

Institution: University of Hull		
Unit of Assessment: 03 – Allied Health Professions, Dentistry, Nursing and Pharmacy		
Title of case study: Supervised Exercise Programmes – a non-invasive, clinical and cost-effective intervention for intermittent claudication		
Period when the underpinning research was undertaken: 1996 – to date		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Prof Ian Chetter	Professor	1999 – present
Mr Dan Carradice	NIHR Lecturer (Clinical)	2012-2017
	Senior Lecturer (Clinical)	2017 – present
Mr George Smith	NIHR Lecturer (Clinical)	2012-2017
	Senior Lecturer (Clinical)	2017 – present
Miss Amy Harwood	PhD student	2013-2016
	Post Doctoral Fellow (Clinical)	2016-2018
Mr Patrick Coughlin	Lecturer (Clinical)	2012-2014
Ms Risha Lane (nee Gohil)	MD Fellow	2012-2014
Ms Katherine Mockford	MD Fellow	2010-2012
Mr Fayyaz Mazari	MD Fellow	2010-2012
Period when the claimed impact occurred: 2014 – to date		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact		
<p>Research in the Hull Academic Vascular Surgical Unit (AVSU) has directly impacted policy, practice and clinical education in the management of intermittent claudication (IC) a condition that affects 5% of the western adult population. Invasive revascularisation was frequently the first-line intervention for IC