Burke N, et al. These Shoes Are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps. *PLoS One*. 2016;11(5):e0154956.

[13] Chen, M. D., Kuo, C. C., Pellegrini, C. A., and Hsu, M. J., "Accuracy of Wristband Activity Monitors during Ambulation and Activities," *Med Sci Sports Exerc,* May 13 2016.

[14] Sellers, C., Dall, P., Grant, M., and Stansfield, B., "Validity and reliability of the activPAL3 for measuring posture and stepping in adults and young people," *Gait Posture,* vol. 43, pp. 42-7, Jan 2016.

[15] Kang, M., Marshall, S. J., Barreira, T. V., and Lee, J. O., "Effect of pedometer-based physical activity interventions: a meta-analysis," *Res Q Exerc Sport,* vol. 80, no. 3, pp. 648-55, Sep 2009.

[16] Tudor-Locke, C., Leonardi, C., Johnson, W. D., Katzmarzyk, P. T., and Church, T. S., "Accelerometer steps/day translation of moderate-to-vigorous activity," *Prev Med,* vol. 53, no. 1-2, pp. 31-3, Jul-Aug 2011.

[17] National Transport Authority. Taximeter Survey 2015. [Internet] Available: https://www.nationaltransport.ie/public-transport-services/taxi/

[18] Stackpool, C. M., Porcari, J. P., Mikat, R. P., and Gilette, C., "The accuracy of various activity trackers in estimating steps taken and energy expenditure," *J Fit Res,* vol. 3, no. 3, pp. 32-48, 2014.

Chapter 6

Effectiveness of a Home-Based Neuromuscular Electrical Stimulation (NMES) Programme to Assist Functional Recovery in the Acute Phase Following Total Knee Arthroplasty Discharge: A Randomised Controlled Trial

Background

Within this thesis, NMES has been investigated as a method of improving haemodynamic measures with regard to preventing venous stasis and DVT. The development of venous stasis and DVT, with its subsequent morbidities, can have a major negative effect on the recovery process following TKA. Results from Chapter 3 suggest that NMES has great potential in improving haemodynamic measures as compared to the currently utilised mechanical method of IPC. In addition to contributing to the prevention of venous stasis and DVT, an improvement in haemodynamic measures may have positive effects on functional recovery following surgery.

As such, an aim of this thesis was to assess the use of NMES as a method of enhancing functional recovery through outcomes of physical activity levels, knee range of motion and lower limb swelling. NMES is a beneficial therapy utilised to improve both lower limb haemodyanamics and muscle strength and has previously been reported to improve muscle strength and decrease muscle wasting in individuals with osteoarthritis and following TKA [1-3]. Applied to the calf muscles, essential in ambulation and musculovenous health, NMES may provide a beneficial method of enhancing physical activity levels, knee range of motion and decreasing swelling post-TKA. These measures play a major role in functional recovery post-TKA, with improvements in physical activity an important goal for many patients following surgery. When the measurement of physical activity is utilised as an indicator of functional recovery, its accurate quantification is of the utmost importance.

As further aim within this thesis to investigate the sensitivity and specificity of a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery. As such, chapters 4 and 5 were carried out to investigate their sensitivity and specificity as methods of monitoring physical activity levels through the measure of step count. While many of these monitors may be of great use for TKA patients for monitoring physical activity levels post-surgery, this current study utilised the research-grade ActivPAL^{TM} activity monitor.

In addition to providing step count as an output, the ActivPAL^{TM} monitor provides information on the time spent in various body positions and gives an event and raw data output that can be utilised to generate a number of other measures. Within this chapter, these measures (namely time spent sitting/lying, time spent upright and number of Stepping Bouts) were utilised to fully assess the effectiveness of NMES as a method of improving physical activity levels, an important indicator of functional recovery post-TKA.

Contribution to work

Study design: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

Data collection:

- Subject consent: Sandra O'Connell, Jane Campbell.
- Subject testing: Sandra O'Connell.

Data Analysis: Sandra O'Connell.

Interpretation of results: Sandra O'Connell, Gearoid ÓLaighin, Leo R Quinlan.

Programming: Evismar Andrade.

Drafting of manuscript: Sandra O'Connell.

Critical review of manuscript: Sandra O'Connell, Gearoid ÓLaighin, Paraic Murray, Jane Campbell, Leo R Quinlan.

6.1 Abstract

Background: Total knee arthroplasty (TKA) is an extremely beneficial surgery that is becoming more prevalent as the average age of the general population increases. TKA is generally considered to be a very effective and successful surgery. However, functional recovery post-surgery can be less than optimal. NMES is a beneficial therapy proven to improve haemodynamics and muscle strength and may be of great benefit in improving functional recovery in the acute phase post-TKA.

Objective: The objective of this study was to assess the effectiveness of a home-based NMES programme to assist in functional recovery in the short-term phase immediately following TKA discharge (up to the sixth post-surgery week).

Methods: Twenty-six TKA patients were randomised into a stimulation or placebo-controlled group. Each group was given a research muscle stimulator to use at home post-discharge for 90 minutes per day over a period of 5 weeks. In the stimulation group, application of stimulation resulted in an electrically activated contraction of the soleus muscle. Patients in the placebo-controlled group received sensory stimulation only. Physical activity levels, joint range of motion and lower limb swelling were measured pre-surgery and on a weekly basis post-discharge up until the sixth post-surgical week.

Results: NMES significantly increased the time spent upright ($P = 0.045$ week 1 post-discharge), decreased the time spent sitting/lying ($P < 0.05$ weeks 1 to 3 post-discharge) and increased the number of Stepping Bouts carried out ($P < 0.05$ weeks 1 to 4 post-discharge) in the early post-discharge phase. While there was a trend towards a greater knee flexion with use of NMES, this did not reach statistical significance ($P = 0.722$). No effect of NMES was observed on swelling measures during the post-discharge period ($P > 0.05$ for all measures). Compliance was measured on an on-board SIM card in the NMES device, with a 95% and 94% time compliance rate for the stimulation and placebo-controlled groups respectively.

Conclusions: The results of this study suggest that NMES may be very useful in improving functional recovery through increasing physical activity levels in the early post-TKA discharge phase. The results of this study warrant further investigation into the use of an optimised NMES protocol.

6.2 Introduction

Total knee arthroplasty (TKA) is an extremely beneficial surgery for the patient and is becoming more prevalent as the average age of the general population continues to rise. The absolute increase in the number of people aged 65 and older, and associated increased incidence of arthritis, means a concurrent increase in the number of TKAs to be performed worldwide [1, 2]. Indeed, TKA procedures are predicted to increase by up to 110% and 117% by 2030 in the United States and in the UK respectively [1, 2]. TKA is carried out primarily as a treatment for end-stage knee osteoarthritis to improve both quality of life and physical functional capacity [3]. Indeed, limitations in daily physical activity and function due to osteoarthritis are some of the foremost reasons for performing TKA [4]. However, while TKA is a beneficial and successful surgery with good long-term prognosis, physical functional recovery and performance immediately post-discharge can be impaired [5], due to factors such as post-operative swelling [6-9], impaired knee range of motion (ROM) [10] and unimproved physical activity levels [11, 12].

Concerning physical activity levels, the American Association of Orthopaedic Surgeons (AAOS) have stated that physical activity is a critical component of home-based self-care, especially in the first few weeks following TKA as patients are expected to resume most normal activities of daily living in the short-term, i.e. within 3 to 6 weeks post-surgery [10]. Adequate reduction of swelling and improvement of knee ROM within this timeframe are also essential for assisting in rehabilitation and enhancing physical function post-TKA [10]. For example, post-operative knee and calf swelling can be an issue in the short-term following TKA and have been investigated from 1-week to 1-month post-surgery [6, 8, 9]. These conditions can result in decreased functional capacity and impaired mobilisation post-TKA, and hence can impair rehabilitation and functional recovery [7-9, 13]. An increase in knee ROM is also essential in the short-term post-TKA, with a minimum flexion of 90° considered standard prior to discharge [14-17].

With regard to swelling of the knee and calf post-TKA, compression therapy, utilising compression stockings and intermittent pneumatic compression foot pumps, has been investigated as a method of combatting this issue [6, 8, 9]. The efficacy of compression stockings as a method of decreasing post-operative swelling remains unclear. When Munk et al (2013) utilised compression stockings for up to 4 weeks post- TKA, the authors reported no significant difference in knee, calf or ankle swelling measurements taken on days 1, 2, 7, 14 or 1-month post-TKA versus controls [9].

However, some success has been reported with the use of foot pumps for up to 8 days post-TKA [6, 8]. Tamir et al (1999) reported success utilising the Walkcare sequential foot compression pneumatic inflatable sandal. The Walkcare compression sandal covers the complete sole of the foot and consists of four pressure chambers that independently and sequentially apply pressure to the heel, plantar arch, metatarsals and toes in order to mimic walking. Use of this device was started immediately post-operation and used continuously for approximately seven days after surgery. A maximum pressure of 200 mmHg was utilised in each chamber and compression was applied for 40 minutes out of each hour. The authors reported significantly decreased swelling one-week post-TKA in the foot, ankle, calf and thigh when compared to controls [6].

In a similar study, Windisch et al (2011) utilised the AV-Impulse foot pump in TKA patients from shortly after the operation to day 8 post-operation, aiming for 24 hours usage per day. This device consists of one chamber that covers and applies compression simultaneously to the entire foot. While the authors did not report on the pressure utilised in their study, the manufacturers of the AV-Impulse system recommend a 3-second compression at a pressure of 130 mmHg for DVT prevention. The authors reported significantly decreased swelling on post-operative day eight in the thigh and knee joint compared to controls. However, no significant difference was observed in the calf or foot [8]. The authors reported good compliance with the use of the foot pump between days one and four post-operation with a gradual decrease observed thereafter. The decline in the rate of compliance, combined with the difference between the Walkcare and AV-Impulse devices (sequential and non-

sequential compression respectively) may account for the lack of significance observed by Windisch et al in the calf and foot swelling measurements [8].

While compression therapy utilising foot pumps provides some benefit in reducing swelling in the short-term post-TKA, the use of foot pumps remains unstandardized and their true efficacy unknown [18].

However it is achieved, a reduction in swelling post-TKA is likely to be of great benefit with regard to improving knee ROM, with post-operative maximum knee ROM a commonly utilised functional outcome measure following TKA [19]. While an improvement in knee ROM is a goal of knee arthroplasty, restoration of full ROM is uncommon and it is generally expected that an average knee flexion of 115° will be achieved after TKA [10]. According to the AAOS, approximately 3 to 6 weeks post-surgery, the majority of patients can expect to achieve nearly full straightening of the knee and to bend the knee sufficiently to get in and out of a car and to climb stairs [10]. The improvement and maintenance of an adequate knee ROM within this timeframe is essential for the resumption of normal activities of daily living and for improvements in function and physical activity levels [10].

Similarly, increases in physical activity levels following TKA are essential for achieving gains in functional recovery post-surgery [12]. To achieve improvements in function, the AAOS recommend that an activity program consisting of a graduated walking program, normal household activities such as sitting, standing and climbing stairs, and specific exercises to restore movement and strengthen the knee be carried out within the first 6 weeks post-TKA [10]. Increasing physical activity levels within this timeframe will allow patients to progress from limited mobility and the need for ambulatory aids, such as crutches, to increased functional abilities, independence and quality of life, all primary reasons for undergoing TKA [3, 20].

While there are many methods of monitoring and measuring physical activity levels, physical activity monitors are popular tools and are commonly utilised. They provide objective real time quantification of activity data that is unaffected by the recall and

response bias associated with questionnaires and diaries [21, 22]. Step count is one of the foremost outputs utilised from physical activity monitors and the relationship between step count and activity levels has been widely studied [11, 23-26]. When utilising step count as a measure of physical activity levels, it is important to consider the sensitivity and specificity of the activity monitors, i.e. their ability to correctly detect and register a step while also disregarding non-stepping movements. Many factors must be considered when utilising step count as a measure of physical activity levels, as the sensitivity and specificity of activity monitors can vary between monitors and under various conditions and circumstances [27-35].

A targeted therapy programme, which would attempt to accelerate reductions in swelling, improvements in knee ROM and improvements in physical activity levels in the immediate post-discharge period (up to the sixth week post-TKA), could correct impaired functional performance post-discharge. Neuromuscular Electrical Stimulation (NMES) is a therapy that may be of benefit in doing so. NMES involves delivering an electrical stimulus to a targeted muscle/group of muscles to elicit muscular contractions. Regarding the reduction of lower limb swelling post-TKA, NMES has the advantage over compression therapy in that it induces a muscular contraction, activating the muscle itself, while also providing compression to the veins in and surrounding the muscle. NMES has been reported to enhance venous haemodynamics [36-43]. Its application in the first 6 weeks post-joint arthroplasty has been shown to enhance venous blood flow [42] and there is a possibility that it may also assist in the lymphatic removal of excess fluid from the lower limb [44], allowing for enhanced functional recovery in the short-term post-TKA. Additionally, NMES has been reported to improve muscle strength, prevent muscle decline and enhance motor function and control [45-49], as well as increase energy expenditure [50] and improve functional exercise capacity [51]. These reports suggest that NMES has the potential to be a beneficial method of increasing knee ROM and enhancing physical activity levels. NMES-elicited activation of the lower limb muscles and the reduced knee swelling achieved through enhanced NMES-assisted lymph drainage (leading to enhanced knee ROM) are both likely to contribute to enhancing overall physical activity levels post-discharge and to counteract limitations in physical activity and function experienced immediately post-discharge.

In this study, we focused upon assessing the effectiveness of a home-based NMES programme to assist in functional recovery in the short-term phase immediately following TKA discharge (up to the sixth post-surgery week). Outcomes of interest included physical activity levels, joint ROM and lower limb swelling.

6.3 Methods

6.3.1 Patients

The Research Assessment Group in the Galway clinic, Doughiska, Co. Galway, approved this study (ClinicalTrials.gov NCT02343198). All patients presenting to a single surgeon practice in the Galway clinic for total knee arthroplasty surgery with a diagnosis of osteoarthritis were considered for inclusion in this study. Patients who consented to participate in this study were randomised to either group A, the stimulation group, or to group B, the placebo-controlled group once written informed consent was obtained. Randomisation was derived from a computer-generated sequence. Exclusion criteria were a history of symptomatic heart disease or severe arterial disease, history of deep venous thrombosis or pulmonary embolism, pregnancy, the presence of a cardiac pacemaker, history of a neurological disorder or the presence of cognitive difficulties, which would prevent the patient or his/her carers from using the stimulator correctly. Criteria for discontinuation included the patient wishing to withdraw for any reason, intolerable discomfort due to the treatment protocol, inability to adhere to the treatment protocol and repeated misuse of the stimulator unit, which could result in injury to the patient.

6.3.2 In-Hospital Protocol

One surgeon performed all surgeries and all patients received an intra-articular infusion with local anaesthetic for the first 24 hours post-surgery. While in hospital, patients received Clexane 20 sc daily and 25mg Lyrica (Pfizer Inc., New York, U.S.A.) three times a day over a period of four days. While at home, patients received 75mg Aspirin daily and 50mg Lyrica at night. Patients also received 100mg Celebrex (Pfizer Inc., New York, U.S.A.) two times a day (am and pm). All patients were given thigh-high anti-embolism stockings (T.E.D. Anti-Embolism Stockings, Covidien, Ireland) to wear for 6 weeks post-surgery. On Day 0, the day of the surgery, if awake, all patients were advised to do ankle exercises for five minutes hourly in addition to deep breathing exercises hourly. On day 0/day 1 patients mobilised a short distance with a walking frame and a physiotherapist and also commenced an exercise programme to strengthen the quadriceps muscle, increase joint range of motion and allow for full knee extension. On day 1/day 2 the distance

covered using either a walking frame or elbow crutches was increased and the exercise programme targeted an active knee flexion of 55–65°. On day 2/day 3, progression with the use of elbow crutches was continued and walking distance was increased. Using the exercise programme patients targeted an active knee flexion of 70°. By day 3/day 4 patients mobilised independently and targeted an active knee flexion of 80-90°. By day 4/day 5 patients were able to do a straight leg raise and aimed to achieve 100° knee flexion. All patients were required to achieve an active knee flexion of 90° prior to discharge.

6.3.3 At-Home Protocol

Post-discharge, all patients were given exercises to be carried out three times a day to improve range of motion and quadriceps femoris function and strength: straight leg raises, ankle pumps, knee straightening exercises, bed- supported knee bends and sitting supported knee bends. No other exercises or activities were prescribed to patients as part of the study protocol. On the day after discharge (5-6 days post-surgery), all patients were provided with a research muscle stimulator for use at home for five weeks (same period of anti-embolism stockings use at home). Stimulation was delivered to the operated leg of every patient through the use of two 5x5cm square electrodes (Ultrastim wire electrodes, Axelgaard Manufacturing Co., Ltd., CA, USA). The researcher positioned these electrodes over the motor points of the soleus muscle. In both groups, following the correct positioning of the electrodes, waterproof bandages (Opsite Post-Op, Smith & Nephew Medical Limited, Hull HU3 2BN England) were placed over the electrodes with the electrode wires hanging down (Figure 6.1). While using the stimulator, the wires connecting the electrodes to the stimulator were worn under the anti-embolism stocking. These wires were disconnected and removed only for showering, unless a patient felt discomfort with them in place under the thigh high anti-embolism stockings, which were worn for the duration of the study.

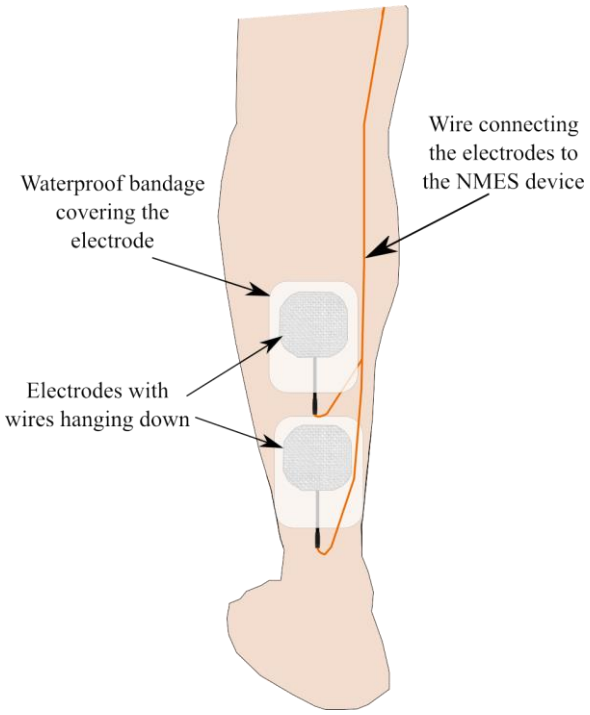

Figure 6.1 Placement of the electrodes for stimulation of the operated leg soleus muscle. Waterproof bandages are positioned in place over the electrodes. The wire connecting the electrodes to the NMES device was worn underneath the anti-embolism stocking (not shown in image). This wire was removed for showering.

6.3.4 Stimulation Protocol

Patients in both groups carried out the same stimulation protocol, which consisted of three 30-minute sessions of comfortable stimulation per day, with a period of at least 2 hours between each session. Patients were advised to set the stimulator voltage to the highest comfortable level possible for each session.

6.3.5 NMES Device

The NMES device used was a constant-voltage, dual-channel, EN60601-1 certified research muscle stimulator (Human Movement Laboratory, NUI Galway) designed as a "coffee table" device for the delivery of a home programme of NMES therapy (Figure 6.2). The stimulator has a built-in compliance log, which logged digitally, using on-board memory, the number of days of use, number of minutes of use each day, the percentage session compliance and the percentage time compliance. These

compliance data were downloaded via the device's USB port for analysis. The stimulator was set to provide a balanced biphasic waveform with a pulse frequency of 36Hz, a pulse width of 350μs, a ramp up time of 0.5s, a contraction time of 1s, a ramp down time of 0.5s and a rest time of 6s.

Figure 6.2 Research muscle stimulator used at home for 5 weeks post-discharge. Patients were encouraged to adjust the voltage to the highest comfortable level during each stimulation session.

Group A, the stimulation group, received a stimulator with a maximum voltage output of 72V. Group B, the placebo-controlled group, received the same stimulator but with the maximum voltage output attenuated to 20V. In Group A, application of stimulation resulted in an electrically activated, visible contraction of the soleus muscle. In Group B, application of stimulation resulted in sensory stimulation only, i.e. patients felt the stimulation on their skin but did not achieve an electrically activated muscle contraction.

6.3.6 Measurements

Measurements of physical activity, joint range of motion and lower limb swelling were recorded one week before the surgery (baseline measures) and on a weekly basis for 5 weeks beginning the day after discharge from hospital. Stimulator compliance was recorded throughout the study period. All measurements were carried out in the home of each patient or in the physiotherapy unit in the Galway clinic if the day of measures coincided with the patient being present in the clinic.

6.3.7 Physical Activity Levels

Physical activity levels were quantified using the ActivPAL micro™ research activity monitor (PAL Technologies Ltd., Glasgow, UK). The ActivPAL micro™ device was chosen for use in this study as it is one of the most widely utilised and validated research-grade activity monitors in physical activity research [52]. The ActivPAL ™ has been utilised extensively across all age groups to investigate physical behaviours and activity in a number of patient groups, including TKA patients. Investigations in chapters 4 and 5 have shown the ActivPAL™ to be sensitive and specific in step detection. In addition to step count, the ActivPAL™ device also outputs the time spent in various body positions and outputs event and raw data. These outputs allow for a more in-depth investigation into the effects of NMES on physical activity in TKA patients post-discharge.

Patients wore the ActivPAL™ monitor for a week prior to surgery to collect baseline data. The ActivPAL™ was worn on the anterior aspect of the thigh, as recommended by the manufacturers, on the non-operated leg. The ActivPAL™ was wrapped in a waterproof nitrile flexible sleeve (PAL Technologies Ltd., Glasgow, UK) and was attached directly to the thigh using Tegaderm transparent dressing (3M Health Care, Minnesota, USA). Following discharge, the ActivPAL™ was worn under the anti-embolism stockings for the duration of the study. Activity data were recorded for 5 weeks during the recovery period, immediately post discharge. Five full days of data from each week were used for analysis. Each week, the device was removed from the thigh and the data downloaded. Once the device was recharged (approximately 1 hour elapsed), it was put back in place on the anterior aspect of the thigh of the non-operated leg. Outputs of interest included step count, stepping time, standing time and sitting/lying time. The step counts, stepping time, standing time and sitting/lying time data were read from the output generated when the ActivPAL™ data were downloaded to a PC using the ActivPAL™ software program.

Additional parameters were derived from the ‘events’ file containing all the ActivPAL™ activity code changes (code 0 = sitting/lying, code 1= standing & code 2 = stepping) captured during the time the patient wore the ActivPAL™ device and which was output to a cvs file.

A Python (Python Software Foundation, Delaware, USA) programme was utilised to read each 'Events' cvs file for each individual patient. A flow chart of the ActivPAL^{TM} data extraction and analysis process is shown in Figure 6.3. A Python algorithm read data for five days of each week and generated an Excel file containing both a daily and weekly report for each individual patient and for each group of patients (Figure 6.3). Using the generated Excel files, it was possible to plot charts and visualise the evolution of the physical activity profile of both groups over time.

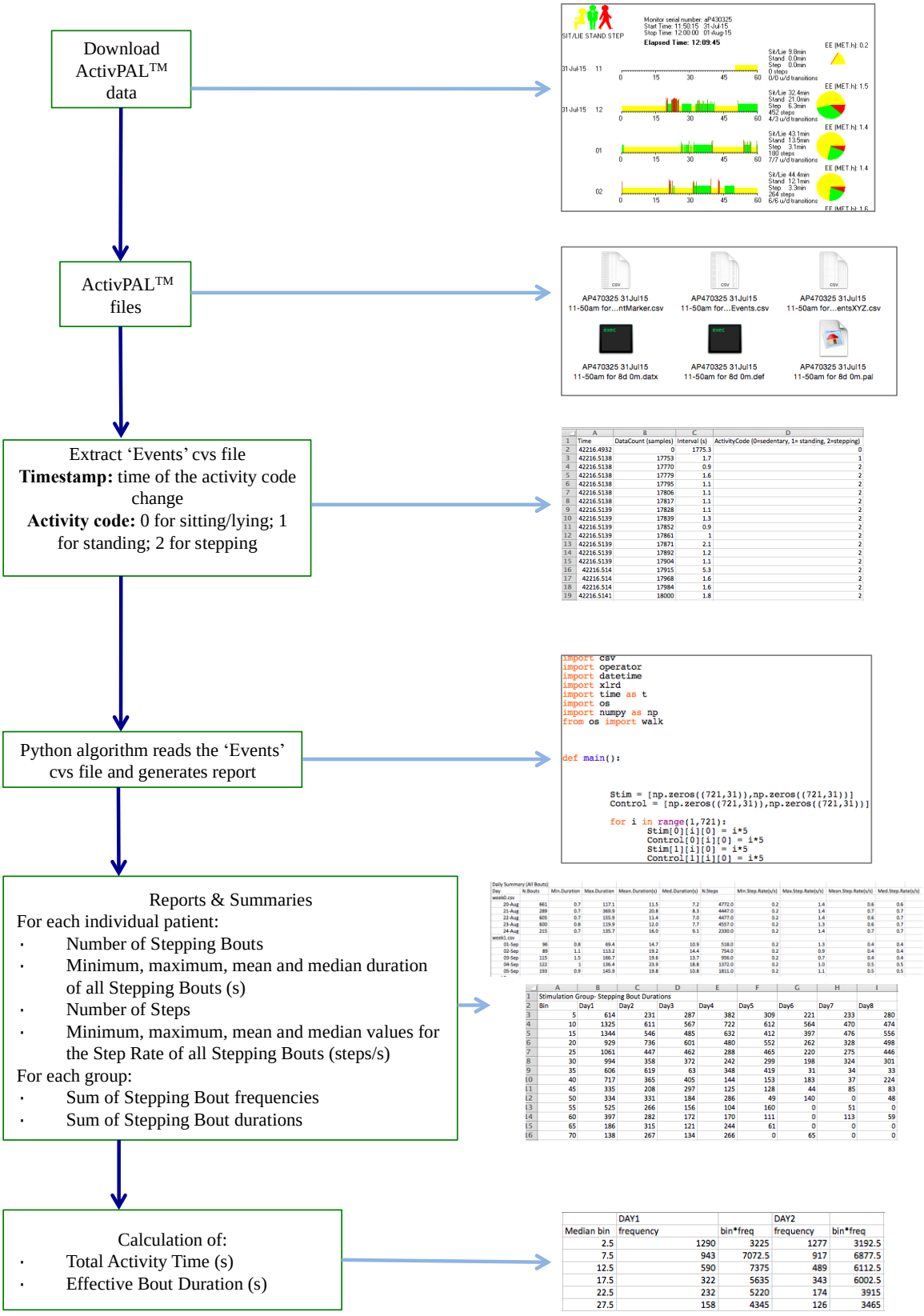

Figure 6.3 Flow diagram of the ActivPAL™ data analysis process.

As part of this analysis process, the following new parameters were derived:

6.3.7.1 Stepping Bout

S*tepping Bout* is defined as the duration of time when the activity is continuously coded as stepping by the ActivPAL^{TM} device (activity code = 2). The number of Stepping Bouts is utilised as a measure of functional recovery.

6.3.7.2 Effective Bout Duration (Centroid)

To visualise the distribution of durations of the parameter Stepping Bout over time and across groups, Stepping Bout durations were graphed using 5-second bins. The Centroid value (in seconds), calculated using Equation 6.1, provides a representative value (balancing point) of Stepping Bout duration for that patient on a daily basis (Figure 6.4).

$$Effective\ Bout\ Duration\ (Centroid) = \frac{\sum_{i=1}^{n}(f_i).(\tau_{Median\ i})}{\sum_{i=1}^{n}(f_i)}$$

Equation 6.1 Equation utilised to calculate the Effective Bout Duration in seconds (Centroid): f_i = Stepping Bout bin frequency for the ith term; $\tau_{Median\ i}$ = median Stepping Bout bin duration for the ith term..

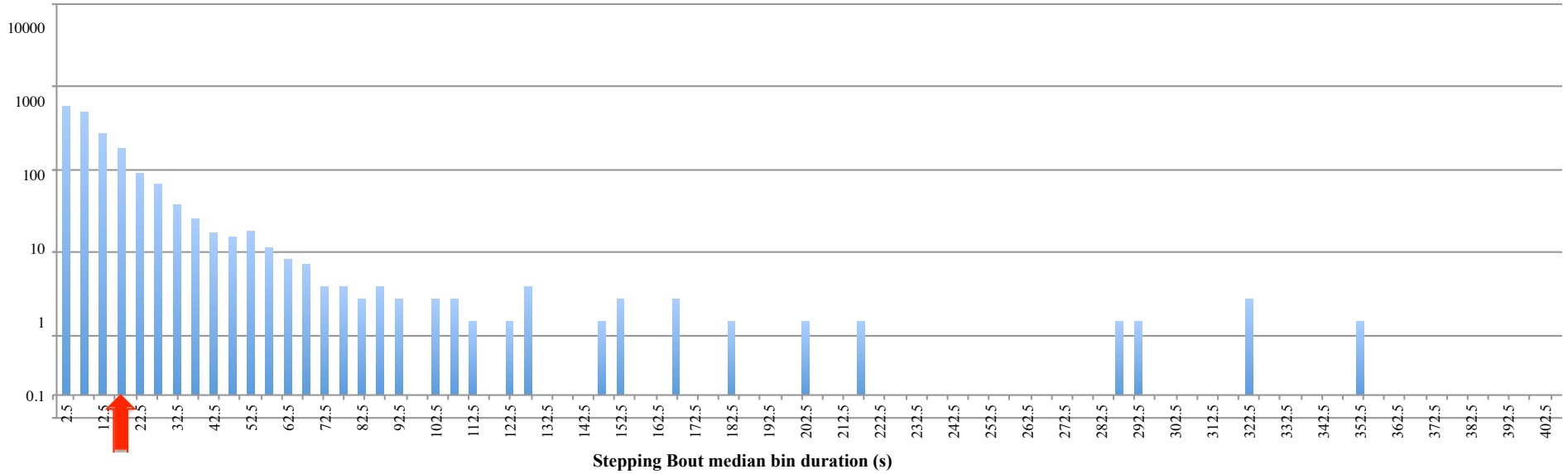

Figure 6.4 Graphical representation of the Centroid. The red arrow indicates the position of the Centroid, which provides a representative value (balancing point) of Stepping Bout duration on a daily basis.

6.3.7.3 Sum of Stepping Bout Durations ≥ 1 minute

The sum of the Stepping Bouts that were of a duration of equal to or greater than 1 minute.

6.3.7.4 Sum of Stepping Bout Durations ≥ 5 minutes

The sum of the Stepping Bouts that were of a duration of equal to or greater than 5 minutes.

6.3.7.5 Sum of Stepping Bout Durations ≥ 10 minutes

The sum of the Stepping Bouts that were of a duration of equal to or greater than 10 minutes.

For statistical analysis, data was normalised and expressed as a percentage of pre-surgery values. Percentage of pre-surgery values were calculated using Equation 6.2.

$$\frac{Raw\ data\ value}{\bar{x}\ pre-surgery\ days\ 1-5} * 100$$

Equation 6.2 Equation utilised to calculate the percentage of pre-surgery (normalised) values. Each raw data value, for every day both pre-surgery and post-discharge, is divided by the mean ( ) of the five pre-surgery days value and multiplied by 100.

This equation was utilised to obtain normalised values for each daily measure of number of Stepping Bouts, Effective Bout Duration (Centroid), the sum of Stepping Bouts of duration ≥ 1 minute, ≥ 5 minutes and ≥ 10 minutes.

6.3.8 Knee and Ankle Range of Motion

Knee ROM was carried out with the patient in a semi-recumbent position with both knees straight. The knee was moved into Knee Flexion and joint angle recorded with a goniometer (Saehan plastic goniometer 30cm, MSD Europe bvba, Belgium) at the point where there was resistance to further motion. To measure Ankle ROM, patients began with their ankle in a 90-degree position and were then asked to pull their toes back towards themselves as much as possible (dorsiflexion) and then to put their toes down towards the floor as much as possible (plantar flexion). The reading on the goniometer (PEL Supply Company, Cleveland, OH 44135) was recorded at resistance to further motion. All measurements were carried out three times with the average of the three measures used for statistical analysis.

6.3.9 Lower Limb Swelling

Lower limb swelling was assessed using the Figure-of-8 measurement, whereby the beginning of the tape is placed midway between the tibialis anterior tendon and the lateral malleolus. The tape is then wrapped around the foot in a figure-of-8 pattern across the subtalar and talar joints to end where it began [53, 54]. Circumference measurements of both the ankle and mid-calf were assessed using a Gulick II tape measure (Country Technology Inc., Gay Mills, WI).

6.3.10 Stimulator Compliance

Stimulator compliance was logged on the NMES device itself and checked on a weekly basis. Patients were aware that stimulator compliance was being logged and of the need for compliance with use of the NMES device and those unable to adhere to the stimulation protocol were withdrawn from the study. A compliance rate of 90% within the first two weeks of the study was necessary in order to ensure proper compliance and allow assessment of the effect of stimulation. The overall stimulator compliance was downloaded from the stimulator at the end of the 5-week period of usage.

6.3.11 Statistical Analysis

All statistical analyses were carried out using SPSS (SPSS for Mac, version 23, IBM Corporation). The Shapiro-Wilk test was used to analyse normality of the data. As

this study follows a repeated measures design, data were fitted to a general linear repeated measures model to assess differences in time and between the stimulation and placebo-controlled groups. The Greenhouse-Geisser correction was used to correct any violations to the assumption of sphericity. Where appropriate, unpaired T test/ Mann Whitney U Test was carried out to assess group differences.

6.4 Results

A total of thirty-seven patients took part in this study. Data from twenty-six patients were included in the final analysis. Six patients withdrew from the study, while five patients were excluded due to issues of low compliance; patients who were unable to attain a compliance rate of 90% within the first two weeks of the study were excluded. This compliance rate was necessary in order to allow assessment of the effect of stimulation. The demographic details for the twenty-six patients included in this study are shown in Table 6.1.

Table 6.1 Demographic Details of Patients in Each Group

	Stimulation Group	Placebo-Controlled Group	Total Range
Age (years)	65 ± 7.30	66 ± 5.29	51 – 79
Gender	7 female; 6 male	6 female; 7 male	————
Weight (kg)	83.93 ± 22.58	86.94 ± 17.99	60.32 – 149.23
BMI (kg/ m^2)	30 ± 7.30	30 ± 5.17	22 – 50
Length of hospital stay (days)	5 ± 0.28	5 ± 0.55	4 – 6
Physiotherapy	12/13	11/13	————

Demographics represent Mean ± SD. There were 13 patients in each group; physiotherapy figures represent the number of patients out of 13 that attended physiotherapy in the post-discharge period.

6.4.1 Physical Activity Levels

Five full days of data from each week was used for analysis. Data from four patients were excluded from analysis, as a full five days of data was not collected due to the ActivPAL^{TM} battery prematurely losing power. This resulted in an analysis that included 22 patients in total, with eleven patients in each group. The data were normalised and expressed as a percentage of pre-surgery values.

6.4.1.1 Step Count and Stepping Time

As expected, the normalised number of steps taken per week significantly reduced immediately following discharge in both groups. The normalised step count increased week on week over the study period but remained significantly lower post-discharge versus pre-surgery (Figure 6.5, Table 6.2). There was no significant difference in normalised step counts between the two groups (P = 0.946). The total normalised time patients spent performing a stepping activity mirrored the normalised step count results. While the normalised stepping time did increase over the post-discharge period for both groups (Figure 6.6), there were no significant differences observed between the two groups (P = 0.874).

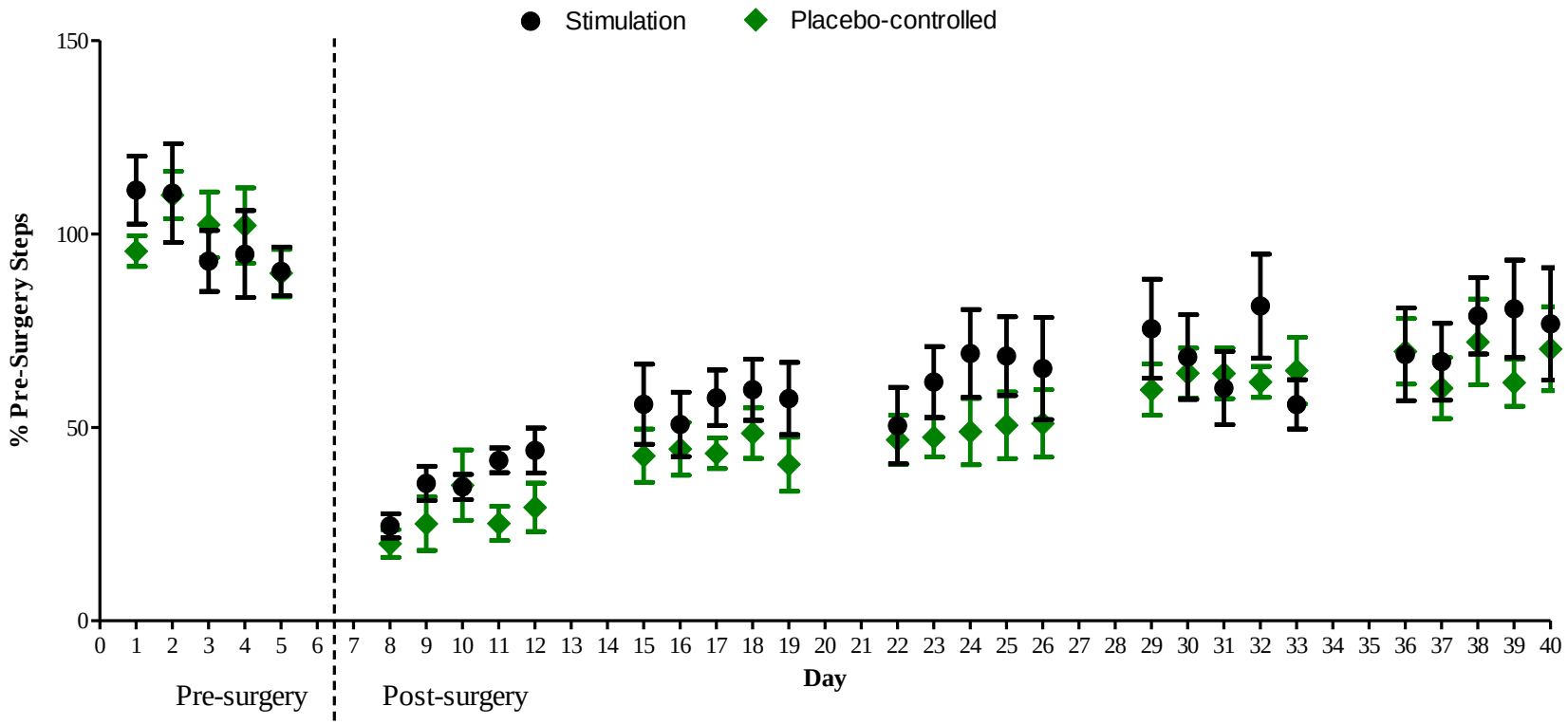

Figure 6.5 Normalised step counts. No significant differences between groups. All data represent mean ± SEM. N = 22.

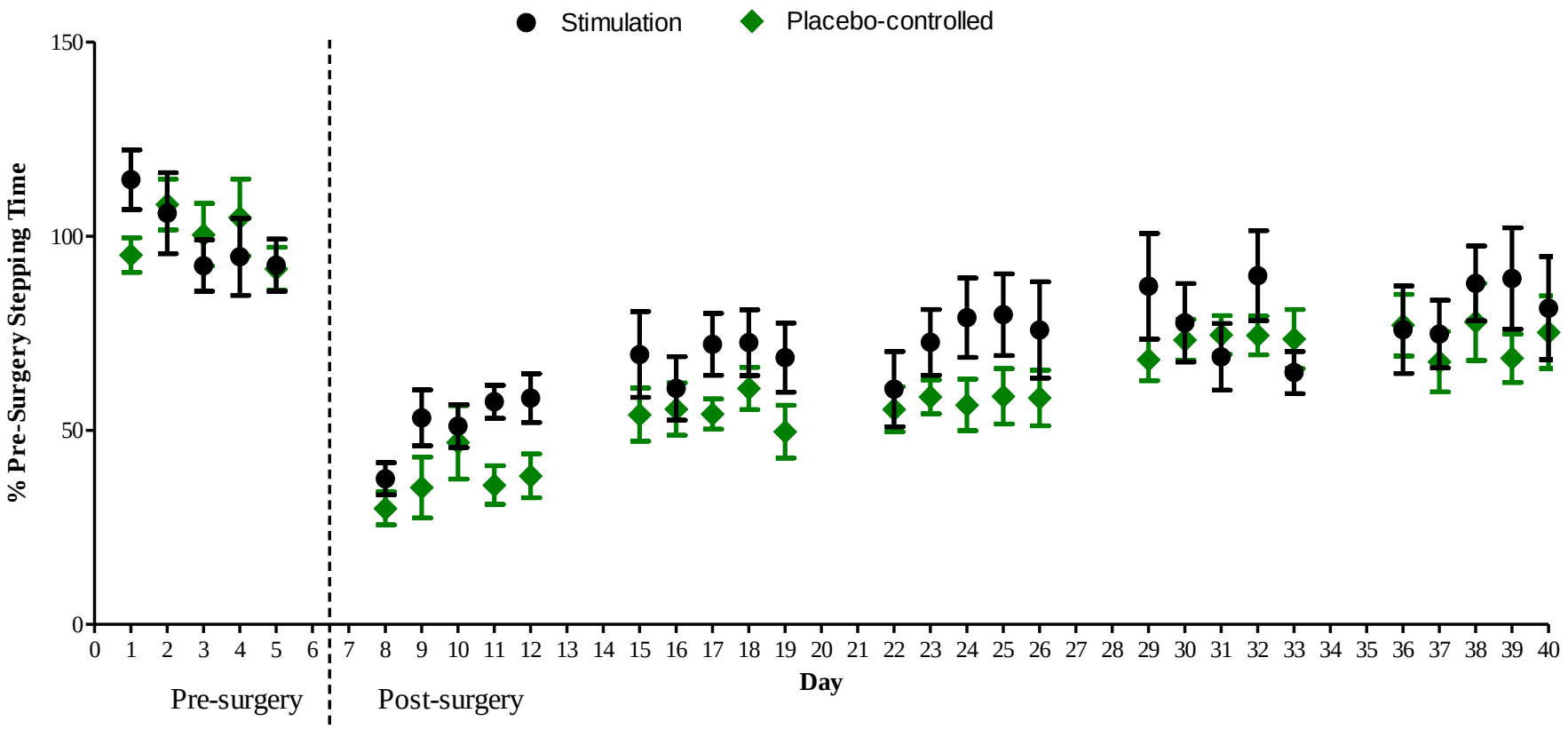

Figure 6.6 Normalised time spent stepping. No significant differences between groups. All data represent mean ± SEM. N = 22.

Table 6.2 Descriptive Statistics for the Step Counts taken by Each Group

	Pre-surgery	2 weeks post-surgery	3 weeks post-surgery	4 weeks post-surgery	5 weeks post-surgery	6 weeks post-surgery
Stimulation Group Step Counts						
Mean	35052	11964	17931	19510	21085	22899
SD	13010	3964	5189	6493	5226	7126
Minimum	18048	5536	6446	9534	14130	12814
Maximum	60268	18678	25646	28234	28628	35472
Placebo-controlled group Step Counts						
Mean	36435	10241	16456	18283	23254	25187
SD	13524	7515	9075	11265	11003	15083
Minimum	16420	980	5478	5550	7660	6444
Maximum	61680	27598	34546	39306	41994	55178

SD = standard deviation.

6.4.1.2 Sitting/lying Time

The normalised time spent sitting/lying increased significantly immediately following discharge but remained relatively constant over the 5 weeks post discharge (Figure 6.7). The placebo-controlled group spent a significantly greater normalised time sitting/lying during weeks 1, 2 and 3 post-surgery (P = 0.020, 0.041 and 0.025 respectively; Figure 6.7).

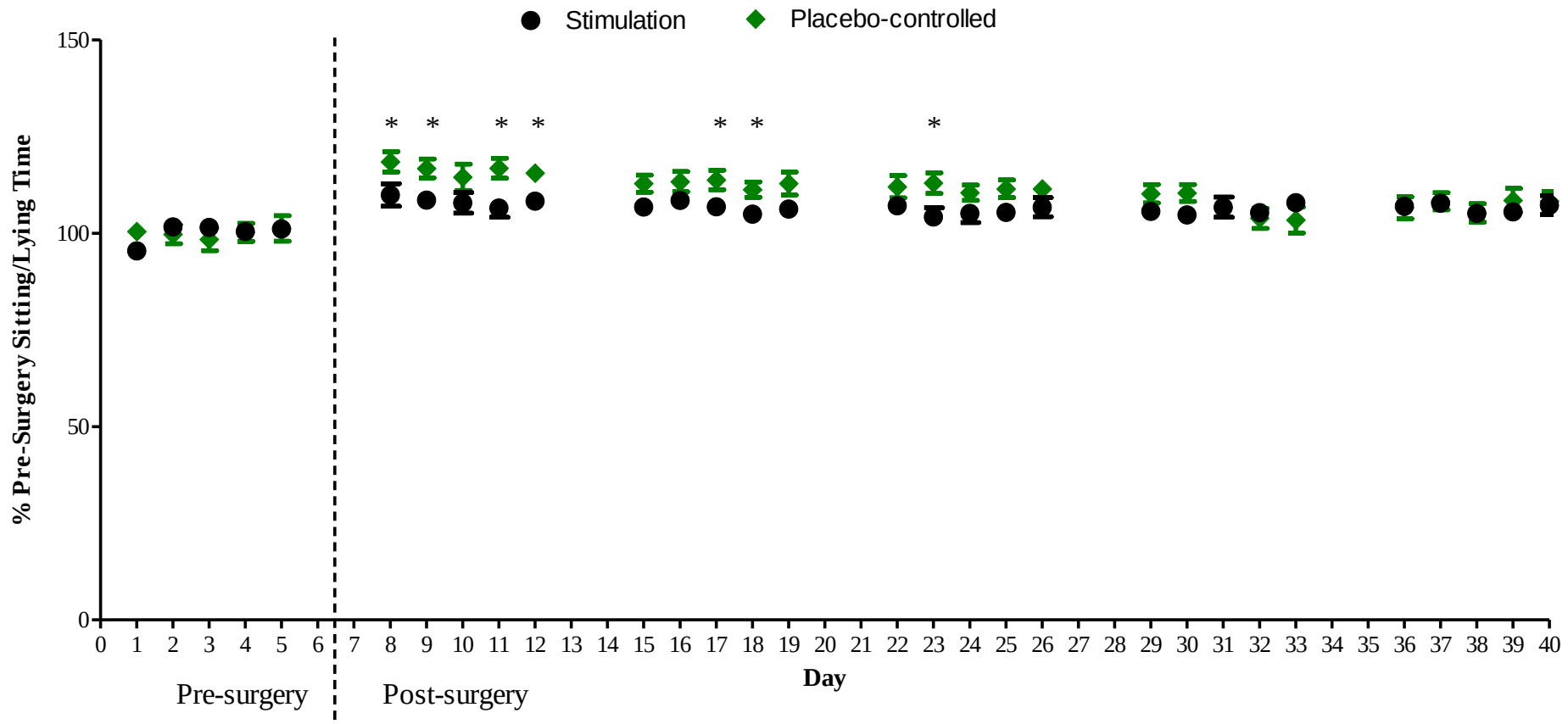

Figure 6.7 Normalised time sitting/lying. * P < 0.05 vs. stimulation (NMES) group at the same time point. All data represent mean ± SEM. N = 22.

6.4.1.3 Standing Time

As expected, the normalised time spent standing decreased immediately following surgery. The normalised time spent standing increased significantly from 2 and 3 weeks post-surgery to 5 weeks post-surgery bur remained below pre-surgery values (Figure 6.8). There was no significant difference in normalised time spent standing between the two groups ($P > 0.05$; Figure 6.8).

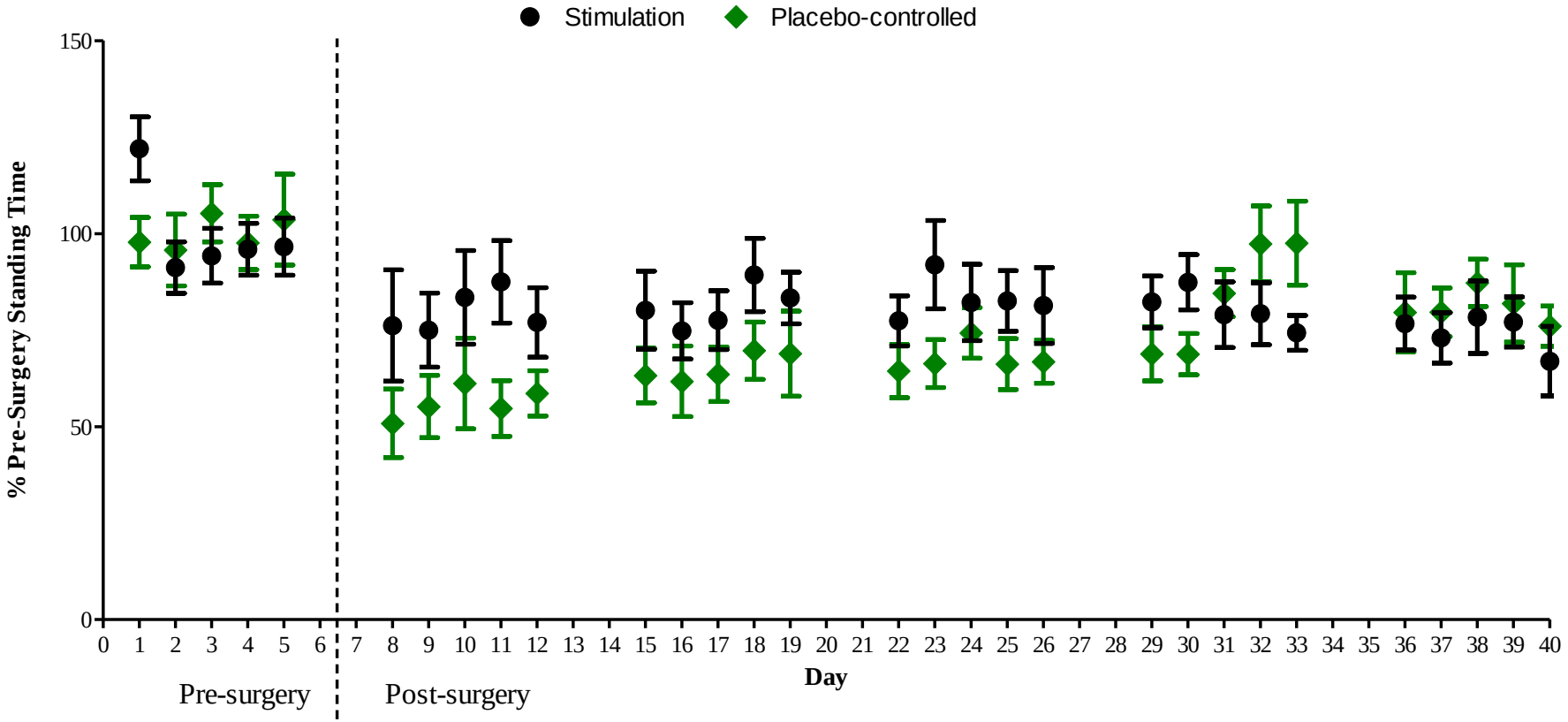

Figure 6.8 Normalised time spent standing. No significant differences between groups. All data represent mean ± SEM. N = 22.

6.4.1.4 Upright Time

Upright time is the sum of the stepping time and standing time. The normalised time spent upright was significantly greater in the stimulation group in week 1 post-discharge ($P = 0.045$; Figure 6.9). While the normalised time spent upright increased during the post-discharge phase examined, it remained below pre-surgery levels (Figure 6.9).

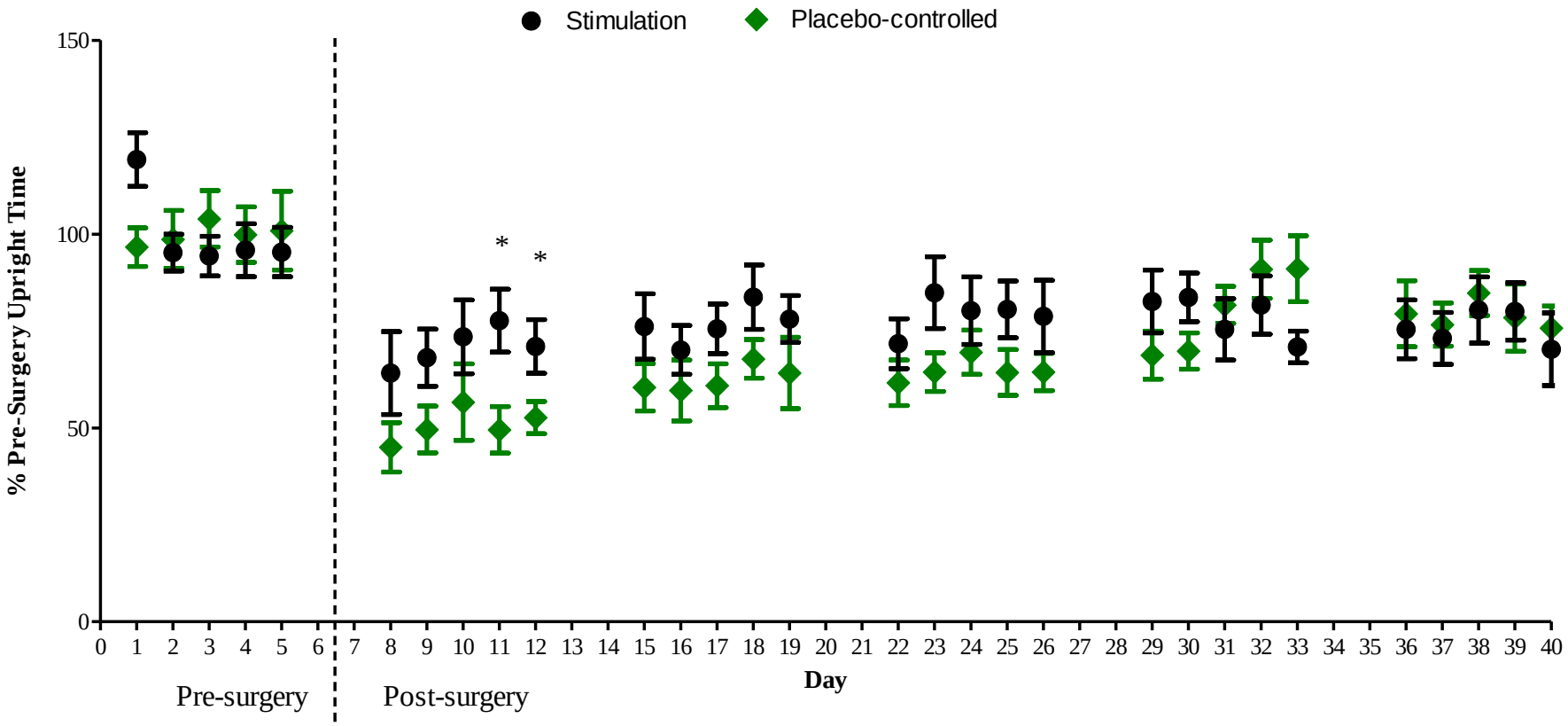

Figure 6.9 Normalised upright time. * P < 0.05 vs. placebo-controlled group at the same time point. All data represent mean ± SEM. N = 22.

To assess the effects of NMES on physical activity levels in greater detail, Stepping Bout data was extracted from the ActivPAL^{TM} monitor.

6.4.1.5 Effective Bout Duration (Centroid)

The normalised Effective Bout Duration (Centroid) remained steady throughout the study period and did not differ between the two groups ($P > 0.05$; Figure 6.10).

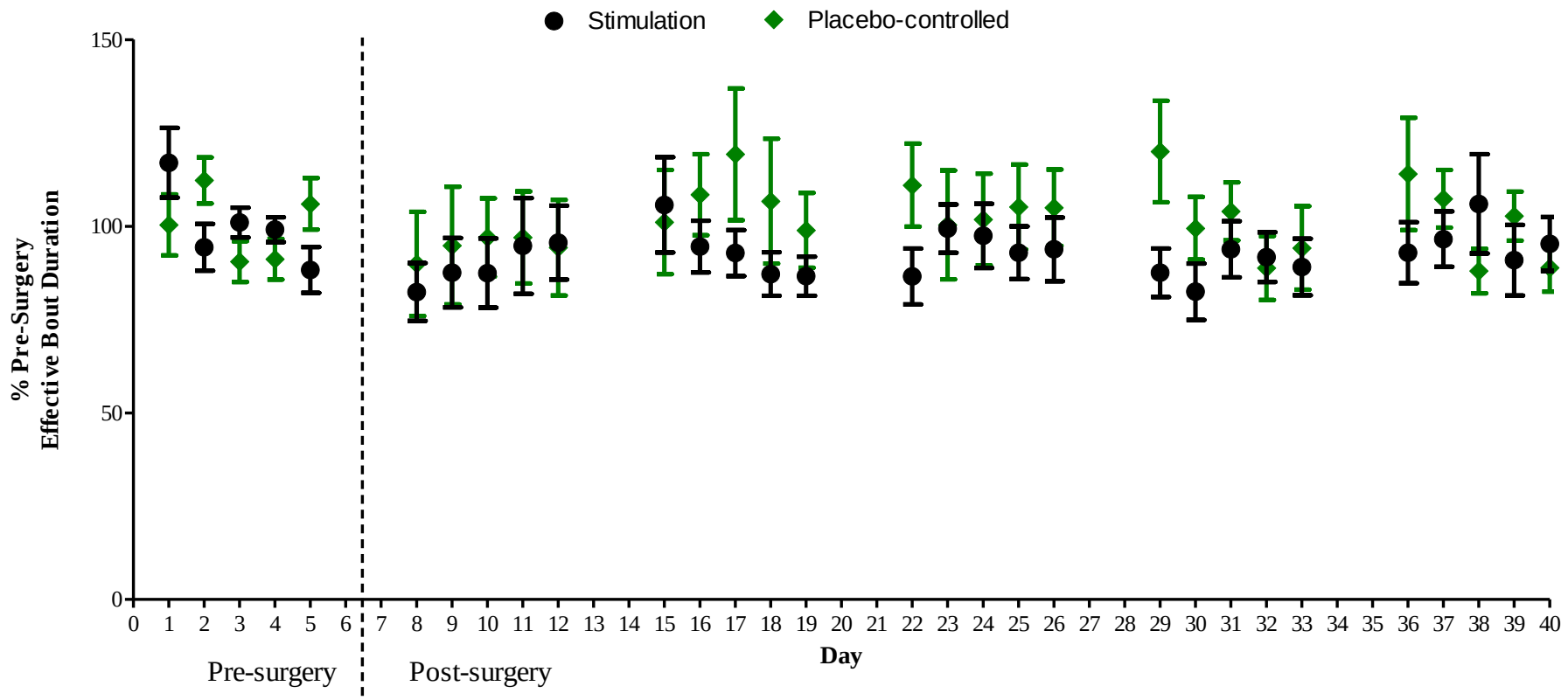

Figure 6.10 Normalised effective bout duration. No significant differences between groups. All data represent mean ± SEM. N = 22.

6.4.1.6 Number of Stepping Bouts

Significant differences were observed between the two groups for normalised number of Stepping Bouts (Figure 6.11). The stimulation group was found to have significantly greater normalised number of Stepping Bouts during the first four weeks post-discharge (P = 0.003, 0.013, 0.002, 0.011 for weeks 1, 2, 3, and 4 post-discharge respectively; Figure 6.11).

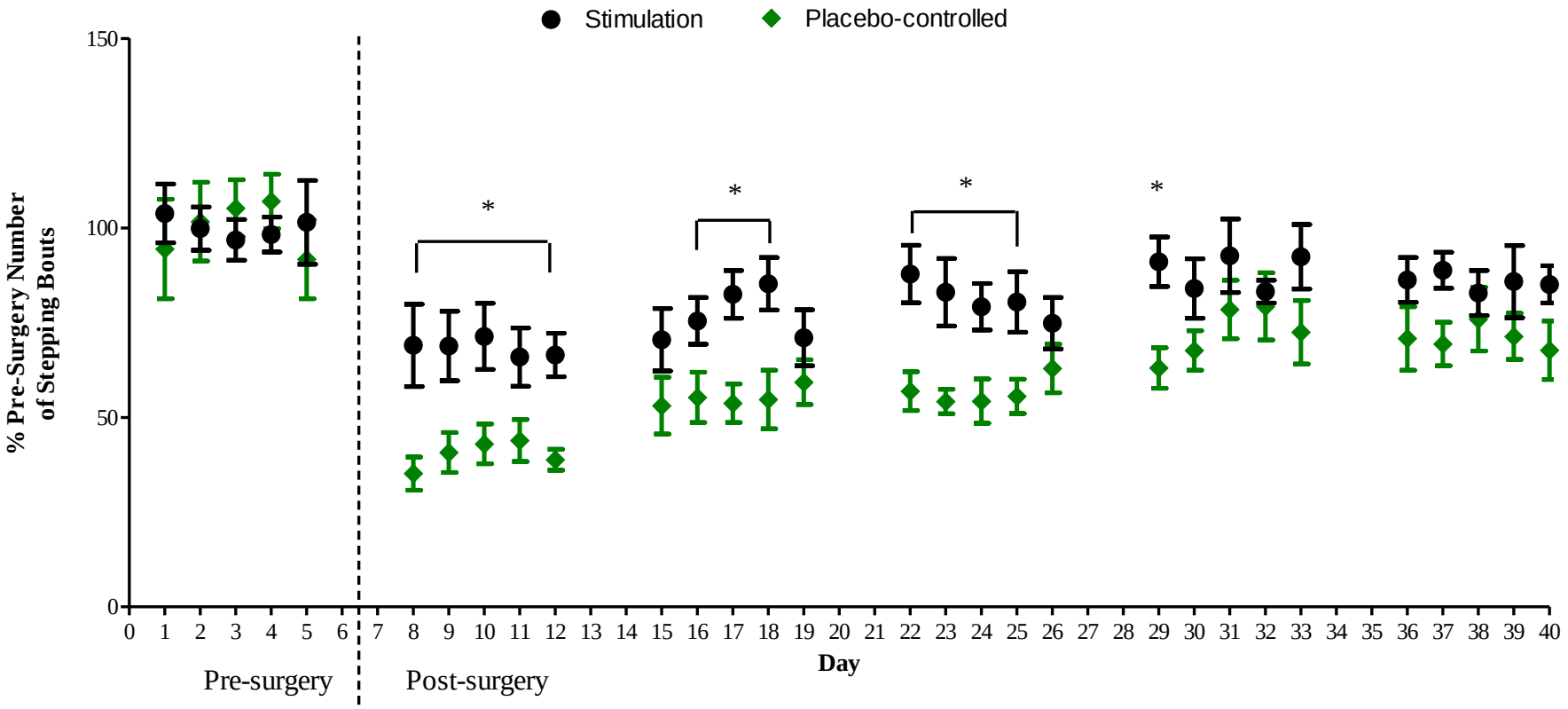

Figure 6.11 Normalised number of Stepping Bouts. * P < 0.05 vs. placebo-controlled group at the same time point. All data represent mean ± SEM. N = 22.

6.4.1.7 Sum of Stepping Bouts of Duration ≥ 1, ≥ 5 and ≥ 10 Minutes

The normalised sum of Stepping Bouts of duration ≥ 1, ≥ 5 or ≥ 10 minutes did not differ between the two groups ($P > 0.05$ for all; Figures 6.12, 6.13 and 6.14 respectively).

Further analysis on physical activity measures was carried out looking at changes per subject, whereby the same conclusions were found as with the analysis looking at changes per group.

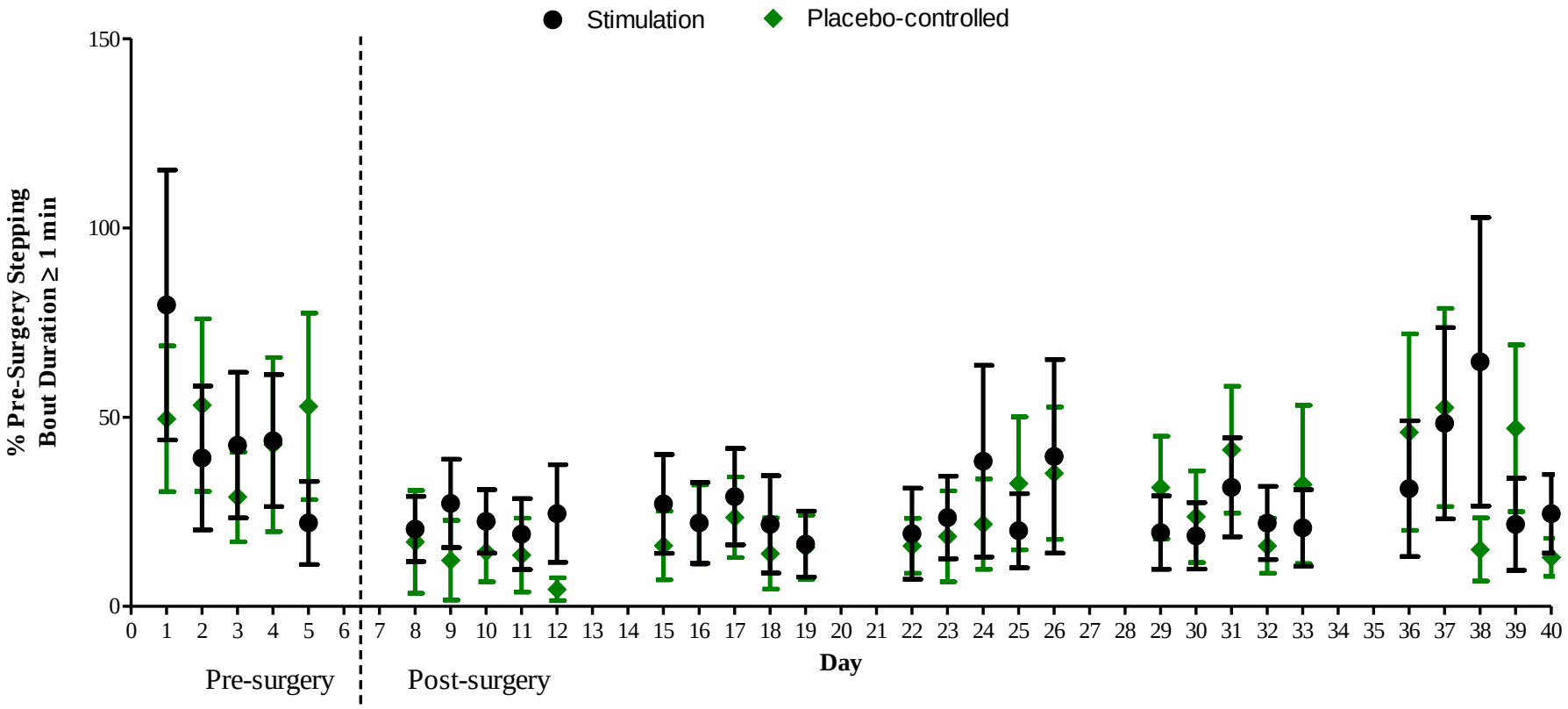

Figure 6.12 Normalised sum of Stepping Bouts of duration ≥ 1 minute. No significant differences between groups. All data represent mean ± SEM. N = 22.

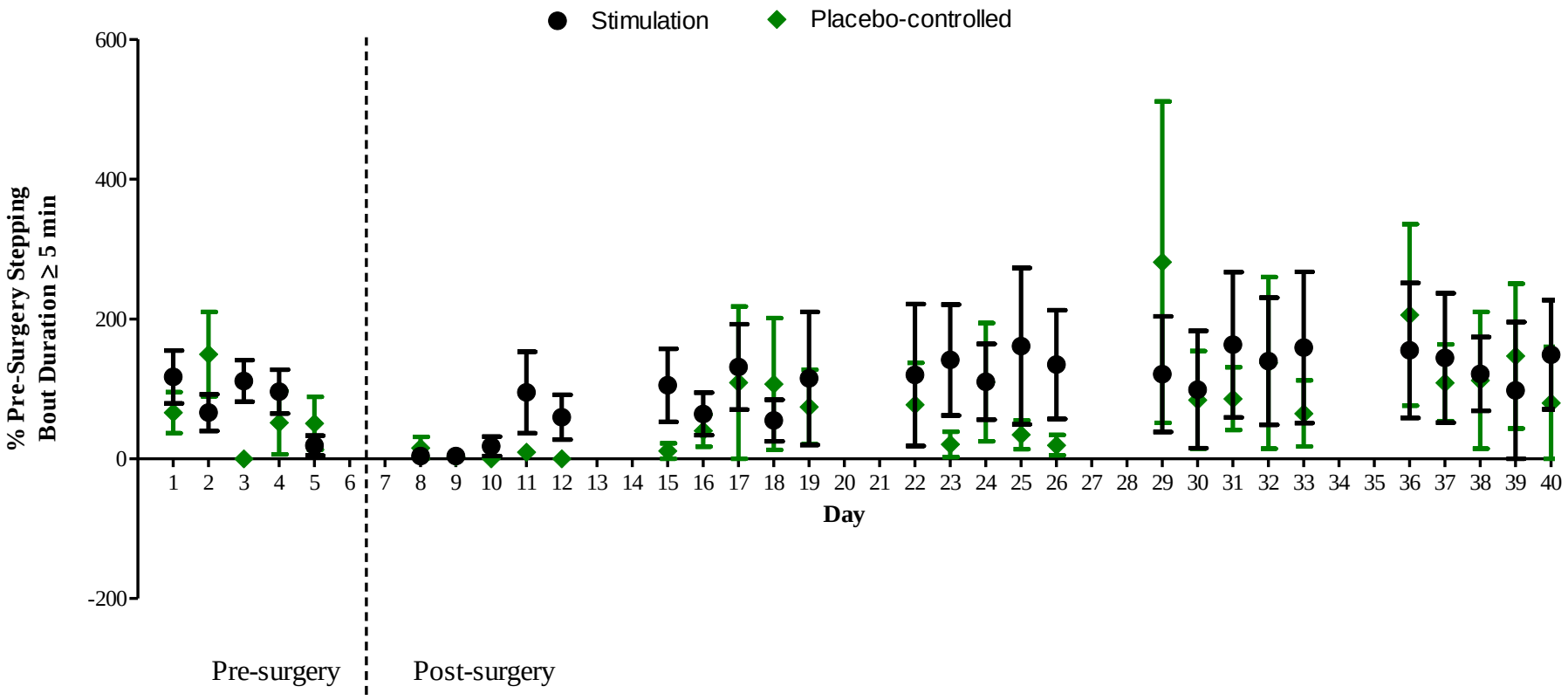

Figure 6.13 Normalised sum of Stepping Bout durations of ≥ 5 minutes. No significant differences between groups. All data represent mean ± SEM. N = 22.

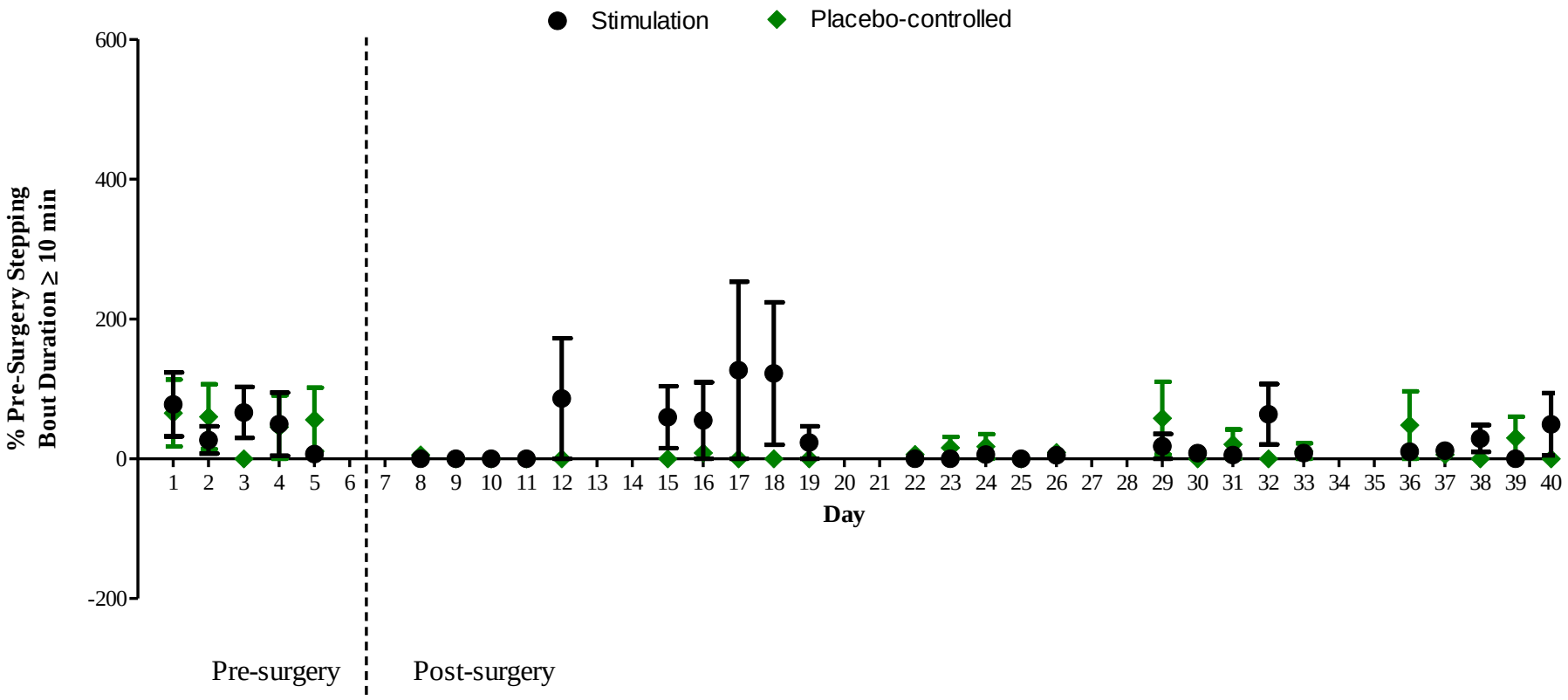

Figure 6.14 Normalised sum of Stepping Bout durations of 10 ≥ minutes. No significant differences between groups. All data represent mean ± SEM. N = 22.

6.4.2 Knee and Ankle Range of Motion

No significant differences were observed in ankle ROM measures between groups or over time (data not shown). There were no differences in knee flexion ROM between the NMES and placebo-controlled groups (P = 0.722). While flexion in the operated knee was reduced following surgery for both groups, it improved over the study period from the day after discharge until 6 weeks post-surgery (Figure 6.15). By week 4 post-surgery, knee flexion had returned to a level similar to that achieved pre-surgery.

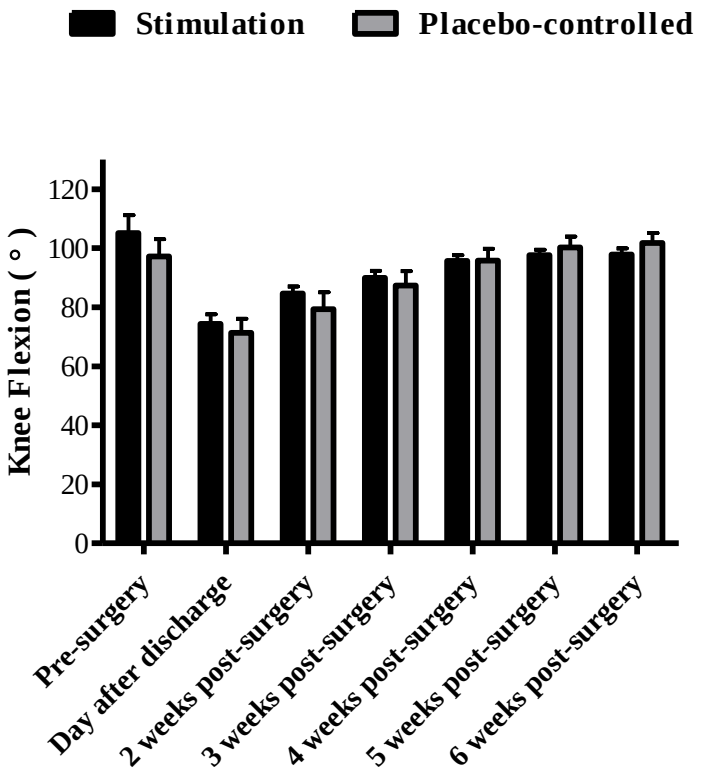

Figure 6.15 Knee flexion (in degrees). No significant differences between groups. Data represents mean ± SEM. N = 22.

When taken as the change in knee flexion (in degrees) from the day after discharge, there was a trend towards the stimulation group achieving a greater change in knee flexion in each successive week following the day after discharge. However, this did not reach statistical significance (P = 0.477; Figure 6.16). There was no significant difference in the rate of change of knee flexion (% change) between groups (data not shown).

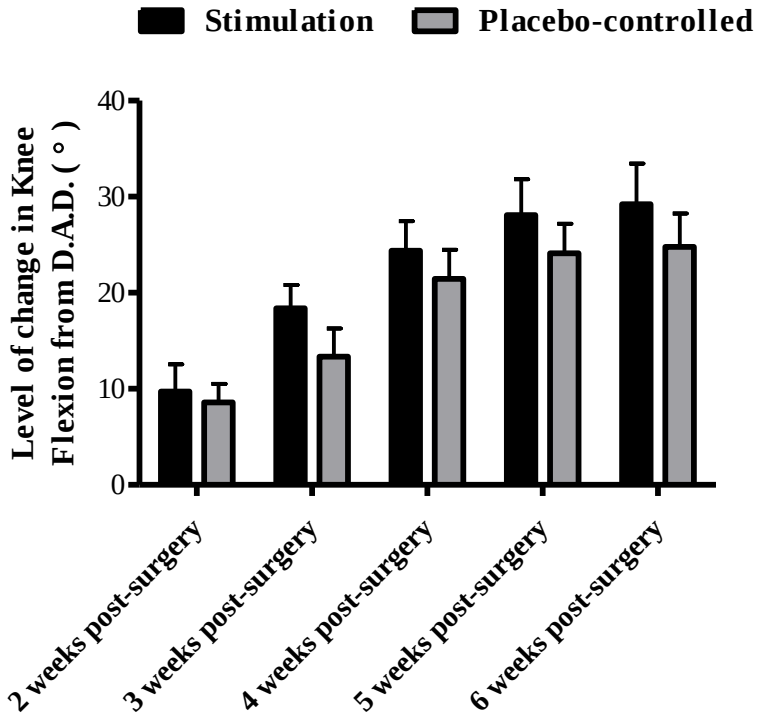

Figure 6.16 Change in knee flexion (in degrees) from the day after discharge. No significant differences between groups Data represent mean ± SEM. N = 22.

6.4.3 Lower Limb Swelling

No changes were observed in figure-of-8 measures between the NMES and placebo-controlled groups (P>0.05 for all measures, Figure 6.17).

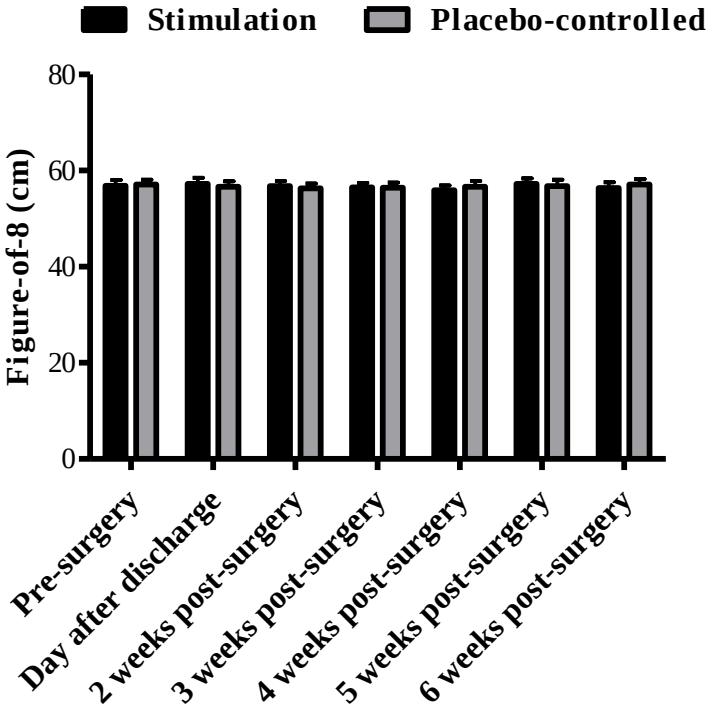

Figure 6.17 Figure-of-8 measures(cm). No significant differences between groups. Data represent mean ± SEM. N =22.

Calf circumference and ankle circumference measures were carried out in a subset of twelve patients. While the stimulation group had a greater calf circumference throughout the study, there was no significant difference in calf circumference between the NMES and placebo-controlled groups (P=0.357). Overall, calf circumference significantly increased on the day after discharge compared to pre-surgery (P=0.038) and decreased over time for the remainder of the study period. This decrease in calf circumference was significant from 3 to 6 weeks post-surgery versus day after discharge measures (Figure 6.18). There was no difference in ankle circumference measurements between the NMES and placebo-controlled groups (P > 0.05 for all measures; data not shown).

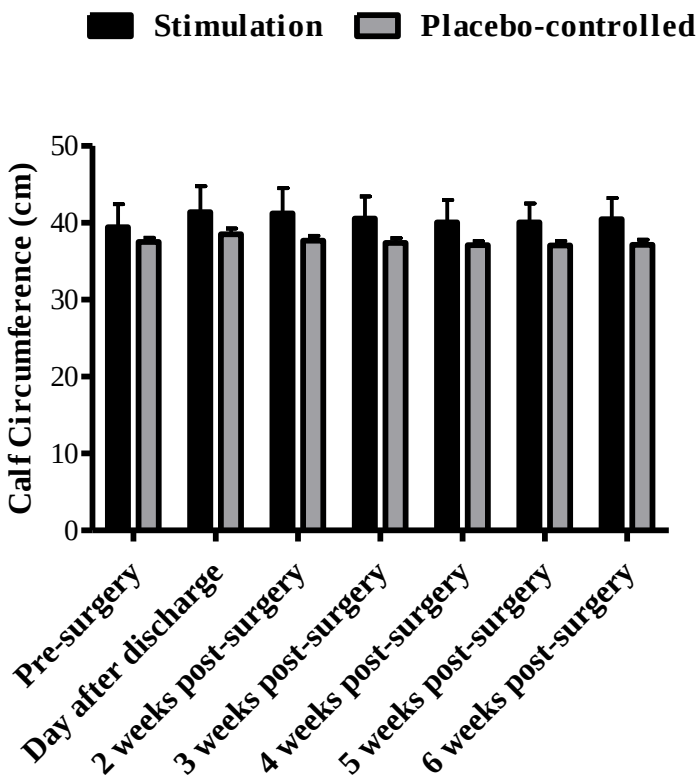

Figure 6.18 Calf circumference measures (cm). No significant differences between groups. Data represent mean ± SEM. N = 12.

6.4.4 NMES Therapy Compliance

The compliance to the NMES therapy was measured on the stimulator for the duration of the post-discharge period of the study. Over this period, the stimulation group had an average session compliance rate of 95% and an average time compliance rate of 95%. The placebo-controlled group had an average session compliance rate of 93% and an average time compliance rate of 94%.

6.5 Discussion

TKA is carried out primarily due to the presence of osteoarthritis and the limitation on daily physical activity and function it imposes. While it is largely considered to be a very successful surgery, functional recovery post-TKA can often be less than desirable [5, 55, 56]. This study assessed the effectiveness of a home-based NMES programme as an aid to functional recovery in the acute phase following TKA discharge, with a focus on measures of physical activity levels, joint range of motion and lower limb swelling. Improvements in these measures are essential for achieving functional recovery post-TKA.

Physical activity provides a protective effect against osteoarthritis and is recommended to reduce pain and improve function [12, 57]. Post-surgery, the benefit of increased physical activity levels is well recognised. The American Academy of Orthopaedic Surgeons recommend physical activity as a vital component of home care in the first 3 to 6 weeks post-TKA, with patients expected to resume normal activities of daily living within this timeframe [10]. However, gains in functional performance post-TKA are often variable and can remain limited after TKA [12]. While physical activity does not directly measure functional performance, functional performance can be enhanced and indirectly measured by increases in physical activity [12].

The overall influence of TKA on physical activity levels in the short-term is relatively unknown [12]. When Paxton et al (2015) carried out a review of the literature examining physical activity post-TKA, several studies reported on physical activity levels at a variety of time points post-surgery [12]. The majority of the studies included for review reported upon physical activity levels measured in the intermediate to long-term post-surgery phase, i.e. from 3 months to 20 years post- TKA. These studies utilised a variety of different physical activity assessment methods, including self-report questionnaires and accelerometry [12]. Only two of the included studies reported upon activity levels assessed by accelerometry within the short-term post-TKA phase, i.e. up to 6-weeks post-TKA [58, 59].

Hayes et al (2011) utilised the Intelligent Device for Energy Expenditure and Activity (IDEEA), a system of five accelerometers, to assess the percentage of time TKA patients spent sitting, standing, lying/reclining and in walking/stepping/transitions between movements [58]. Activity data was collected at five different time points: pre-surgery, 6 weeks post-surgery, 3 months post-surgery, 6 months post-surgery and 12 months post-surgery. The type of activity carried out did not significantly change over the five recording periods and patients were reported to spend less than 5% of the recorded time walking, stepping or in transitions between movements. There were no significant differences observed in the percentage of time patients spent walking, stepping or in transitions between movements between any time points [58]. Krenk et al (2013) also assessed physical activity levels in the short-term post-TKA using actigraphy [59]. The authors compared activity counts per day at pre-surgery to 4 and 6 days post-surgery. Unsurprisingly, counts per day were reduced at both 4 and 6 days post-surgery compared to pre-surgery.

Krenk et al has shown that in the immediate days following TKA, up to the sixth post-operative day, there is a decrease in activity performed by patients. While this result is to be expected so soon after surgery, results presented by Hayes et al are somewhat surprising with no increase in activity carried out by patients at any time point from 6 weeks post-surgery to 12 months post-surgery compared to pre-surgery levels. The results of our study demonstrate the beneficial effects of NMES in enhancing physical activity levels within the 6-week post-TKA phase.

NMES is a proven beneficial therapy used to enhance both blood flow and muscle strength within the lower limbs [36, 42, 46] and in this study was applied to the calf muscle in the home to assist in recovery post-TKA. The calf muscle is a key muscle involved in both ambulation and musculo-venous health, and thus its activation/use is key in aiding recovery post-TKA. Results of this study demonstrate the effectiveness of NMES applied to the calf muscle in enhancing physical activity levels in the early post-discharge phase.

Although there were no significant differences observed between the two groups for measures of step counts, time spent stepping, time spent standing, or effective bout duration (centroid), patients in the NMES group were found to spend a significantly greater time upright (Figure 6.9) and to carry out a significantly greater number of Stepping Bouts (Figure 6.11) within the early post-discharge period. In addition, patients in the NMES group spent significantly lesser time sitting/lying in the early post-discharge period compared to the placebo-controlled group (Figure 6.7). These results demonstrate the ability of NMES to enhance functional recovery post-TKA in the early post-discharge period as they show that use of NMES encourages physical activity by decreasing the time patients spend sitting/lying, increasing the time patients spend upright and increasing the number of Stepping bouts carried out while upright. These results demonstrate the benefit of NMES in aiding in the progression from limited mobility to increased functional ability and independence in the early post-discharge phase.

There were also no group differences observed for the sum of Stepping Bout durations $\geq$ 1 minute, $\geq$ 5 minutes or $\geq$ 10 minutes. These bout durations were investigated as it has been suggested within the literature that accumulating activity in several short bouts, such as $\geq$ 1, 5 or 10 minutes, may be as beneficial as one continuous bout of activity of similar total duration [60-62]. MacFarlane et al (2006) investigated activity bouts of 30 minutes and of $\leq$ 6 minutes in sedentary adults aged between 35 and 50 years. While one group carried out 30-minute continuous activity bouts per day, 3 to 4 days per week, the second group carried out 6-minute activity bouts 5 times per day, 4 to 5 days per week [61]. The authors reported no significant differences in energy expenditure between the two groups and found both groups to significantly improve their VO_2 max (measure of aerobic fitness). In conclusion, the authors stated that accumulating several short bouts of physical activity can provide significant improvements in sedentary adult fitness and is not too unalike one continuous bout of activity of similar total duration [61].

Similarly, Schmidt et al (2001) investigated if three 10-minute bouts of activity per day were as effective as one continuous bout of 30-minutes in overweight, female college students [60]. VO_2 max was found to increase significantly while measures of weight, body mass index and circumference were found to significantly decrease in all groups. Similar to the conclusion reached by MacFarlane et al, Schmidt et al concluded that activity accumulated in several short bouts has similar effects on fitness and weight loss as one continuous bout of similar duration [60]. When Glazer et al (2013) investigated activity bouts of both < 10 minutes and ≥ 10 minutes in women involved in a heart study, the authors concluded that bouts of activity < 10 minutes may favourably influence cardiovascular risk in a similar manner to bouts ≥ 10 minutes [63]. In addition, several physical activity guidelines recommend that activity be carried out in bouts of at least ten minutes to achieve health benefits [63, 64]. As such, the sum of Stepping Bout durations of ≥ 1, 5 or 10 minutes were investigated within this current study. No significant differences were observed between the two groups for any sum of Stepping Bout durations.

Within this study, TKA patients carried out very few Stepping Bouts of greater than or equal to 10 minutes, which may not be completely surprising within the early post-discharge phase assessed, combined with findings that walking activities associated with daily living most likely involve short walking bouts with only a few consecutive steps without a break accumulated in periods of less than one minute [65, 66]. The majority of Stepping Bouts carried out by TKA patients in this study were of duration of 2 minutes or less for patients in both groups (data not shown) during the early post-discharge phase examined. As the addition of NMES increases the number of these Stepping Bouts carried out (Figure 6.11), this further suggests NMES is a beneficial method of enhancing physical activity and hence aiding in functional recovery post-discharge.

However, while the application of NMES led to increased physical activity levels in the early post-discharge phase, no significant effect of NMES was observed on either knee range of motion or swelling measurements.

The importance of an increased knee flexion post-TKA is well known, with a greater knee flexion corresponding to a greater functional capacity. While use of NMES did result in a trend towards a greater knee flexion in the early post-discharge phase, this was not significant. NMES was not found to have any significant effect on swelling measures, but the observed results suggest that lower limb swelling is not a major issue in TKA patients post-discharge. Swelling may be of greater consequence immediately post-surgery and application of NMES pre-discharge may provide benefit with regard to swelling reduction.

NMES is a beneficial haemodynamic and muscle strengthening therapy that has also now been shown to support increased physical activity levels in the short-term early post-TKA discharge phase. The overall results of this study show great promise and suggest that optimisation of an NMES protocol applied at an earlier time point post-surgery is likely to provide even further benefit in functional recovery in the early stages of recovery post-TKA. Moreover, the rate of compliance with use of the NMES device was excellent with a 95% time compliance rate observed in the stimulation group over the five-week period of usage, further adding to its promise as a method of assisting functional recovery post-TKA.

6.5.1 Limitations

Information regarding the extent patients fully adhered to the prescribed physiotherapy exercises to be carried out three times daily is lacking, as the clinical team did not monitor this element. The therapeutic effect of these exercises is not fully known nor is the effect that these exercises may have had on the effectiveness of the NMES protocol. This is an important consideration for future studies. Furthermore, with regard to physical activity levels, the effect of crutch walking was not accounted for with regard to step count. There is currently little information regarding the effect crutch walking may have, and while all patients utilised crutches post-surgery, this is certainly a consideration for future studies.

6.5.2 Conclusions

The results of this study demonstrate the beneficial effect of NMES in enhancing physical activity levels during the short-term post-discharge phase by significantly increasing the time patients spend upright, decreasing the time patients spend sitting/lying and increasing the number of Stepping Bouts carried out. These results warrant further investigation into the use of an optimised NMES protocol pre-discharge whereby improvements in knee ROM and swelling may also be observed. Application of NMES at an earlier time point post-TKA or for a greater duration post-discharge is likely to provide excellent functional benefit for TKA patients in the short-term.

6.6 References

[1] Kurtz, S., Ong, K., Lau, E., Mowat, F., and Halpern, M., "Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030," *J Bone Joint Surg Am,* vol. 89, no. 4, pp. 780-5, Apr 2007.

[2] Patel, A., Pavlou, G., Mujica-Mota, R. E., and Toms, A. D., "The epidemiology of revision total knee and hip arthroplasty in England and Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset," *Bone Joint J,* vol. 97-B, no. 8, pp. 1076-81, Aug 2015.

[3] Carr, A. *et al.*, "Knee replacement," *Lancet,* vol. 379, no. 9823, pp. 1331-40, Apr 7 2012.

[4] de Groot, I. B., Bussmann, H. J., Stam, H. J., and Verhaar, J. A., "Small increase of actual physical activity 6 months after total hip or knee arthroplasty," *Clin Orthop Relat Res,* vol. 466, no. 9, pp. 2201-8, Sep 2008.

[5] Bade, M., Kohrt, W., and Stevens-Lapsley, J., "Outcomes before and after total knee arthroplasty compared to healthy adults," *J Orthop Sports Phys Ther,* vol. 40, no. 9, pp. 559-67, Sep 2010.

[6] Tamir, L., Hendel, D., Neyman, C., Eshkenazi, A., Ben-Zvi, Y., and Zomer, R., "Sequential foot compression reduces lower limb swelling and pain after total knee arthroplasty," *J Arthroplasty,* vol. 14, no. 3, pp. 333-8, Apr 1999.

[7] Holm, B., Kristensen, M., Bencke, J., Husted, H., Kehlet, H., and Bandholm, T., "Loss of knee-extension strength is related to knee swelling after total knee arthroplasty," *Arch Phys Med Rehabil,* vol. 91, no. 11, pp. 1770-6, Nov 2010.

[8] Windisch, C., Kolb, W., Kolb, K., Grutzner, P., Venbrocks, R., and Anders, J., "Pneumatic compression with foot pumps facilitates early postoperative mobilisation in total knee arthroplasty," *Int Orthop,* vol. 35, no. 7, pp. 995-1000, Jul 2011.

[9] Munk, S., Jensen, N., Andersen, I., Kehlet, H., and Hansen, T., "Effect of compression therapy on knee swelling and pain after total knee arthroplasty," *Knee Surg Sports Traumatol Arthrosc,* vol. 21, no. 2, pp. 388-92, Feb 2013.

[10] American Academy of Orthopaedic Surgeons. 2015. Total Knee Replacement. http://orthoinfo.aaos.org/topic.cfm?topic=A00389. Archived at: http://www.webcitation.org/6pQUlT33t

[11] Tudor-Locke, C., Washington, T. L., and Hart, T. L., "Expected values for steps/day in special populations," *Prev Med,* vol. 49, no. 1, pp. 3-11, Aug 2009.

[12] Paxton, R., Melanson, E., Stevens-Lapsley, J., and Christiansen, C., "Physical activity after total knee arthroplasty: A critical review," *World J Orthop,* vol. 6, no. 8, pp. 614-22, Sep 18 2015.

[13] Brock, T., Sprowson, A., Muller, S., and Reed, M., "Short-stretch inelastic compression bandage in knee swelling following total knee arthroplasty study (STICKS): study protocol for a randomised controlled feasibility study," *Trials,* vol. 16, p. 87, Mar 11 2015.

[14] Chan, E., Teo, Y., Assam, P., and Fransen, M., "Functional discharge readiness and mobility following total knee arthroplasty for osteoarthritis: a comparison of analgesic techniques," *Arthritis Care Res (Hoboken),* vol. 66, no. 11, pp. 1688-94, Nov 2014.

[15] Husted, H., Gromov, K., Malchau, H., Freiberg, A., Gebuhr, P., and Troelsen, A., "Traditions and myths in hip and knee arthroplasty: A narrative review," *Acta Orthopaedica*, vol. 85, no. 6, pp. 548-555, 09/11/accepted 2014.

[16] UPMC Beacon Centre for Orthopaedics. Guidelines for Patients having a Total Knee Replacement. http://www.beaconhospital.ie/images/physio/Knee_replacement.pdf http://www.webcitation.org/6pQVDPGXy

[17] UF Health Rehab Centre- Shands Hospital, "Knee Replacement Surgery Patient Information Manual: Maximizing Your New Knee(s)," UFHealth University of Florida Health. https://www.ortho.ufl.edu/sites/ortho.ufl.edu/files/pdf/education/KneeReplacementSurgeryMaximizingYourNewKnee.pdf http://www.webcitation.org/6pQVNTvjA

[18] O'Connell, S. *et al.*, "The Use of Intermittent Pneumatic Compression in Orthopedic and Neurosurgical Postoperative Patients: A Systematic Review and Meta-analysis," *Ann Surg,* vol. 263, no. 5, pp. 888-9, May 2016.

[19] Devers, B., Conditt, M., Jamieson, M., Driscoll, M., Noble, P., and Parsley, B., "Does greater knee flexion increase patient function and satisfaction after total knee arthroplasty?," *J Arthroplasty,* vol. 26, no. 2, pp. 178-86, Feb 2011.

[20] de Groot, I., Bussmann, J., Stam, H., and Verhaar, J., "Actual everyday physical activity in patients with end-stage hip or knee osteoarthritis compared with healthy controls," *Osteoarthritis Cartilage,* vol. 16, no. 4, pp. 436-42, Apr 2008.

[21] Shephard, R., "Limits to the measurement of habitual physical activity by questionnaires," *Br J Sports Med,* vol. 37, no. 3, pp. 197-206; discussion 206, Jun 2003.

[22] Prince, S., Adamo, K., Hamel, M., Hardt, J., Gorber, S. C., and Tremblay, M., "A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review," *Int J Behav Nutr Phys Act,* vol. 5, p. 56, 2008.

[23] Tudor-Locke, C. and Bassett, D. R., Jr., "How many steps/day are enough? Preliminary pedometer indices for public health," *Sports Med,* vol. 34, no. 1, pp. 1-8, 2004.

[24] Tudor-Locke, C., Hatano, Y., Pangrazi, R. P., and Kang, M., "Revisiting "how many steps are enough?"," *Med Sci Sports Exerc,* vol. 40, no. 7 Suppl, pp. S537-43, Jul 2008.

[25] Kang, M., Marshall, S. J., Barreira, T. V., and Lee, J. O., "Effect of pedometer-based physical activity interventions: a meta-analysis," *Res Q Exerc Sport,* vol. 80, no. 3, pp. 648-55, Sep 2009.

[26] Brandes, M., Ringling, M., Winter, C., Hillmann, A., and Rosenbaum, D., "Changes in physical activity and health-related quality of life during the first year after total knee arthroplasty," *Arthritis Care Res (Hoboken),* vol. 63, no. 3, pp. 328-34, Mar 2011.

[27] Dahlgren, G., Carlsson, D., Moorhead, A., Hager-Ross, C., and McDonough, S., "Test-retest reliability of step counts with the ActivPAL device in common daily activities," *Gait Posture,* vol. 32, no. 3, pp. 386-90, Jul 2010.

[28] Dondzila, C., Swartz, A., Miller, N., Lenz, E., and Strath, S., "Accuracy of uploadable pedometers in laboratory, overground, and free-living conditions in young and older adults," *Int J Behav Nutr Phys Act,* vol. 9, p. 143, 2012.

[29] Storm, F., Heller, B., and Mazza, C., "Step detection and activity recognition accuracy of seven physical activity monitors," *PLoS One,* vol. 10, no. 3, p. e0118723, 2015.

[30] O'Connell, S. *et al.*, "These Shoes Are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps," *PLoS One,* vol. 11, no. 5, p. e0154956, 2016.

[31] O'Connell, S., ÓLaighin, G., and Quinlan, L., "When a Step Is Not a Step! Specificity Analysis of Five Physical Activity Monitors," *PLoS One,* vol. 12, no. 1, p. e0169616, 2017.

[32] Howe, T. and Rafferty, D., "Quadriceps activity and physical activity profiles over long durations in patients with osteoarthritis of the knee and controls," *J Electromyogr Kinesiol,* vol. 19, no. 2, pp. e78-83, Apr 2009.

[33] Tonelli, S., Rakel, B., Cooper, N., Angstom, W., and Sluka, K., "Women with knee osteoarthritis have more pain and poorer function than men, but similar physical activity prior to total knee replacement," *Biol Sex Differ,* vol. 2, p. 12, Nov 10 2011.

[34] Peiris, C., Taylor, N., and Shields, N., "Patients receiving inpatient rehabilitation for lower limb orthopaedic conditions do much less physical activity than recommended in guidelines for healthy older adults: an observational study," *J Physiother,* vol. 59, no. 1, pp. 39-44, Mar 2013.

[35] Taraldsen, K. *et al.*, "Physical behavior and function early after hip fracture surgery in patients receiving comprehensive geriatric care or orthopedic care--a randomized controlled trial," *J Gerontol A Biol Sci Med Sci,* vol. 69, no. 3, pp. 338-45, Mar 2014.

[36] Faghri, P., Votto, J., and Hovorka, C., "Venous hemodynamics of the lower extremities in response to electrical stimulation," *Arch Phys Med Rehabil,* vol. 79, no. 7, pp. 842-8, Jul 1998.

[37] Clarke-Moloney, M., Lyons, G., Breen, P., Burke, P., and Grace, P., "Haemodynamic study examining the response of venous blood flow to electrical stimulation of the gastrocnemius muscle in patients with chronic venous disease," *Eur J Vasc Endovasc Surg*, vol. 31, no. 3, pp. 300-5, Mar 2006.

[38] Corley, G. J., Breen, P. P., Grace, P. A., and G, ÓLaighin, "The effect of surface neuromuscular electrical stimulation and compression hosiery applied to the lower limb, on the comfort and blood flow of healthy subjects," *Conf Proc IEEE Eng Med Biol Soc*, vol. 2008, pp. 703-6, 2008.

[39] Broderick, B., O'Briain, D., Breen, P., Kearns, S., and ÓLaighin, G., "A pilot evaluation of a neuromuscular electrical stimulation (NMES) based methodology for the prevention of venous stasis during bed rest," *Med Eng Phys*, vol. 32, no. 4, pp. 349-55, May 2010.

[40] Griffin, M., Nicolaides, A., Bond, D., Geroulakos, G., and Kalodiki, E., "The efficacy of a new stimulation technology to increase venous flow and prevent venous stasis," *Eur J Vasc Endovasc Surg*, vol. 40, no. 6, pp. 766-71, Dec 2010.

[41] Corley, G., Breen, P., Birlea, S., Serrador, J., Grace, P., and ÓLaighin, G., "Hemodynamic effects of habituation to a week-long program of neuromuscular electrical stimulation," *Med Eng Phys*, vol. 34, no. 4, pp. 459-65, May 2012.

[42] Broderick, B., Breathnach, O., Condon, F., Masterson, E., and ÓLaighin, G., "Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty," *J Orthop Surg Res*, vol. 8, pp. 3-10, 2013.

[43] Broderick, B. *et al.*, "Comparative lower limb hemodynamics using neuromuscular electrical stimulation (NMES) versus intermittent pneumatic compression (IPC)," *Physiol Meas*, vol. 35, no. 9, pp. 1849-59, Sep 2014.

[44] Moini J. Anatomy and Physiology for Health Professionals. 2nd edition. Burlington, MA: Jones & Bartlett; 2011. ISBN: 1284090353.

[45] Popovic, M., Curt, A., Keller, T., and Dietz, V., "Functional electrical stimulation for grasping and walking: indications and limitations," *Spinal Cord,* vol. 39, no. 8, pp. 403-12, Aug 2001.

[46] Stevens-Lapsley, J., Balter, J., Wolfe, P., Eckhoff, D., and Kohrt, W., "Early neuromuscular electrical stimulation to improve quadriceps muscle strength after total knee arthroplasty: a randomized controlled trial," *Phys Ther,* vol. 92, no. 2, pp. 210-26, Feb 2012.

[47] Kern, H. *et al.*, "Electrical stimulation counteracts muscle decline in seniors," *Front Aging Neurosci,* vol. 6, p. 189, 2014.

[48] Dirks, M., Hansen, D., Assche, A. V., Dendale, P., and Loon, L. V., "Neuromuscular electrical stimulation prevents muscle wasting in critically ill comatose patients," *Clin Sci (Lond),* vol. 128, no. 6, pp. 357-65, Mar 2015.

[49] Wang, Y., Meng, F., Zhang, Y., Xu, M., and Yue, S., "Full-movement neuromuscular electrical stimulation improves plantar flexor spasticity and ankle active dorsiflexion in stroke patients: A randomized controlled study," *Clin Rehabil,* Aug 20 2015.

[50] Hsu, M.-J., Wei, S.-H., and Chang, Y.-J., "Effect of Neuromuscular Electrical Muscle Stimulation on Energy Expenditure in Healthy Adults," *Sensors (Basel, Switzerland),* vol. 11, no. 2, pp. 1932-1942, 2011.

[51] Maddocks, M. *et al.*, "Neuromuscular electrical stimulation to improve exercise capacity in patients with severe COPD: a randomised double-blind, placebo-controlled trial," *The Lancet Respiratory Medicine,* vol. 4, no. 1, pp. 27-36, 2016.

[52] PAL Technologies bibliography. Available at: http://www.paltechnologies.com/bibliography/

[53] Esterson, P. S., "Measurement of ankle joint swelling using a figure of 8*," *J Orthop Sports Phys Ther,* vol. 1, no. 1, pp. 51-2, 1979.

[54] Petersen, E. J. *et al.*, "Reliability of water volumetry and the figure of eight method on subjects with ankle joint swelling," *J Orthop Sports Phys Ther,* vol. 29, no. 10, pp. 609-15, Oct 1999.

[55] Walsh, M., Woodhouse, L., Thomas, S., and Finch, E., "Physical impairments and functional limitations: a comparison of individuals 1 year after total knee arthroplasty with control subjects," *Phys Ther,* vol. 78, no. 3, pp. 248-58, Mar 1998.

[56] Noble, P., Gordon, M., Weiss, J., Reddix, R., Conditt, M., and Mathis, K., "Does total knee replacement restore normal knee function?," Clin Orthop Relat Res, no. 431, pp. 157-65, Feb 2005.

[57] Hochberg, M. *et al.*, "American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee," *Arthritis Care Res (Hoboken)*, vol. 64, no. 4, pp. 465-74, Apr 2012.

[58] Hayes, D., Watts, M., Anderson, L., and Walsh, W., "Knee arthroplasty: a cross-sectional study assessing energy expenditure and activity," *ANZ J Surg*, vol. 81, no. 5, pp. 371-4, May 2011.

[59] Krenk, L., Jennum, P., and Kehlet, H., "Activity, sleep and cognition after fast-track hip or knee arthroplasty," *J Arthroplasty*, vol. 28, no. 8, pp. 1265-9, Sep 2013.

[60] Schmidt, W., Biwer, C., and Kalscheuer, L., "Effects of long versus short bout exercise on fitness and weight loss in overweight females," *J Am Coll Nutr*, vol. 20, no. 5, pp. 494-501, Oct 2001.

[61] Macfarlane, D., Taylor, L., and Cuddihy, T., "Very short intermittent vs continuous bouts of activity in sedentary adults," *Prev Med*, vol. 43, no. 4, pp. 332-6, Oct 2006.

[62] Glazer, N. L. *et al.*, "Sustained and shorter bouts of physical activity are related to cardiovascular health," *Med Sci Sports Exerc*, vol. 45, no. 1, pp. 109-15, Jan 2013.

[63] World Health Organization. 2010. Global Recommendations on Physical Activity for Health. http://apps.who.int/iris/bitstream/10665/44399/1/9789241599979_eng.pdf http://www.webcitation.org/6pQWG7Jps.

[64] "Physical Activity and Public Health in Older Adults," *Recommendation From the American College of Sports Medicine and the American Heart Association*, vol. 116, no. 9, pp. 1094-1105, 2007.

[65] Orendurff, M., Schoen, J., Bernatz, G., Segal, A., and Klute, G., "How humans walk: bout duration, steps per bout, and rest duration," *J Rehabil Res Dev*, vol. 45, no. 7, pp. 1077-89, 2008.

[66] Dall, P., McCrorie, P., Granat, M., and Stansfield, B., "Step accumulation per minute epoch is not the same as cadence for free-living adults," *Med Sci Sports Exerc*, vol. 45, no. 10, pp. 1995-2001, Oct 2013.

Chapter 7

General Discussion

The management/mitigation of factors associated with clinical complications and functional recovery are key aspects associated with a successful TKA. The main objectives of the research presented in this thesis were (1) to investigate the use of NMES as a method of preventing venous stasis and DVT, (2) to investigate the sensitivity and specificity of a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery and (3) to investigate the use of NMES in enhancing recovery post-TKA through measures of physical activity, joint range of motion and lower limb swelling.

In this context NMES was employed as a method to aid recovery following total knee arthroplasty focusing on two main areas: the complication of venous stasis and functional recovery assessment based on changes in physical activity, joint range of motion and lower limb swelling. The first two studies focused on investigating (1) the effectiveness of intermittent pneumatic compression (IPC) devices in mitigating the risk of venous stasis and developing deep vein thrombosis (DVT) (chapter 2) and (2) the effect of IPC and NMES on lower limb venous haemodynamics (chapter 3).

In chapter 2, a comprehensive systematic review and meta-analysis focused upon IPC devices and their use in patients at high-risk for developing DVT, namely orthopaedic and neurosurgical patients. While IPC is commonly utilised in these high-risk patients post-surgery, the true efficacy and the standardisation of use with these devices has yet to be established. From an extensive search of the literature, data from nine randomised controlled trials was analysed. These trials compared the use of an IPC device- with or without additional chemoprophylaxis- versus chemoprophylaxis alone, in high-risk surgical patients. The results of chapter 2 report the use of IPC in combination with other prophylaxis methods is associated with a significantly lesser number of patients diagnosed with DVT. The only study reporting on DVT/PE-related mortality did not show any significant difference between IPC and control groups. The data presented in chapter 2 suggests that use of an IPC device is neither superior nor inferior to use of chemoprophylaxis. However, a limitation of the report includes the heterogeneous nature of both of the intervention and control groups pooled for the meta-analysis. Some studies combined the use of IPC with chemoprophylaxis whereas other studies utilised IPC alone.

Further to this, the control groups were randomised to receive different forms of chemoprophylaxis and even when receiving the same chemoprophylactic agent, received different doses. Additionally, both the duration of follow-up, hospital stay and the test utilised to detect DVT varied greatly between studies. Although IPC is commonly utilised for the prevention of venous stasis and DVT post-surgery, the data presented in Chapter 2 emphasises the need for improved reporting and standardisation of usage with IPC devices in order to evaluate their true efficacy.

Following the examination of IPC usage within the literature, it was desirable to compare the haemodynamic capabilities of IPC to that of NMES. The use of electrical stimulation for the improvement of venous haemodynamics is not a new concept. Electrical stimulation has been utilised to directly stimulate muscles to prevent venous stasis as early as the 1960s. NMES has been investigated as a method of DVT prophylaxis in general surgical patients [1-7], neurosurgical patients [8], spinal cord injured (SCI) patients [9] and trauma patients [10]. While most of these studies reported a lesser incidence of DVT when utilising NMES [1, 2, 4, 6, 7], some studies reported no significant difference [3, 5]. It is important to note that the majority of studies were carried out over 20 years ago. A vast amount of research has since been carried out to enhance both stimulation parameters and the way in which they are delivered. Although the benefits of NMES in improving venous haemodynamics and preventing venous stasis have been established more recently [11-15], it is not widely utilised as a method of venous stasis or DVT prevention.

The data presented in chapter 3 assessed the use of NMES in preventing venous stasis and compared it to the currently utilised method of IPC. This study demonstrated an increase in measures of peak velocity, time averaged mean velocity and ejected volumes with use of both NMES and IPC in young healthy participants. These results contribute to current knowledge within the literature and demonstrate the potential benefits of NMES over IPC in enhancing lower limb venous haemodynamics. While NMES and IPC of the calf compartment were found to produce a greater peak velocity and time averaged mean velocity versus IPC of the foot, NMES was also found to produce a greater ejected volume versus both IPC of the foot and of the calf compartment.

As the haemodynamic measure that acts as the best indicator of improved blood flow is as yet unknown, it is important to consider both the velocities and the volumes produced with the use of venous stasis prevention methods. In addition to an increase in blood flow velocity, it would follow that the greater the volume of blood ejected from the lower limb, the less blood that is then present in stasis and the less likely the development of DVT. Chapter 3 presents promising data suggesting that NMES improves both velocities and volumes to a greater degree than IPC, suggesting that NMES might be of greater benefit in improving lower limb venous haemodynamics for the prevention of venous stasis and DVT.

It is important to consider the limitations associated with this study. While these findings support use of NMES as a potentially superior method of venous stasis prevention, it is important to note that the data presented are based upon values obtained during application of stimulation and compression for five-minute periods only. It would be of interest to further assess the haemodynamic capabilities of both mechanical methods over a greater duration of application. This would provide a more in-depth understanding of the abilities of NMES in preventing venous stasis compared to IPC. Additionally, it is important to note that this study was carried out in young, healthy participants. Results may differ in an older patient population, such as TKA patients, whereby there are likely to be greater periods of immobilisation and bed rest following surgery, leading to a greater chance of venous stasis.

Improvements in haemodynamic measures are of great importance following TKA as they can reduce the incidence of clinical complications that can negatively affect recovery. Following TKA, functional recovery is a vital aspect. This can comprise the ability to walk on a flat surface, bend to the floor to pick up an object, the ability to walk up or down stairs, or put on a pair of stockings for example. While there are any measures that can assess functional recovery, this thesis has focused upon measures of physical activity levels, joint range of motion and lower limb swelling.

Increases in measures such as physical activity levels are of the utmost importance following TKA, as restrictions in daily physical activity and function are primary reasons for performing TKA [16]. One of the most commonly utilised methods of

quantifying physical activity levels is through use of activity monitors. Physical activity monitors are extremely useful devices for quantifying physical activity levels, most commonly through the output of cumulative step count per day, week or month. Commercial activity monitors have screens and/or smart phone applications that allow for the easy visualisation of activity data. These devices may be extremely beneficial to patients following TKA as they provide an easy-to-use method of quantifying physical activity and providing motivation. When utilised as a method of measuring functional recovery through step count, the accuracy of these activity monitors comes into question. It is necessary for physical activity monitors to be both sensitive and specific in their ability to detect and correctly register steps. An over- or underestimation of step count could negatively affect a patient's perception of functional recovery improvement and consequently impair recovery.

As an aim within this thesis was to investigate the sensitivity and specificity of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery, data presented in chapters 4 and 5 focused on the investigation of both the sensitivity and specificity of a range of activity monitors. Within chapter 4, the sensitivity of a number of commercial-grade activity monitors was comprehensively evaluated under conditions that could be encountered while achieving the recommended daily step count goal of 10,000 steps. This study investigated effects of underfoot surface and footwear type on the sensitivity of the Garmin Vivofit™, NL-2000™ pedometer, Withings Smart Activity Monitor Tracker (Pulse O2)™ and Fitbit One™ activity monitors during prescribed walking. In this study, the ActivPAL™ research-grade monitor was worn as a reference device as this device is one of the most widely utilised activity monitors in physical activity research and has been utilised in all age groups and in both healthy and patient groups. Results of this study reported all monitors tested to be sensitive in step detection on natural lawn grass, gravel, ceramic tile, tarmacadam/asphalt and linoleum surfaces while wearing both running and hard soled shoes.

These results are promising and would suggest users can have confidence in these activity monitors in quantifying physical activity following TKA. However, the specificity of the monitors is also important to consider. When utilising step count as

an output for physical activity quantification, non-stepping movements may contribute to false positives. Chapter 5 assessed the specificity of the ActivPAL micro™, NL-2000™ pedometer, Withings Smart Activity Monitor Tracker (Pulse O2)™, Fitbit One™ and Jawbone UP™ activity monitors. Unlike the sensitivity of the activity monitors, the specificity of the monitors varied a great deal under the various conditions tested. The activities prescribed during this study differed in intensity and type and this was reflected in the results. The majority of the activity monitors were least specific during the more intense 'active' non-stepping activities tested, including indoor cycling, outdoor cycling and indoor rowing. However, it was also clear that the body-worn position of the activity monitors most likely contributed to the reduced specificity observed. For example, the Jawbone™ is a wrist-worn monitor and was least specific during the 'moderate' non-stepping activities that involved quite a bit of arm and hand movement. In addition to this, the ActivPAL™ monitor is worn on the anterior aspect of the thigh and was least specific during the cycling activities, whereby the thigh was constantly moving between the vertical and horizontal planes.

The lack of specificity and overestimation of step count for the majority of the tested activity monitors presented in chapter 5 would suggest that further evaluation is necessary before recommending their use for physical activity measurement in TKA patients. However, the detection and registration of steps during non-stepping activities may not be a completely negative finding. All physical activity is of benefit and positively contributes to functional recovery post-TKA. It would be of interest to develop a method of translating non-stepping activities into step count equivalents. This would allow for a more accurate quantification of physical activity and gain a more in-depth view of functional recovery post-TKA and in wider clinical applications when utilising step count as an output.

While data presented in chapters 4 and 5 highlight the sensitivity and specificity that can be observed in a number of activity monitors under various conditions, there were some limitations within these studies. Primary among them is that both studies were carried out in healthy participants. The sensitivity and specificity associated with their use could differ significantly in TKA patients, whereby slow walking speeds and the

use of ambulatory aids are present. Slow walking speeds, as present in the early post-TKA recovery phase, are reported to decrease activity monitor step detection accuracy [17-19] and the use of ambulatory aids, such as crutches, on activity monitor step detection has not been extensively examined. Out of the few studies that have investigated step detection accuracy when utilising ambulatory aids, mixed results have been reported [20, 21]. A combination of slow walking speeds and the use of crutches may affect the ability of activity monitors to accurately quantify physical activity and may subsequently affect functional recovery. For example, if a patient is adequately active but believes they are more active than in reality, they may become complacent and decrease the amount of physical activity they perform, thereby negatively affecting their functional recovery. Alternatively, if a patient is adequately active but believes they are doing less activity than in reality, this could potentially lead to disappointment and a lack of motivation with regard to carrying out physical activity. Again, this could have a negative impact on functional recovery. These factors are important to consider for future studies in this area.

Further to this, while the activity monitors were tested extensively under various circumstances and conditions, some of the non-stepping activities did not fully reflect the activities that could be carried out by TKA patients in the early post-discharge period. Further investigation into TKA patient-specific activities would be of benefit. A further limitation exists in the activity monitors tested. Only a handful of commercial monitors were tested, chosen based upon their popularity and reasonable price range at the time of investigation. The results of these studies cannot be generalised to other activity monitors.

In chapter 6 the ActivPAL^{TM}, a research-grade activity monitor, was used to assess levels of physical activity in TKA patients. Step count, time spent stepping, standing, upright and sitting/lying as well as Stepping Bout data were evaluated. Measures of joint range of motion and lower limb swelling were also evaluated to assess functional recovery in the short-term post-TKA discharge phase. TKA patients received an NMES device to use at home for 5 weeks post-discharge and were randomised to stimulation or placebo-controlled groups, receiving motor stimulation (inducing a muscular contraction) or sensory stimulation (no muscular contraction)

respectively. The results of this study report no significant effect of NMES on reducing lower limb swelling, but changes were observed in knee range of motion and physical activity measures. While there were no significant group differences for knee range of motion measures, there was a trend towards a greater increase in knee ROM in the early post-discharge weeks with use of NMES.

The use of NMES resulted in significantly greater time spent upright, a significantly lesser time sitting/lying and a significantly greater number of Stepping Bouts carried out. These results demonstrate the effectiveness of NMES applied to the calf muscle in enhancing physical activity levels in the early post-discharge phase and are very promising with regard to enhancing functional recovery rates post-TKA. An increase in the time spent upright combined with a decrease in the time spent sitting/lying and an increase in the number of Stepping Bouts carried out will aid in the progression from limited mobility to increased functional ability and independence in the early post-discharge phase. In combination with the excellent rates of compliance observed with the NMES device, these results suggest that NMES has great potential as a method of enhancing functional recovery outcomes following TKA. This is the first study to assess the effects of NMES as part of the post-operative care regime in TKA patients in the early post-discharge period and adds greatly to current literature surrounding the use of NMES as a method of enhancing functional recovery post-surgery.

However, while NMES increased the time spent upright, decreased the time spent sitting/lying and an increased the number of Stepping Bouts carried out by patients post-discharge, the effect of the physiotherapy-prescribed exercises carried out by all patients is lacking. Both the therapeutic effect and the interaction effect of the prescribed exercise programme on the effect of NMES are unknown and this would be an important consideration for future studies. Additionally, the effect of crutch walking was not accounted for with regard to step count and while all patients utilised crutches post-surgery, this is a consideration for future studies.

In summary, this thesis has described in detail the potential for NMES to play a role in the early phase post-operative care regime of TKA patients. The aims of this thesis

were to (1) to investigate the use of NMES as a method of preventing venous stasis and DVT, (2) to investigate the sensitivity and specificity of a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery and (3) to investigate the use of NMES in enhancing recovery post-TKA through measures of physical activity, joint range of motion and lower limb swelling.

The investigation into the use of NMES as a method of preventing venous stasis and DVT was achieved within chapters 2 and 3. The work presented within these chapters emphasises the need for improved reporting and standardisation of use with IPC for DVT prevention and highlights the promising benefits of NMES in promoting venous haemodynamics to a greater degree than IPC. This work adds to existing literature reporting on the benefits of NMES in venous stasis prevention [22-29].

The investigation into the sensitivity and specificity of a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery was achieved within chapters 4 and 5. The work presented within these chapters emphasises the variability that can exist in the step detection abilities of a range of activity monitors in terms of sensitivity and specificity. These results add greatly to existing literature regarding the sensitivity and specificity of a number of activity monitors. Few studies have been carried out assessing the specificity of activity monitors [30, 31] and studies assessing the sensitivity of activity monitors have not carried out as comprehensive an examination as was carried out in chapter 4 [32-37].

The investigation into the use of NMES in enhancing recovery post-TKA through measures of physical activity, joint range of motion and lower limb swelling was achieved within chapter 6, whereby NMES was utilised for five weeks post-TKA discharge. Its benefit was observed through measures of physical activity, significantly increasing the time patients spent upright, decreasing the time spent sitting/lying and increasing the number of Stepping Bouts they performed. This study adds greatly to existing literature in this area, as it is the first study assessing the use of NMES in TKA patients in this early post-discharge phase.

The work within this thesis highlights the potential of NMES as both a method of

improving lower limb haemodynamic measures and enhancing functional recovery measures. This work supports the use of NMES as part of the post-operative care regime in TKA patients post-surgery and highlights a number of physical activity monitors that have the potential to be utilised by TKA-patients post-surgery.

7.1 Recommendations for Future Work

It would be of interest to further assess the haemodynamic capabilities of both NMES and IPC when applied for periods of greater than 5 minutes and when applied to adults of an age more reflective of TKA patients. This would provide a more in-depth understanding of the abilities of NMES in preventing venous stasis in TKA patients. It would also be of interest to investigate the sensitivity and specificity of a greater selection of commercial activity monitors during a range of physical activities more reflective of the activities carried out by TKA patients in the early post-discharge period. This would allow for selection of a commercial activity monitor that would be most effective for physical activity monitoring in TKA patients. With regard to the use of NMES as a method of enhancing functional activity post-TKA, an optimised NMES protocol applied for a greater duration per day would most likely provide great benefit. Further work assessing both the therapeutic and the interaction effect of the post-TKA prescribed exercise programme on the effect of NMES should also be considered.

7.2 References

[1] Doran, F. and White, H., "A demonstration that the risk of postoperative deep venous thrombosis is reduced by stimulating the calf muscles electrically during the operation," , *Br J Surg,* vol. 54, no. 8, pp. 686-9, Aug 1967.

[2] Browse, N. and Negus, D., "Prevention of postoperative leg vein thrombosis by electrical muscle stimulation. An evaluation with 125I-labelled fibrinogen," , *Br Med J,* vol. 3, no. 5723, pp. 615-8, Sep 12 1970.

[3] Moloney, G., Morrell, M., and Fell, R., "The effect of electrical stimulation of the legs on postoperative thrombosis," , *Br J Surg,* vol. 59, no. 1, pp. 65-8, Jan 1972.

[4] Nicolaides, A., Kakkar, V., Field, E., and Fish, P., "Optimal electrical stimulus for prevention of deep vein thrombosis," , *Br Med J,* vol. 3, no. 5829, pp. 756-8, Sep 23 1972.

[5] Dejode, L., Khurshid, M., and Walther, W., "The influence of electrical stimulation of the leg during surgical operations on the subsequent development of deep-vein thrombosis," , *Br J Surg,* vol. 60, no. 1, pp. 31-2, Jan 1973.

[6] Rosenberg, I., Evans, M., and Pollock, A., "Prophylaxis of postoperative leg vine thrombosis by low dose subcutaneous heparin or peroperative calf muscle stimulation: a controlled clinical trial," , *Br Med J,* vol. 1, no. 5959, pp. 649-51, Mar 22 1975.

[7] Lindstrom, B. *et al.*, "Prediction and prophylaxis of postoperative thromboembolism--a comparison between peroperative calf muscle stimulation with groups of impulses and dextran 40," , *Br J Surg,* vol. 69, no. 11, pp. 633-7, Nov 1982.

[8] Bostrom, S. *et al.*, "Post-operative thromboembolism in neurosurgery. A study on the prophylactic effect of calf muscle stimulation plus dextran compared to low-dose heparin," , *Acta Neurochir (Wien),* vol. 80, no. 3-4, pp. 83-9, 1986.

[9] Merli, G. *et al.*, "Deep vein thrombosis: prophylaxis in acute spinal cord injured patients," , *Arch Phys Med Rehabil,* vol. 69, no. 9, pp. 661-4, Sep 1988.

[10] Velmahos, G., Petrone, P., Chan, L., Hanks, S., Brown, C., and Demetriades, D., "Electrostimulation for the prevention of deep venous thrombosis in patients with major trauma: a prospective randomized study," , *Surgery,* vol. 137, no. 5, pp. 493-8, May 2005.

[11] Faghri, P., Meerdervort, H. V., Glaser, R., and Figoni, S., "Electrical stimulation-induced contraction to reduce blood stasis during arthroplasty," , *IEEE Trans Rehabil Eng,* vol. 5, no. 1, pp. 62-9, Mar 1997.

[12] Broderick, B., O'Briain, D., Breen, P., Kearns, S., and ÓLaighin, G., "A hemodynamic study of popliteal vein blood flow: the effect of bed rest and electrically elicited calf muscle contractions," , *Conf Proc IEEE Eng Med Biol Soc,* vol. 2009, pp. 2149-52, 2009.

[13] Czyrny, J., Kaplan, R., Wilding, G., Purdy, C., and Hirsh, J., "Electrical foot stimulation: a potential new method of deep venous thrombosis prophylaxis," *Vascular,* vol. 18, no. 1, pp. 20-7, Jan-Feb 2010.

[14] Corley, G., Breen, P., Birlea, S., Serrador, J., Grace, P., and ÓLaighin, G., "Hemodynamic effects of habituation to a week-long program of neuromuscular electrical stimulation," , *Med Eng Phys,* vol. 34, no. 4, pp. 459-65, May 2012.

[15] Broderick, B., Breathnach, O., Condon, F., Masterson, E., and ÓLaighin, G., "Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty," , *J Orthop Surg Res,* vol. 8, pp. 3-10, 2013.

[16] de Groot, I., Bussmann, H., Stam, H., and Verhaar, J., "Small increase of actual physical activity 6 months after total hip or knee arthroplasty," , *Clin Orthop Relat Res,* vol. 466, no. 9, pp. 2201-8, Sep 2008.

[17] Cyarto, E., Myers, A., and Tudor-Locke, C., "Pedometer accuracy in nursing home and community-dwelling older adults," , *Med Sci Sports Exerc,* vol. 36, no. 2, pp. 205-9, Feb 2004.

[18] Harrington, D., Welk, G., and Donnelly, A., "Validation of MET estimates and step measurement using the ActivPAL physical activity logger," , *J Sports Sci,* vol. 29, no. 6, pp. 627-33, Mar 2011.

[19] Giannakidou, D. *et al.*, "The validity of two Omron pedometers during treadmill walking is speed dependent," , *Eur J Appl Physiol,* vol. 112, no. 1, pp. 49-57, Jan 2012.

[20] Bussmann, J., Culhane, K., Horemans, H., Lyons, G., and Stam, H., "Validity of the prosthetic activity monitor to assess the duration and spatio-temporal characteristics of prosthetic walking," , *IEEE Trans Neural Syst Rehabil Eng,* vol. 12, no. 4, pp. 379-86, Dec 2004.

[21] Wendland, D. and Sprigle, S., "Activity monitor accuracy in persons using canes," , *J Rehabil Res Dev,* vol. 49, no. 8, pp. 1261-8, 2012.

[22] Faghri, P., Votto, J., and Hovorka, C., "Venous hemodynamics of the lower extremities in response to electrical stimulation," *Arch Phys Med Rehabil,* vol. 79, no. 7, pp. 842-8, Jul 1998.

[23] Clarke-Moloney, M., Lyons, G., Breen, P., Burke, P., and Grace, P., "Haemodynamic study examining the response of venous blood flow to electrical stimulation of the gastrocnemius muscle in patients with chronic venous disease," *Eur J Vasc Endovasc Surg,* vol. 31, no. 3, pp. 300-5, Mar 2006.

[24] Corley, G. J., Breen, P. P., Grace, P. A., and G, ÓLaighin, "The effect of surface neuromuscular electrical stimulation and compression hosiery applied to the lower limb, on the comfort and blood flow of healthy subjects," *Conf Proc IEEE Eng Med Biol Soc,* vol. 2008, pp. 703-6, 2008.

[25] Broderick, B., O'Briain, D., Breen, P., Kearns, S., and ÓLaighin, G., "A pilot evaluation of a neuromuscular electrical stimulation (NMES) based methodology for the prevention of venous stasis during bed rest," *Med Eng Phys,* vol. 32, no. 4, pp. 349-55, May 2010.

[26] Griffin, M., Nicolaides, A., Bond, D., Geroulakos, G., and Kalodiki, E., "The efficacy of a new stimulation technology to increase venous flow and prevent venous stasis," *Eur J Vasc Endovasc Surg,* vol. 40, no. 6, pp. 766-71, Dec 2010.

[27] Corley, G., Breen, P., Birlea, S., Serrador, J., Grace, P., and ÓLaighin, G., "Hemodynamic effects of habituation to a week-long program of neuromuscular electrical stimulation," *Med Eng Phys,* vol. 34, no. 4, pp. 459- 65, May 2012.

[28] Broderick, B., Breathnach, O., Condon, F., Masterson, E., and ÓLaighin, G., "Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty," *J Orthop Surg Res,* vol. 8, pp. 3-10, 2013.

[29] Broderick, B. *et al.*, "Comparative lower limb hemodynamics using neuromuscular electrical stimulation (NMES) versus intermittent pneumatic compression (IPC)," *Physiol Meas,* vol. 35, no. 9, pp. 1849-59, Sep 2014.

[30] Chen, M. D., Kuo, C. C., Pellegrini, C. A., and Hsu, M. J., "Accuracy of Wristband Activity Monitors during Ambulation and Activities," *Med Sci Sports Exerc,* May 13 2016.

[31] Sellers, C., Dall, P., Grant, M., and Stansfield, B., "Validity and reliability of the activPAL3 for measuring posture and stepping in adults and young people," *Gait Posture,* vol. 43, pp. 42-7, Jan 2016.

[32] Dahlgren, G., Carlsson, D., Moorhead, A., Hager-Ross, C., and McDonough, S. M., "Test-retest reliability of step counts with the ActivPAL device in common daily activities," *Gait Posture,* vol. 32, no. 3, pp. 386-90, Jul 2010.

[33] Dondzila, C. J., Swartz, A. M., Miller, N. E., Lenz, E. K., and Strath, S. J., "Accuracy of uploadable pedometers in laboratory, overground, and free-living conditions in young and older adults," *Int J Behav Nutr Phys Act,* vol. 9, p. 143, 2012.

[34] Giannakidou, D. M. *et al.*, "The validity of two Omron pedometers during treadmill walking is speed dependent," *Eur J Appl Physiol,* vol. 112, no. 1, pp. 49-57, Jan 2012.

[35] Storm, F. A., Heller, B. W., and Mazza, C., "Step detection and activity recognition accuracy of seven physical activity monitors," *PLoS One,* vol. 10, no. 3, p. e0118723, 2015.

[36] Takacs, J., Pollock, C. L., Guenther, J. R., Bahar, M., Napier, C., and Hunt, M. A., "Validation of the Fitbit One activity monitor device during treadmill walking," *J Sci Med Sport,* vol. 17, no. 5, pp. 496-500, Sep 2014.

[37] Taraldsen, K. *et al.*, "Evaluation of a body-worn sensor system to measure physical activity in older people with impaired function," *Phys Ther,* vol. 91, no. 2, pp. 277-85, Feb 2011.

Bibliography

Aglietti, P., Buzzi, R. & Gaudenzi, A. 1988. Patellofemoral functional results and complications with the posterior stabilized total condylar knee prosthesis. *J Arthroplasty,* 3**,** 17-25.

Agnelli, G. 2004. Prevention of venous thromboembolism in surgical patients. *Circulation,* 110**,** IV4-12.

American Academy of Orthopaedic Surgeons 2015 'Total Knee Replacement'. Available: http://orthoinfo.aaos.org/topic.cfm?topic=A00389. Archived at: http://www.webcitation.org/6pQUl T33t

Arabi, Y., Khedr, M., Dara, S., Dhar, G., Bhat, S., Tamim, H. & Afesh, L. 2013. Use of intermittent pneumatic compression and not graduated compression stockings is associated with lower incident VTE in critically ill patients: a multiple propensity scores adjusted analysis. *Chest,* 144**,** 152-9.

Avramidis, K., Karachalios, T., Popotonasios, K., Sacorafas, D., Papathanasiades, A. A. & Malizos, K. N. 2011. Does electric stimulation of the vastus medialis muscle influence rehabilitation after total knee replacement? *Orthopedics,* 34**,** 175.

Bade, M., Kohrt, W., and Stevens-Lapsley, J. 2010. Outcomes before and after total knee arthroplasty compared to healthy adults, *J Orthop Sports Phys Ther,* vol. 40, no. 9, pp. 559-67.

Badley, E. M. & Crotty, M. 1995. An international comparison of the estimated effect of the aging of the population on the major cause of disablement, musculoskeletal disorders. *J Rheumatol,* 22**,** 1934-40.

Bergqvist, D. 1997. Prolonged prophylaxis in postoperative medicine. *Semin Thromb Hemost,* 23**,** 149-54.

Bockheim, H. M., Mcallen, K. J., Baker, R. & Barletta, J. F. 2009. Mechanical prophylaxis to prevent venous thromboembolism in surgical patients: a prospective trial evaluating compliance. *J Crit Care,* 24**,** 192-6.

Bogachev, V. Y., Golovanova, O. V., Kuznetsov, A. N., Shekoyan, A. O. & Bogacheva, N. V. 2011. Electromuscular stimulation with VEINOPLUS(R) for the treatment of chronic venous edema. *Int Angiol,* 30**,** 567-90.

Bostrom, S., Holmgren, E., Jonsson, O., Lindberg, S., Lindstrom, B., Winso, I. & Zachrisson, B. 1986. Post-operative thromboembolism in neurosurgery. A study on the prophylactic effect of calf muscle stimulation plus dextran compared to low-dose heparin. *Acta Neurochir (Wien),* 80**,** 83-9.

Brandes, M., Schomaker, R., Mollenhoff, G. & Rosenbaum, D. 2008. Quantity versus quality of gait and quality of life in patients with osteoarthritis. *Gait Posture,* 28**,** 74-9.

Brandes, M., Ringling, M., Winter, C., Hillmann, A. & Rosenbaum, D. 2011. Changes in physical activity and health-related quality of life during the first year after total knee arthroplasty. *Arthritis Care Res (Hoboken),* 63**,** 328-34.

Breen, P., Corley, G., O'Keeffe, D., Conway, R. & ÓLaighin, G. 2009. A programmable and portable NMES device for drop foot correction and blood flow assist applications. *Med Eng Phys,* 31**,** 400-8.

Breen, P., Galvin, O., Quondamatteo, F., Grace, P. & ÓLaighin, G. 2012. Comparison of single- and two-channel neuromuscular electrical stimulation sites for enhancing venous return. *IEEE Trans Neural Syst Rehabil Eng,* 20**,** 389-94.

Brock, T., Sprowson, A., Muller, S., and Reed, M. 2015. Short-stretch inelastic compression bandage in knee swelling following total knee arthroplasty study (STICKS): study protocol for a randomised controlled feasibility study, *Trials*, vol. 16, p. 87.

Broderick, B., O'Briain, D., Breen, P., Kearns, S. & ÓLaighin, G. 2009. A hemodynamic study of popliteal vein blood flow: the effect of bed rest and electrically elicited calf muscle contractions. *Conf Proc IEEE Eng Med Biol Soc,* 2009**,** 2149-52.

Broderick, B., O'Briain, D., Breen, P., Kearns, S. & ÓLaighin, G. 2010. A pilot evaluation of a neuromuscular electrical stimulation (NMES) based methodology for the prevention of venous stasis during bed rest. *Med Eng Phys,* 32**,** 349-55.

Broderick, B. J., Kennedy, C., Breen, P. P., Kearns, S. R. & ÓLaighin, G. 2011. Patient tolerance of neuromuscular electrical stimulation (NMES) in the presence of orthopaedic implants. *Med Eng Phys,* 33**,** 56-61.

Broderick, B., Breathnach, O., Condon, F., Masterson, E. & ÓLaighin, G. 2013. Haemodynamic performance of neuromuscular electrical stimulation (NMES) during recovery from total hip arthroplasty. *J Orthop Surg Res,* 8**,** 3-10.

Broderick, B. *et al.*, 2014. Comparative lower limb hemodynamics using neuromuscular electrical stimulation (NMES) versus intermittent pneumatic compression (IPC). *Physiol Meas,* vol. 35, no. 9, pp. 1849-59.

Brown, D. K., Grimwade, D., Martinez-Bussion, D., Taylor, M. J. & Gladwell, V. F. 2013. The validity of the ActiPed for physical activity monitoring. *Int J Sports Med,* 34**,** 431-7.

Browse, N. & Negus, D. 1970. Prevention of postoperative leg vein thrombosis by electrical muscle stimulation. An evaluation with 125I-labelled fibrinogen. *Br Med J,* 3**,** 615-8.

Busse, M. E., Van Deursen, R. W. & Wiles, C. M. 2009. Real-life step and activity measurement: reliability and validity. *J Med Eng Technol,* 33**,** 33-41.

Bussmann, J., Culhane, K., Horemans, H., Lyons, G.M. & Stam, H. 2004. Validity of the prosthetic activity monitor to assess the duration and spatio-temporal characteristics of prosthetic walking. *IEEE Trans Neural Syst Rehabil Eng,* 12**,** 379-86.

Carman, T., Kanner, A., Barnett, G. & Deitcher, S. 2003. Prevention of thromboembolism after neurosurgery for brain and spinal tumors. *South Med J,* 96**,** 17-22.

Carr, A. J., Robertsson, O., Graves, S., Price, A. J., Arden, N. K., Judge, A. & Beard, D. J. 2012. Knee replacement. *Lancet,* 379**,** 1331-40.

Centers for Disease Control. 2008. 'Physical Activity Guidelines for Americans. U.S. Department of Health and Human Services.' Available from: http://www.health.gov/paguidelines/guidelines/summary.aspx

Chan, E., Teo, Y., Assam, P., and Fransen, M. 2014. Functional discharge readiness and mobility following total knee arthroplasty for osteoarthritis: a comparison of analgesic techniques, *Arthritis Care Res (Hoboken),* vol. 66, no. 11, pp. 1688-94.

Chang, C. & Cormier, J. 2013. Lymphedema interventions: exercise, surgery, and compression devices. *Semin Oncol Nurs,* 29**,** 28-40.

Chen, M. D., Kuo, C. C., Pellegrini, C. A. & Hsu, M. J. 2016. Accuracy of Wristband Activity Monitors during Ambulation and Activities. *Med Sci Sports Exerc*.

Chin, P., Amin, M., Yang, K., Yeo, S. & Lo, N. 2009. Thromboembolic prophylaxis for total knee arthroplasty in Asian patients: a randomised controlled trial. *J Orthop Surg (Hong Kong),* 17**,** 1-5.

Chouhan, V., Comerota, A., Sun, L., Harada, R., Gaughan, J. & Rao, A. 1999. Inhibition of tissue factor pathway during intermittent pneumatic compression: A possible mechanism for antithrombotic effect. *Arterioscler Thromb Vasc Biol,* 19**,** 2812-7.

Clarke-Moloney, M., Lyons, G.M., Breen, P., Burke, P. & Grace, P. 2006. Haemodynamic study examining the response of venous blood flow to electrical stimulation of the gastrocnemius muscle in patients with chronic venous disease. *Eur J Vasc Endovasc Surg,* 31**,** 300-5.

Colbert, L. H., Matthews, C. E., Havighurst, T. C., Kim, K. & Schoeller, D. A. 2011. Comparative validity of physical activity measures in older adults. *Med Sci Sports Exerc,* 43**,** 867-76.

Colwell, C. J., Kwong, L., Turpie, A. & Davidson, B. 2006. Flexibility in administration of fondaparinux for prevention of symptomatic venous thromboembolism in orthopaedic surgery. *J Arthroplasty,* 21**,** 36-45.

Colwell, C. J., Froimson, M., Mont, M., Ritter, M., Trousdale, R., Buehler, K., Spitzer, A., Donaldson, T. & Padgett, D. 2010. Thrombosis prevention after total hip arthroplasty: a prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin. *J Bone Joint Surg Am,* 92**,** 527-35.

Colwell, C. J., Froimson, M., Anseth, S., Giori, N., Hamilton, W., Barrack, R., Buehler, K., Mont, M., Padgett, D., Pulido, P. & Barnes, C. 2014. A mobile compression device for thrombosis prevention in hip and knee arthroplasty. *J Bone Joint Surg Am,* 96**,** 177-83.

Comerota, A., Chouhan, V., Harada, R., Sun, L., Hosking, J., Veermansunemi, R., Comerota, A. J., Schlappy, D. & Rao, A. 1997. The fibrinolytic effects of intermittent pneumatic compression: mechanism of enhanced fibrinolysis. *Ann Surg,* 226**,** 306-13; discussion 313-4.

Corley, G. J., Breen, P. P., Grace, P. A., and G ÓLaighin. 2008. The effect of surface neuromuscular electrical stimulation and compression hosiery applied to the lower limb, on the comfort and blood flow of healthy subjects. *Conf Proc IEEE Eng Med Biol Soc,* vol. 2008, pp. 703-6.

Corley, G., Breen, P., Birlea, S., Serrador, J., Grace, P. & ÓLaighin, G. 2012. Hemodynamic effects of habituation to a week-long program of neuromuscular electrical stimulation. *Med Eng Phys,* 34**,** 459-65.

Crouter, S. E., Schneider, P. L., Karabulut, M. & Bassett, D. R., Jr. 2003. Validity of 10 electronic pedometers for measuring steps, distance, and energy cost. *Med Sci Sports Exerc,* 35**,** 1455-60.

Cushner, F., Agnelli, G., Fitzgerald, G. & Warwick, D. 2010. Complications and functional outcomes after total hip arthroplasty and total knee arthroplasty: results from the Global Orthopaedic Registry (GLORY). *Am J Orthop (Belle Mead NJ),* 39**,** 22-8.

Cyarto, E., Myers, A. & Tudor-Locke, C. 2004. Pedometer accuracy in nursing home and community-dwelling older adults. *Med Sci Sports Exerc,* 36**,** 205-9.

Czyrny, J., Kaplan, R., Wilding, G., Purdy, C. & Hirsh, J. 2010. Electrical foot stimulation: a potential new method of deep venous thrombosis prophylaxis. *Vascular,* 18**,** 20-7.

Dahlgren, G., Carlsson, D., Moorhead, A., Hager-Ross, C. & McDonough, S. M. 2010. Test-retest reliability of step counts with the ActivPAL device in common daily activities. *Gait Posture,* 32**,** 386-90.

Dall, P., McCrorie, P., Granat, M., and Stansfield, B. 2013. Step accumulation per minute epoch is not the same as cadence for free-living adults. *Med Sci Sports Exerc,* vol. 45, no. 10, pp.

Danish, S., Burnett, M., Ong, J., Sonnad, S., Maloney-Wilensky, E. & Stein, S. 2005. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery,* 56**,** 1286-92; discussion 1292-4.

Dawson, J., Fitzpatrick, R., Murray, D. & Carr, A. 1998. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br,* 80**,** 63-9.

de Groot, I. B., Bussmann, J., Stam, H., and Verhaar, J. 2008. Actual everyday physical activity in patients with end-stage hip or knee osteoarthritis compared with healthy controls, *Osteoarthritis Cartilage,* vol. 16, no. 4, pp. 436-42.

de Groot, I. D., Bussmann, H., Stam, H. & Verhaar, J. 2008. Small increase of actual physical activity 6 months after total hip or knee arthroplasty. *Clin Orthop Relat Res,* 466**,** 2201-8.

Dejode, L., Khurshid, M. & Walther, W. 1973. The influence of electrical stimulation of the leg during surgical operations on the subsequent development of deep-vein thrombosis. *Br J Surg,* 60**,** 31-2.

Delis, K., Slimani, G., Hafez, H. & Nicolaides, A. 2000. Enhancing venous outflow in the lower limb with intermittent pneumatic compression. A comparative haemodynamic analysis on the effect of foot vs. calf vs. foot and calf compression. *Eur J Vasc Endovasc Surg,* 19**,** 250-60.

Dennis, D. A., Clayton, M. L., O'Donnell, S., Mack, R. P. & Stringer, E. A. 1992. Posterior cruciate condylar total knee arthroplasty. Average 11-year follow-up evaluation. *Clin Orthop Relat Res***,** 168-76.

Dennis, M., Sandercock, P., Reid, J., Graham, C., Forbes, J. & Murray, G. 2013. Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial. *Lancet,* 382**,** 516-24.

DerSimonian, R. & Laird, N. 1983. Evaluating the effect of coaching on SAT scores: a meta-analysis. *Harvard Educational Review,* 53**,** 1-15.

Devers, B. N., Conditt, M. A., Jamieson, M. L., Driscoll, M. D., Noble, P. C. & Parsley, B. S. 2011. Does greater knee flexion increase patient function and satisfaction after total knee arthroplasty? *J Arthroplasty,* 26**,** 178-86.

Diaz, K. M., Krupka, D. J., Chang, M. J., Peacock, J., Ma, Y., Goldsmith, J., Schwartz, J. E. & Davidson, K. W. 2015. Fitbit(R): An accurate and reliable device for wireless physical activity tracking. *Int J Cardiol,* 185**,** 138-40.

Dirks, M. L., Hansen, D., Van Assche, A., Dendale, P. & Van Loon, L. J. 2015. Neuromuscular electrical stimulation prevents muscle wasting in critically ill comatose patients. *Clin Sci (Lond),* 128**,** 357-65.

Dondzila, C. J., Swartz, A. M., Miller, N. E., Lenz, E. K. & Strath, S. J. 2012. Accuracy of uploadable pedometers in laboratory, overground, and free-living conditions in young and older adults. *Int J Behav Nutr Phys Act,* 9**,** 143.

Doran, F. & White, H. 1967. A demonstration that the risk of postoperative deep venous thrombosis is reduced by stimulating the calf muscles electrically during the operation. *Br J Surg,* 54**,** 686-9.

Douketis, J., Gu, C., Schulman, S., Ghirarduzzi, A., Pengo, V. & Prandoni, P. 2007. The risk for fatal pulmonary embolism after discontinuing anticoagulant therapy for venous thromboembolism. *Ann Intern Med,* 147**,** 766-74.

Downs, S. & Black, N. 1998. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health,* 52**,** 377-84.

Edwards, J., Pulido, P., Ezzet, K., Copp, S., Walker, R. & Colwell, C. J. 2008. Portable compression device and low-molecular-weight heparin compared with low-molecular-weight heparin for thromboprophylaxis after total joint arthroplasty. *J Arthroplasty,* 23**,** 1122-7.

Eisele, R., Kinzl, L. & Koelsch, T. 2007. Rapid-inflation intermittent pneumatic compression for prevention of deep venous thrombosis. *J Bone Joint Surg Am,* 89**,** 1050-6.

Emmerson, K. P., Moran, C. G. & Pinder, I. M. 1996. Survivorship analysis of the Kinematic Stabilizer total knee replacement: a 10- to 14-year follow-up. *J Bone Joint Surg Br,* 78**,** 441-5.

Epley, D. 2000. Pulmonary emboli risk reduction. *J Vasc Nurs,* 18**,** 61-8; quiz 69-70.

Eriksson, B., Kalebo, P., Ekman, S., Lindbratt, S., Kerry, R. & Close, P. 1994. Direct thrombin inhibition with Rec-hirudin CGP 39393 as prophylaxis of thromboembolic complications after total hip replacement. *Thromb Haemost,* 72**,** 227-31.

Esterson, P. S. 1979. Measurement of ankle joint swelling using a figure of 8*. *J Orthop Sports Phys Ther,* 1**,** 51-2.

Ethgen, O., Bruyere, O., Richy, F., Dardennes, C. & Reginster, J. Y. 2004. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. *J Bone Joint Surg Am,* 86-A**,** 963-74.

Faghri, P., Meerdervort, H. V., Glaser, R. & Figoni, S. 1997. Electrical stimulation-induced contraction to reduce blood stasis during arthroplasty. *IEEE Trans Rehabil Eng,* 5**,** 62-9.

Faghri, P., Votto, J. & Hovorka, C. 1998. Venous hemodynamics of the lower extremities in response to electrical stimulation. *Arch Phys Med Rehabil,* 79**,** 842-8.

Ferguson, T., Rowlands, A. V., Olds, T. & Maher, C. 2015. The validity of consumer-level, activity monitors in healthy adults worn in free-living conditions: a cross-sectional study. *Int J Behav Nutr Phys Act,* 12**,** 42.

Fitbit. [Internet]. "How does my tracker count steps?" Available from: https://help.fitbit.com/articles/en_US/Help_article/How-does-my-tracker-count-steps

Francis, C., Pellegrini, V. J., Totterman, S., Boyd, A. J., Marder, V., Liebert, K., Stulberg, B., Ayers, D., Rosenberg, A., Kessler, C. & Johanson, N. 1997. Prevention of deep-vein thrombosis after total hip arthroplasty. Comparison of warfarin and dalteparin. *J Bone Joint Surg Am,* 79**,** 1365-72.

Fujisawa, M., Naito, M., Asayama, I., Kambe, T. & Koga, K. 2003. Effect of calf-thigh intermittent pneumatic compression device after total hip arthroplasty: comparative analysis with plantar compression on the effectiveness of reducing thrombogenesis and leg swelling. *J Orthop Sci,* 8**,** 807-11.

Geerts, W. H., Pineo, G. F., Heit, J. A., Bergqvist, D., Lassen, M. R., Colwell, C. W. & Ray, J. G. 2004. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest,* 126**,** 338S-400S.

Gelfer, Y., Tavor, H., Oron, A., Peer, A., Halperin, N. & Robinson, D. 2006. Deep vein thrombosis prevention in joint arthroplasties: continuous enhanced circulation therapy vs low molecular weight heparin. *J Arthroplasty,* 21**,** 206-14.

Giannakidou, D., Kambas, A., Ageloussis, N., Fatouros, I., Christoforidis, C., Venetsanou, F., Douroudos, I. & Taxildaris, K. 2012. The validity of two Omron pedometers during treadmill walking is speed dependent. *Eur J Appl Physiol,* 112**,** 49-57.

Glazer, N. L, Lyass A., Esliger D.W., Blease S.J., Freedson P.S., Massaro J.M., Murabito J.M., Vasan R.S. 2013 "Sustained and shorter bouts of physical activity are related to cardiovascular health," *Med Sci Sports Exerc,* vol. 45, no. 1, pp. 109-15, Jan.

Gnanalingham, K. & Holland, J. 2003. Attitudes to the use of prophylaxis for thrombo-embolism in neurosurgical patients. *J Clin Neurosci,* 10**,** 467-9.

Godfrey, A., Culhane, K. M. & Lyons, G. M. 2007. Comparison of the performance of the activPAL Professional physical activity logger to a discrete accelerometer-based activity monitor. *Med Eng Phys,* 29**,** 930-4.

Goldberg, V. M., Figgie, M. P., Figgie, H. E., 3rd, Heiple, K. G. & Sobel, M. 1988. Use of a total condylar knee prosthesis for treatment of osteoarthritis and rheumatoid arthritis. Long-term results. *J Bone Joint Surg Am,* 70**,** 802-11.

Grant, P. M., Dall, P. M., Mitchell, S. L. & Granat, M. H. 2008. Activity-monitor accuracy in measuring step number and cadence in community-dwelling older adults. *J Aging Phys Act,* 16**,** 201-14.

Griffin, M., Nicolaides, A., Bond, D., Geroulakos, G. & Kalodiki, E. 2010. The efficacy of a new stimulation technology to increase venous flow and prevent venous stasis. *Eur J Vasc Endovasc Surg,* 40**,** 766-71.

Hardwick, M., Pulido, P. & Colwell, C. J. 2011. A mobile compression device compared with low-molecular-weight heparin for prevention of venous thromboembolism in total hip arthroplasty. *Orthop Nurs,* 30**,** 312-6.

Harrington, D., Welk, G. & Donnelly, A. 2011a. Validation of MET estimates and step measurement using the ActivPAL physical activity logger. *J Sports Sci,* 29**,** 627-33.

Harrington, D. M., Tudor-Locke, C., Champagne, C. M., Broyles, S. T., Harsha, D. W., Kennedy, B. M., Johnson, W. D., Allen, R. & Katzmarzyk, P. T. 2011b. Step-based translation of physical activity guidelines in the Lower Mississippi Delta. *Appl Physiol Nutr Metab,* 36**,** 583-5.

Hayes, D., Watts, M., Anderson, L., and Walsh, W. 2011. Knee arthroplasty: a cross-sectional study assessing energy expenditure and activity. *ANZ J Surg,* vol. 81, no. 5, pp. 371-4.

Heck, D. A., Robinson, R. L., Partridge, C. M., Lubitz, R. M. & Freund, D. A. 1998. Patient outcomes after knee replacement. *Clin Orthop Relat Res***,** 93-110.

Hilding, M. B., Backbro, B. & Ryd, L. 1997. Quality of life after knee arthroplasty. A randomized study of 3 designs in 42 patients, compared after 4 years. *Acta Orthop Scand,* 68**,** 156-60.

Hochberg, M. C., Altman, R. D., April, K. T., Benkhalti, M., Guyatt, G., Mcgowan, J., Towheed, T., Welch, V., Wells, G. & Tugwell, P. 2012. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken),* 64**,** 465-74.

Holm, B., Kristensen, M. T., Bencke, J., Husted, H., Kehlet, H. & Bandholm, T. 2010. Loss of knee-extension strength is related to knee swelling after total

knee arthroplasty. *Arch Phys Med Rehabil,* 91**,** 1770-6.

Howe, T. and Rafferty, D., Quadriceps activity and physical activity profiles over long durations in patients with osteoarthritis of the knee and controls 2009. *J Electromyogr Kinesiol,* vol. 19, no. 2, pp. e78-83.

Huber, O., Bounameaux, H., Borst, F. & Rohner, A. 1992. Postoperative pulmonary embolism after hospital discharge. An underestimated risk. *Arch Surg,* 127**,** 310-3.

Hull, R., Raskob, G., Pineo, G., Rosenbloom, D., Evans, W., Mallory, T., Anquist, K., Smith, F., Hughes, G., Green, D., Elliot, C., Panju, A. & Brant, R. 1993. A comparison of subcutaneous low-molecular-weight heparin with warfarin sodium for prophylaxis against deep-vein thrombosis after hip or knee implantation. *N Engl J Med,* 329**,** 1370-6.

Hull, R., Yusen, R. & Bergqvist, D. 2009. State-of-the-art review: Assessing the safety profiles of new anticoagulants for major orthopedic surgery thromboprophylaxis. *Clin Appl Thromb Hemost,* 15**,** 377-88.

Husted, H., Gromov, K., Malchau, H., Freiberg, A., Gebuhr, P., and Troelsen, A. 2014. Traditions and myths in hip and knee arthroplasty: A narrative review, *Acta Orthopaedica*, vol. 85, no. 6, pp. 548-555.

Hsu, M.-J., Wei, S.-H., and Chang, Y.-J., "Effect of Neuromuscular Electrical Muscle Stimulation on Energy Expenditure in Healthy Adults," *Sensors,* vol. 11, no. 2, pp. 1932-1942, 02/01, 2011.

Iorio, A. & Agnelli, G. 2000. Low-molecular-weight and unfractionated heparin for prevention of venous thromboembolism in neurosurgery: a meta-analysis. *Arch Intern Med,* 160**,** 2327-32.

Izumi, M., Ikeuchi, M., Mitani, T., Taniguchi, S. & Tani, T. 2010. Prevention of venous stasis in the lower limb by transcutaneous electrical nerve stimulation. *Eur J Vasc Endovasc Surg,* 39**,** 642-5.

Jacobs, D., Piotrowski, J., Hoppensteadt, D., Salvator, A. & Fareed, J. 1996. Hemodynamic and fibrinolytic consequences of intermittent pneumatic compression: preliminary results. *J Trauma,* 40**,** 710-16; discussion 716-7.

Jimenez, D., Diaz, G., Marin, E., Vidal, R., Sueiro, A. & Yusen, R. 2006. The risk of recurrent venous thromboembolism in patients with unprovoked symptomatic deep vein thrombosis and asymptomatic pulmonary embolism. *Thromb Haemost,* 95**,** 562-6.

Johnson, R., Green, J. & Charnley, J. 1977. Pulmonary embolism and its prophylaxis following the Charnley total hip replacement. *Clin Orthop Relat Res***,** 123-32.

Johnson, M., Meltz, K., Hart, K., Schmudlach, M., Clarkson, L. & Borman, K. 2015. Validity of the Actical activity monitor for assessing steps and energy expenditure during walking. *J Sports Sci,* 33**,** 769-76.

Kahn, T. & Schwarzkopf, R. 2015. Does Total Knee Arthroplasty Affect Physical Activity Levels? Data from the Osteoarthritis Initiative. *J Arthroplasty,* 30**,** 1521-5.

Kakkos, S., Caprini, J., Geroulakos, G., Nicolaides, A., Stansby, G. & Reddy, D. 2009. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thrombo-embolism in high-risk patients. *Eur J Vasc Endovasc Surg,* 37**,** 364-5.

Kang, M., Marshall, S. J., Barreira, T. V. & Lee, J. O. 2009. Effect of pedometer-based physical activity interventions: a meta-analysis. *Res Q Exerc Sport,* 80**,** 648-55.

Karmisholt, K. & Gotzsche, P. 2005. Physical activity for secondary prevention of disease. Systematic reviews of randomised clinical trials. *Dan Med Bull,* 52**,** 90-4.

Kearon, C. 2003. Natural history of venous thromboembolism. *Circulation,* 107**,** I22-30.

Keeney, J. A., Nunley, R. M., Wright, R. W., Barrack, R. L. & Clohisy, J. C. 2014. Are younger patients undergoing TKAs appropriately characterized as active? *Clin Orthop Relat Res,* 472**,** 1210-6.

Kern, H., Barberi, L., Lofler, S., Sbardella, S., Burggraf, S., Fruhmann, H., Carraro, U., Mosole, S., Sarabon, N., Vogelauer, M., Mayr, W., Krenn, M., Cvecka, J., Romanello, V., Pietrangelo, L., Protasi, F., Sandri, M., Zampieri, S. & Musaro, A. 2014. Electrical stimulation counteracts muscle decline in seniors. *Front Aging Neurosci,* 6**,** 189.

Klassen, T. D., Simpson, L. A., Lim, S. B., Louie, D. R., Parappilly, B., Sakakibara, B. M., Zbogar, D. & Eng, J. J. 2015. "Stepping Up" Activity Poststroke: Ankle-Positioned Accelerometer Can Accurately Record Steps During Slow Walking. *Phys Ther*.

Krenk, L., Jennum, P., and Kehlet, H. 2013. Activity, sleep and cognition after fast-track hip or knee arthroplasty. *J Arthroplasty,* vol. 28, no. 8, pp. 1265-9.

Kurtoglu, M., Yanar, H., Bilsel, Y., Guloglu, R., Kizilirmak, S., Buyukkurt, D. & Granit, V. 2004. Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin. *World J Surg,* 28**,** 807-11.

Kurtz, S., Ong, K., Lau, E., Mowat, F. & Halpern, M. 2007. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am,* 89**,** 780-5.

Lacut, K., Bressollette, L., Gal, G. L., Etienne, E., Tinteniac, A. D., Renault, A., Rouhart, F., Besson, G., Garcia, J., Mottier, D. & Oger, E. 2005. Prevention of venous thrombosis in patients with acute intracerebral hemorrhage. *Neurology,* 65**,** 865-9.

Laverick, M., Mcgivern, R., Crone, M. & Mollan, R. 1990. A comparison of the effects of electrical calf muscle stimulation and the venous foot pump on venous blood flow in the lower leg. *Phlebologie,* 5**,** 285-290.

Lee, J. M., Kim, Y. & Welk, G. J. 2014. Validity of consumer-based physical activity monitors. *Med Sci Sports Exerc,* 46**,** 1840-8.

Leicht, A. S. & Crowther, R. G. 2007. Pedometer accuracy during walking over different surfaces. *Med Sci Sports Exerc,* 39**,** 1847-50.

Liberati, A., Altman, D., Tetzlaff, J., Mulrow, C., Gotzsche, P., Ioannidis, J., Clarke, M., Devereaux, P., Kleijnen, J. & Moher, D. 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol,* 62**,** e1-34.

Line, B. 2001. Pathophysiology and diagnosis of deep venous thrombosis. *Semin Nucl Med,* 31**,** 90-101.

Lindstrom, B., Holmdahl, C., Jonsson, O., Korsan-Bengtsen, K., Lindberg, S., Petrusson, B., Pettersson, S., Wikstrand, J. & Wojciechowski, J. 1982. Prediction and prophylaxis of postoperative thromboembolism--a comparison between peroperative calf muscle stimulation with groups of impulses and dextran 40. *Br J Surg,* 69**,** 633-7.

Lyons, G.M., Leane, G., Clarke-Moloney, M., O'Brien, J. & Grace, P. 2004. An investigation of the effect of electrode size and electrode location on comfort during stimulation of the gastrocnemius muscle. *Med Eng Phys,* 26**,** 873-8.

Lyons, G.M., Leane, G. & Grace, P. 2002. The effect of electrical stimulation of the calf muscle and compression stocking on venous blood flow velocity. *Eur J Vasc Endovasc Surg,* 23**,** 564-6.

Macfarlane, D., Taylor, L., and Cuddihy, T. 2006. "Very short intermittent vs continuous bouts of activity in sedentary adults," *Prev Med,* vol. 43, no. 4, pp. 332-6.

Maclellan, D. & Fletcher, J. 2007. Mechanical compression in the prophylaxis of venous thromboembolism. *ANZ J Surg,* 77**,** 418-23.

Maddocks, M., Petrou, A., Skipper, L. & Wilcock, A. 2010. Validity of three accelerometers during treadmill walking and motor vehicle travel. *Br J Sports Med,* 44**,** 606-8.

Maddocks, M., Nolan C.M., D-C Man, W., Polkey M.I., Hart N., Gao W., Rafferty G.F., Moxham J., Higginson I.J. .2016, "Neuromuscular electrical stimulation to improve exercise capacity in patients with severe COPD: a randomised double-blind, placebo-controlled trial," *The Lancet Respiratory Medicine,* vol. 4, no. 1, pp. 27-36.

Matsuda, S., Kawahara, S., Okazaki, K., Tashiro, Y. & Iwamoto, Y. 2013. Postoperative Alignment and ROM Affect Patient Satisfaction After TKA. *Clinical Orthopaedics and Related Research®,* 471**,** 127-133.

Merli, G., Herbison, G., Ditunno, J., Weitz, H., Henzes, J., Park, C. & Jaweed, M. 1988. Deep vein thrombosis: prophylaxis in acute spinal cord injured patients. *Arch Phys Med Rehabil,* 69**,** 661-4.

Moini, J. 2011. *Anatomy and Physiology for Health Professionals*. Jones & Bartlett Publishers, p. 424. ISBN: 1284090353.

Moloney, G., Morrell, M. & Fell, R. 1972. The effect of electrical stimulation of the legs on postoperative thrombosis. *Br J Surg,* 59**,** 65-8.

Morris, R. & Woodcock, J. 2004. Evidence-based compression: prevention of stasis and deep vein thrombosis. *Ann Surg,* 239**,** 162-71.

Morris, R. 2008. Intermittent pneumatic compression - systems and applications. *J Med Eng Technol,* 32**,** 179-88.

Morris, R. J. & Woodcock, J. P. 2010. Intermittent pneumatic compression or graduated compression stockings for deep vein thrombosis prophylaxis? A systematic review of direct clinical comparisons. *Ann Surg,* 251**,** 393-6.

Munk, S., Jensen, N., Andersen, I., Kehlet, H., and Hansen, T. 2013. Effect of compression therapy on knee swelling and pain after total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc,* vol. 21, no. 2, pp. 388-92.

Murphy, S. L. 2009. Review of physical activity measurement using accelerometers in older adults: considerations for research design and conduct. *Prev Med,* 48**,** 108-14.

National Transport Authority. Taximeter Survey 2015. [Internet] Available: https://www.nationaltransport.ie/public-transport-services/taxi/

New Lifestyles [Internet]. "NL-2000 pedometer User's Guide. Available from: http://www.thepedometercompany.com/instructions.html

Nicolaides, A., Kakkar, V., Field, E. & Fish, P. 1972. Optimal electrical stimulus for prevention of deep vein thrombosis. *Br Med J,* 3**,** 756-8.

Noble, P., Gordon, M., Weiss, J., Reddix, R., Conditt, M., and Mathis, K. 2005. Does total knee replacement restore normal knee function? *Clin Orthop Relat Res,* no. 431, pp. 157-65.

Nunan, D., Mahtani, K., Roberts, N. & Heneghan, C. 2013. Physical activity for the prevention and treatment of major chronic disease: an overview of systematic reviews. *Syst Rev,* 2**,** 56.

O'Connell, S. *et al.* 2016 The Use of Intermittent Pneumatic Compression in Orthopedic and Neurosurgical Postoperative Patients: A Systematic Review and Meta-analysis, *Ann Surg*, vol. 263, no. 5, pp. 888-9.

O'Connell, S., G, ÓLaighin., Kelly, L., Murphy, E., Beirne, S., Burke, N., Kilgannon, O. & Quinlan, L. R. 2016. These Shoes Are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps. *PLoS One,* 11**,** e0154956.

O'Connell, S., ÓLaighin, G., and Quinlan, L. 2017. When a Step Is Not a Step! Specificity Analysis of Five Physical Activity Monitors. *PLoS One*, vol. 12, no. 1, p. e0169616.

Orendurff, M., Schoen, J., Bernatz, G., Segal, A., and Klute, G. 2008. How humans walk: bout duration, steps per bout, and rest duration. *J Rehabil Res Dev,* vol. 45, no. 7, pp. 1077-89.

Patel, A., Pavlou, G., Mujica-Mota, R. E. & Toms, A. D. 2015. The epidemiology of revision total knee and hip arthroplasty in England and Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset. *Bone Joint J,* 97-B**,** 1076-81.

Paxton, R., Melanson, E., Stevens-Lapsley, J., and Christiansen, C. 2015. Physical activity after total knee arthroplasty: A critical review. *World J Orthop,* vol.

6, no. 8, pp. 614-22.

Pedersen, B. K. & Saltin, B. 2006. Evidence for prescribing exercise as therapy in chronic disease. *Scand J Med Sci Sports,* 16 Suppl 1**,** 3-63

Peiris, C., Taylor, N., and Shields, N. 2013. Patients receiving inpatient rehabilitation for lower limb orthopaedic conditions do much less physical activity than recommended in guidelines for healthy older adults: an observational study. *J Physiother,* vol. 59, no. 1, pp. 39-44.

Penedo, F. & Dahn, J. 2005. Exercise and well-being: a review of mental and physical health benefits associated with physical activity. *Curr Opin Psychiatry,* 18**,** 189-93.

Petersen, E. J., Irish, S. M., Lyons, C. L., Miklaski, S. F., Bryan, J. M., Henderson, N. E. & Masullo, L. N. 1999. Reliability of water volumetry and the figure of eight method on subjects with ankle joint swelling. *J Orthop Sports Phys Ther,* 29**,** 609-15.

"Physical Activity and Public Health in Older Adults,"2007 *Recommendation From The American College of Sports Medicine and the American Heart Association,* vol. 116, no. 9, pp. 1094-1105.

Pittman, G. 1989. Peroneal nerve palsy following sequential pneumatic compression. *JAMA,* 261**,** 2201-2.

Pitto, R., Hamer, H., Heiss-Dunlop, W. & Kuehle, J. 2004. Mechanical prophylaxis of deep-vein thrombosis after total hip replacement a randomised clinical trial. *J Bone Joint Surg Br,* 86**,** 639-42.

Popovic, M. R., Curt, A., Keller, T. & Dietz, V. 2001. Functional electrical stimulation for grasping and walking: indications and limitations. *Spinal Cord,* 39**,** 403-12.

Prince, S., Adamo, K., Hamel, M., Hardt, J., Gorber, S. C., and Tremblay, M. 2008. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act,* vol. 5, p. 56.

Ricci, M., Fisk, P., Knight, S. & Case, T. 1997. Hemodynamic evaluation of foot venous compression devices. *J Vasc Surg,* 26**,** 803-8.

Robinson, K., Anderson, D., Gross, M., Petrie, D., Leighton, R., Stanish, W., Alexander, D., Mitchell, M., Mason, W., Flemming, B., Fairhurst-Vaughan,

M. & Gent, M. 1998. Accuracy of screening compression ultrasonography and clinical examination for the diagnosis of deep vein thrombosis after total hip or knee arthroplasty. *Can J Surg,* 41**,** 368-73.

Rosenberg, I., Evans, M. & Pollock, A. 1975. Prophylaxis of postoperative leg vine thrombosis by low dose subcutaneous heparin or peroperative calf muscle stimulation: a controlled clinical trial. *Br Med J,* 1**,** 649-51.

Ryan, C. G., Grant, P. M., Tigbe, W. W. & Granat, M. H. 2006. The validity and reliability of a novel activity monitor as a measure of walking. *Br J Sports Med,* 40**,** 779-84.

Salzman, E., Mcmanama, G., Shapiro, A., Robertson, L., Donovan, A., Blume, H., Sweeney, J., Kamm, R., Johnson, M. & Black, P. 1987. Effect of optimization of hemodynamics on fibrinolytic activity and antithrombotic efficacy of external pneumatic calf compression. *Ann Surg,* 206**,** 636-41.

Schindler, O. & Dalziel, R. 2005. Post-thrombotic syndrome after total hip or knee arthroplasty: incidence in patients with asymptomatic deep venous thrombosis. *J Orthop Surg (Hong Kong),* 13**,** 113-9.

Schmidt, W., Biwer, C., and Kalscheuer, L. 2001. "Effects of long versus short bout exercise on fitness and weight loss in overweight females," *J Am Coll Nutr,* vol. 20, no. 5, pp. 494-501.

Schneider, P. L., Crouter, S. E., Lukajic, O. & Bassett, D. R., Jr. 2003. Accuracy and reliability of 10 pedometers for measuring steps over a 400-m walk. *Med Sci Sports Exerc,* 35**,** 1779-84.

Schneider, P. L., Crouter, S. & Bassett, D. R. 2004. Pedometer measures of free-living physical activity: comparison of 13 models. *Med Sci Sports Exerc,* 36**,** 331-5.

Sellers, C., Dall, P., Grant, M. & Stansfield, B. 2016. Validity and reliability of the activPAL3 for measuring posture and stepping in adults and young people. *Gait Posture,* 43**,** 42-7.

Shephard, R., Limits to the measurement of habitual physical activity by questionnaires 2003. *Br J Sports Med,* vol. 37, no. 3, pp. 197-206.

Silbersack, Y., Taute, B., Hein, W. & Podhaisky, H. 2004. Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression. *J Bone Joint Surg Br,* 86**,** 809-12.

Simpson, L. A., Eng, J. J., Klassen, T. D., Lim, S. B., Louie, D. R., Parappilly, B.,

Sakakibara, B. M. & Zbogar, D. 2015. Capturing step counts at slow walking speeds in older adults: Comparison of ankle and waist placement of measuring device. *J Rehabil Med*.

Sobieraj-Teague, M., Hirsh, J., Yip, G., Gastaldo, F., Stokes, T., Sloane, D., O'Donnell, M. & Eikelboom, J. 2012. Randomized controlled trial of a new portable calf compression device (Venowave) for prevention of venous thrombosis in high-risk neurosurgical patients. *J Thromb Haemost,* 10**,** 229-35.

Stackpool, C. M., Porcari, J. P., Mikat, R. P. & Gilette, C. 2014. The accuracy of various activity trackers in estimating steps taken and energy expenditure. *J Fit Res,* 3**,** 32-48.

Stannard, J., Lopez-Ben, R., Volgas, D., Anderson, E., Busbee, M., Karr, D., Mcgwin, G. J. & Alonso, J. 2006. Prophylaxis against deep-vein thrombosis following trauma: a prospective, randomized comparison of mechanical and pharmacologic prophylaxis. *J Bone Joint Surg Am,* 88**,** 261-6.

Stansfield, B., Hajarnis, M. & Sudarshan, R. 2015. Characteristics of very slow stepping in healthy adults and validity of the activPAL3 activity monitor in detecting these steps. *Med Eng Phys,* 37**,** 42-7.

Sterne, J., Egger, M. & Moher, D. 2011. Chapter 10: Addressing reporting biases. *In:* Higgins, J. & Green, S. (eds.) *Cochrane Handbook for Systematic Reviews of Intervention.* Version 5.1.0 ed.

Stevens-Lapsley, J. E., Balter, J. E., Wolfe, P., Eckhoff, D. G. & Kohrt, W. M. 2012. Early neuromuscular electrical stimulation to improve quadriceps muscle strength after total knee arthroplasty: a randomized controlled trial. *Phys Ther,* 92**,** 210-26.

Storm, F. A., Heller, B. W. & Mazza, C. 2015. Step detection and activity recognition accuracy of seven physical activity monitors. *PLoS One,* 10**,** e0118723.

Strup, S., Gudziak, M., Mulholland, S. & Gomella, L. 1993. The effect of intermittent pneumatic compression devices on intraoperative blood loss during radical prostatectomy and radical cystectomy. *J Urol,* 150**,** 1176-8.

Sugitani, K., Arai, Y., Takamiya, H., Terauchi, R., Nakagawa, S., Ueshima, K. & Kubo, T. 2015. Factors affecting range of motion after total knee arthroplasty in patients with more than 120 degrees of preoperative flexion angle. *International Orthopaedics,* 39**,** 1535-1540.

Sultan, P. G., Most, E., Schule, S., Li, G. & Rubash, H. E. 2003. Optimizing flexion after total knee arthroplasty: advances in prosthetic design. *Clin Orthop Relat Res***,** 167-73.

Takacs, J., Pollock, C. L., Guenther, J. R., Bahar, M., Napier, C. & Hunt, M. A. 2014. Validation of the Fitbit One activity monitor device during treadmill walking. *J Sci Med Sport,* 17**,** 496-500.

Tamir, L., Hendel, D., Neyman, C., Eshkenazi, A. U., Ben-Zvi, Y. & Zomer, R. 1999. Sequential foot compression reduces lower limb swelling and pain after total knee arthroplasty. *J Arthroplasty,* 14**,** 333-8.

Taraldsen, K., Askim, T., Sletvold, O., Einarsen, E. K., Bjastad, K. G., Indredavik, B. & Helbostad, J. L. 2011. Evaluation of a body-worn sensor system to measure physical activity in older people with impaired function. *Phys Ther,* 91**,** 277-85.

Taraldsen, K., Chastin, S. F., Riphagen, Ii, Vereijken, B. & Helbostad, J. L. 2012. Physical activity monitoring by use of accelerometer-based body-worn sensors in older adults: a systematic literature review of current knowledge and applications. *Maturitas,* 71**,** 13-9.

Taraldsen, K. *et al.* 2014. Physical behavior and function early after hip fracture surgery in patients receiving comprehensive geriatric care or orthopedic care--a randomized controlled trial. *J Gerontol A Biol Sci Med Sci,* vol. 69, no. 3, pp. 338-45.

Tarnay, T., Rohr, P., Davidson, A., Stevenson, M., Byars, E. & Hopkins, G. 1980. Pneumatic calf compression, fibrinolysis, and the prevention of deep venous thrombosis. *Surgery,* 88**,** 489-96.

The Nordic Cochrane Centre TCc. Review Manager (RevMan) [Computer Program]. Version 5.2. 2012.

Tonelli, S., Rakel, B., Cooper, N., Angstom, W., and Sluka, K. 2011. Women with knee osteoarthritis have more pain and poorer function than men, but similar physical activity prior to total knee replacement. *Biol Sex Differ,* vol. 2, p. 12.

Tsonga, T., Kapetanakis, S., Papadopoulos, C., Papathanasiou, J., Mourgias, N., Georgiou, N., Fiska, A. & Kazakos, K. 2011. Evaluation of improvement in quality of life and physical activity after total knee arthroplasty in greek elderly women. *Open Orthop J,* 5**,** 343-7.

Tudor-Locke, C., Ainsworth, B. E., Whitt, M. C., Thompson, R. W., Addy, C. L. & Jones, D. A. 2001. The relationship between pedometer-determined ambulatory activity and body composition variables. *Int J Obes Relat Metab Disord,* 25**,** 1571-8.

Tudor-Locke, C. & Bassett, D. R., Jr. 2004. How many steps/day are enough? Preliminary pedometer indices for public health. *Sports Med,* 34**,** 1-8.

Tudor-Locke, C., Hatano, Y., Pangrazi, R. P. & Kang, M. 2008. Revisiting "how many steps are enough?". *Med Sci Sports Exerc,* 40**,** S537-43.

Tudor-Locke, C., Washington, T. L. & Hart, T. L. 2009. Expected values for steps/day in special populations. *Prev Med,* 49**,** 3-11.

Tudor-Locke, C., Leonardi, C., Johnson, W. D., Katzmarzyk, P. T. & Church, T. S. 2011. Accelerometer steps/day translation of moderate-to-vigorous activity. *Prev Med,* 53**,** 31-3.

Turpie, A., Bauer, K., Caprini, J., Comp, P., Gent, M. & Muntz, J. 2007. Fondaparinux combined with intermittent pneumatic compression vs. intermittent pneumatic compression alone for prevention of venous thromboembolism after abdominal surgery: a randomized, double-blind comparison. *J Thromb Haemost,* 5**,** 1854-61.

UF Health Rehab Centre- Shands Hospital, "Knee Replacement Surgery Patient Information Manual: Maximizing Your New Knee(s)," UFHealth University of Florida Health. https://www.ortho.ufl.edu/sites/ortho.ufl.edu/files/pdf/education/KneeReplacementSurgeryMaximizingYourNewKnee.pdf http://www.webcitation.org/6pQVNTvjA

UPMC Beacon Centre for Orthopaedics, "Guidelines for Patients having a Total Knee Replacement," UPMC Beacon. Hospital. http://www.beaconhospital.ie/images/physio/Knee_replacement.pdf http://www.webcitation.org/6pQVDPGXy

Urbankova, J., Quiroz, R., Kucher, N. & Goldhaber, S. 2005. Intermittent pneumatic compression and deep vein thrombosis prevention. A meta-analysis in postoperative patients. *Thromb Haemost,* 94**,** 1181-5.

U.S. Department of Health and Human Services. Physical activity and health: a report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National

Vanek, V. 1998. Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves. *Am Surg,* 64**,** 1050-8.

Van Remoortel, H., Giavedoni, S., Raste, Y., Burtin, C., Louvaris, Z., Gimeno-Santos, E., Langer, D., Glendenning, A., Hopkinson, N. S., Vogiatzis, I., Peterson, B. T., Wilson, F., Mann, B., Rabinovich, R., Puhan, M. A. & Troosters, T. 2012. Validity of activity monitors in health and chronic disease: a systematic review. *Int J Behav Nutr Phys Act,* 9**,** 84.

Vanscheidt, W., Ukat, A. & Partsch, H. 2009. Dose-response of compression therapy for chronic venous edema--higher pressures are associated with greater volume reduction: two randomized clinical studies. *J Vasc Surg,* 49**,** 395-402, 402 e1.

Velmahos, G., Petrone, P., Chan, L., Hanks, S., Brown, C. & Demetriades, D. 2005. Electrostimulation for the prevention of deep venous thrombosis in patients with major trauma: a prospective randomized study. *Surgery,* 137**,** 493-8.

Vissers, M., Bussmann, J., de Groot, I. D., Verhaar, J. & Reijman, M. 2013. Physical functioning four years after total hip and knee arthroplasty. *Gait Posture,* 38**,** 310-5.

Walsh, M., Woodhouse, L., Thomas, S., and Finch, E. 1998. Physical impairments and functional limitations: a comparison of individuals 1 year after total knee arthroplasty with control subjects. *Phys Ther,* vol. 78, no. 3, pp. 248-58.

Wang, Y. H., Meng, F., Zhang, Y., Xu, M. Y. & Yue, S. W. 2015. Full-movement neuromuscular electrical stimulation improves plantar flexor spasticity and ankle active dorsiflexion in stroke patients: A randomized controlled study. *Clin Rehabil*.

Warburton, D. E., Nicol, C. W. & Bredin, S. S. 2006. Health benefits of physical activity: the evidence. *CMAJ,* 174**,** 801-9.

Wendland, D. & Sprigle, S. 2012. Activity monitor accuracy in persons using canes. *J Rehabil Res Dev,* 49**,** 1261-8.

Werbel, G. & Shybut, G. 1986. Acute compartment syndrome caused by a malfunctioning pneumatic-compression boot. A case report. *J Bone Joint Surg Am,* 68**,** 1445-6.

White, R. 2003. The Epidemiology of Venous Thromboembolism. *Circulation,* 107**,** I-4-I-8.

White, L., Volfson, Z., Faulkner, G. & Arbour-Nicitopoulos, K. 2016. Reliability and Validity of Physical Activity Instruments Used in Children and Youth With Physical Disabilities: A Systematic Review. *Pediatr Exerc Sci,* 28**,** 240-63.

Whitelaw, G., Oladipo, O., Shah, B., Demuth, K., Coffman, J. & Segal, D. 2001. Evaluation of intermittent pneumatic compression devices. *Orthopedics,* 24**,** 257-61.

Windisch, C., Kolb, W., Kolb, K., Grutzner, P., Venbrocks, R. & Anders, J. 2011. Pneumatic compression with foot pumps facilitates early postoperative mobilisation in total knee arthroplasty. *Int Orthop,* 35**,** 995-1000.

World Health Organization. Global Recommendations on Physical Activity for Health. 2010. Available from: http://whqlibdoc.who.int/publications/2010/9789241599979_eng.pdf?ua=1 http://www.webcitation.org/6pQWG7Jps

Yilmaz, S., Calbiyik, M., Yilmaz, B. K. & Aksoy, E. 2015. Potential role of electrostimulation in augmentation of venous blood flow after total knee replacement: A pilot study. *Phlebology*.

Young, D., Reynolds, K., Sidell, M., Brar, S., Ghai, N., Sternfeld, B., Jacobsen, S., Slezak, J., Caan, B. & Quinn, V. 2014. Effects of physical activity and sedentary time on the risk of heart failure. *Circ Heart Fail,* 7**,** 21-7.

Yusuf, S., Peto, R., Lewis, J., Collins, R. & Sleight, P. 1985. Beta blockade during and after myocardial infarction: an overview of the randomized trials. *Prog Cardiovasc Dis,* 27**,** 335-71.

Appendix

Journal Publications Arising from this Thesis

The Use of Intermittent Pneumatic Compression in Orthopedic and Neurosurgical Post-Operative Patients: A Systematic Review and Meta-Analysis

This paper is core to this thesis and appears as Chapter 2. The first page that appears in *Annals of Surgery* is listed here.

The Use of Intermittent Pneumatic Compression in Orthopedic and Neurosurgical Postoperative Patients

A Systematic Review and Meta-analysis

Sandra O'Connell, BSc,[*]*Khalid Bashar, MBBS, MRCS,*[‡] *Barry J. Broderick, PhD,*[¶§] *James Sheehan, MD, PhD,*[‖] *Fabio Quondamatteo, MD,*[‖‖] *Stewart R. Walsh, MCh, MSc, FRCS,*[**] *Gearoid ÓLaighin, PhD,*[¶§] *and Leo R. Quinlan, PhD*[*]

Objective: The objective of this systematic review and meta-analysis was to carry out an up-to-date evaluation on the use of compression devices as deep vein thrombosis (DVT) prophylaxis methods in orthopedic and neurological patients.

Summary of Background Data: There is an increased risk of DVT with surgery, particularly in patients who are not expected to mobilize soon after their procedures, such as orthopedic and neurosurgical patients. Compression devices are often employed for DVT prophylaxis in these patients. However, the true efficacy of these devices and the standardization of use with these devices are yet to be established.

Methods: Medline, CINAHL, Embase, Google Scholar, and the Cochrane library electronic databases were searched to identify randomized controlled trials and observational studies reporting on the use of compression devices for DVT prevention.

Results: Nine studies were included for review and meta-analysis. Use of an intermittent pneumatic compression device alone is neither superior nor inferior to chemoprophylaxis.

Conclusions: In the absence of large randomized multicenter trials comparing the use of intermittent pneumatic compression or chemoprophylaxis alone to a combination of both treatments, the current evidence supports the use of a combined approach in high-risk surgical patients.

Keywords: deep venous thrombosis, intermittent pneumatic compression, prophylaxis

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Deep vein thrombosis (DVT), the development of a pathological thrombus in a deep vein, is of particular concern within the orthopedic and neurological communities, especially following surgeries in these fields, where patients are deemed at high risk for developing DVT. The main danger associated with DVT is that of pulmonary embolism (PE), which can occur when the clot breaks away from the vessel wall and travels as far as the lungs, where it can be fatal.[1] Together, DVT and PE are known collectively as venous thromboembolism (VTE). There is an increased risk of DVT with surgery, particularly in patients who are not expected to mobilize soon after their procedures, such as orthopedic patients after total hip arthroplasty (THA)/total knee arthroplasty (TKA) surgery, or neurosurgical patients following spinal/head procedures. To this end, prevention of DVT is more important in those who are considered to be at high risk for developing VTE complications, with the continuing debate on the best modality to achieve a reasonable risk reduction while avoiding complications associated with chemoprophylaxis, such as major bleeding.[2–5]

The increased incidence of osteoarthritis and rheumatoid arthritis in an aging population makes it a particularly worrying concern within the orthopedic community. Combined with the benefit these surgeries provide with regard to both function and quality of life for patients, their prevalence will only continue to increase. For example, in the USA alone, it has been estimated that the demand for primary THA will increase from 293,094 in 2010 to 511,837 in 2020, an increase of 75%, with the demand for TKA estimated to increase from 655,336 to 1,375,574 over the same period, an increase of 110%.[6] According to data from the Global Orthopaedic Registry, the overall incidence of major complications following THA and TKA is low.[7] However, DVT and PE are complications that do occur. Indeed, DVT is one of the most common inhospital complications, occurring in 0.6% and 1.4% of THA and TKA patients, respectively.[7] Overall, DVT was found to occur in up to 1.4% of patients enrolled in the Global Orthopaedic Registry. This would suggest that although many forms of prophylaxis are available, both pharmacological and mechanical, DVT remains an important clinical burden following these surgeries.

DVT is also a prominent concern within the neurological community. Although anticoagulants such as low molecular weight heparin (LMWH) and unfractionated heparin are recommended for DVT prevention in neurological patients, extreme caution must be exercised with their use due to the risk of bleeding in the brain or spine, which could be fatal.[8–12] As such, mechanical methods of prophylaxis including graduated compression stockings (GCS) and intermittent pneumatic compression (IPC) devices are also recommended for neurological patients.

IPC devices are a popular form of mechanical DVT prevention that prevents venous stasis. These devices consist of a pneumatic pump, which connects to 1 or more inflatable cuffs/pads via air hoses. The cuffs are wrapped around a patient's foot or leg. With IPC of the foot, rapid, cyclical inflation and deflation of the cuffs give a nonphysiological compression of the plantar venous plexus. Expulsion of blood from the foot prevents venous stasis. The blood is pushed through the venous system back toward the heart in order to

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Comparative Lower Limb Hemodynamics Using Neuromuscular Electrical Stimulation (NMES) versus Intermittent Pneumatic Compression (IPC)

This paper is core to this thesis and appears as Chapter 3. The first page that appears in *Physiological Measurement* is listed here. My contributions were as follows:

- Assisting in haemodynamic data collection
- Analysis and interpretation of the data
- Drafting of and critical review of manuscript

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Comparative lower limb hemodynamics using neuromuscular electrical stimulation (NMES) versus intermittent pneumatic compression (IPC)

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Abstract

Deep Vein Thrombosis (DVT) is a life threatening condition and a serious concern among hospitalised patients, with death occurring in approximately 6% of cases. Intermittent pneumatic compression (IPC) is commonly used for DVT prevention, however suffers from low compliance and issues of usability and portability. Neuromuscular electrical stimulation (NMES) has been shown to improve lower limb hemodynamics but direct comparison with IPC in terms of hemodynamics is rare but very important to determine the potential effectiveness of NMES in DVT prevention.

Lower limb IPC was compared to calf NMES, in 30 healthy volunteers (18–23 years). Each intervention was carried out on each leg, on the popliteal vein measured using Doppler ultrasound. All interventions produced significantly greater haemodynamic responses compared to baseline. Calf- IPC and NMES produced significant increases in venous blood velocity (cm/s) and volume of blood ejected per cycle (1 cycle of NMES expels 23.22 ml compared to the baseline ejected volume of 2.52 ml, measured over 1 s ($p < 0.001$ versues baseline).

These Shoes are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps

This paper is core to this thesis and appears as Chapter 4. The first page that appears in *PLoS One* is listed here.

PLOS ONE

RESEARCH ARTICLE

These Shoes Are Made for Walking: Sensitivity Performance Evaluation of Commercial Activity Monitors under the Expected Conditions and Circumstances Required to Achieve the International Daily Step Goal of 10,000 Steps

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Competing Interests: The authors have declared that no competing interests exist.

Abstract

Introduction

Physical activity is a vitally important part of a healthy lifestyle, and is of major benefit to both physical and mental health. A daily step count of 10,000 steps is recommended globally to achieve an appropriate level of physical activity. Accurate quantification of physical activity during conditions reflecting those needed to achieve the recommended daily step count of 10,000 steps is essential. As such, we aimed to assess four commercial activity monitors for their sensitivity/accuracy in a prescribed walking route that reflects a range of surfaces that would typically be used to achieve the recommended daily step count, in two types of footwear expected to be used throughout the day when aiming to achieve the recommended daily step count, and in a timeframe required to do so.

Methods

Four commercial activity monitors were worn simultaneously by participants (n = 15) during a prescribed walking route reflective of surfaces typically encountered while achieving the daily recommended 10,000 steps. Activity monitors tested were the Garmin Vivofit™, New Lifestyles' NL-2000™ pedometer, Withings Smart Activity Monitor Tracker (Pulse O_2), and Fitbit One™.

When a Step Is Not a Step! Specificity Analysis of Five Physical Activity Monitors

This paper is core to this thesis and appears as Chapter 5. The first page that appears in *PLoS One* is listed here.

PLOS ONE

RESEARCH ARTICLE

When a Step Is Not a Step! Specificity Analysis of Five Physical Activity Monitors

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Competing Interests: The authors have declared that no competing interests exist.

Abstract

Introduction

Physical activity is an essential aspect of a healthy lifestyle for both physical and mental health states. As step count is one of the most utilized measures for quantifying physical activity it is important that activity-monitoring devices be both sensitive and specific in recording actual steps taken and disregard non-stepping body movements. The objective of this study was to assess the specificity of five activity monitors during a variety of prescribed non-stepping activities.

Methods

Participants wore five activity monitors simultaneously for a variety of prescribed activities including deskwork, taking an elevator, taking a bus journey, automobile driving, washing and drying dishes; functional reaching task; indoor cycling; outdoor cycling; and indoor rowing. Each task was carried out for either a specific duration of time or over a specific distance. Activity monitors tested were the ActivPAL micro™, NL-2000™ pedometer, Withings Smart Activity Monitor Tracker (Pulse O_2)™, Fitbit One™ and Jawbone UP™. Participants were video-recorded while carrying out the prescribed activities and the false positive step count registered on each activity monitor was obtained and compared to the video.

Results

All activity monitors registered a significant number of false positive steps per minute during one or more of the prescribed activities. The Withings™ activity performed best, registering a significant number of false positive steps per minute during the outdoor cycling activity only ($P = 0.025$). The Jawbone™ registered a significant number of false positive steps during the functional reaching task and while washing and drying dishes, which involved arm and hand movement ($P < 0.01$ for both). The ActivPAL™ registered a significant number of false positive steps during the cycling exercises ($P < 0.001$ for both).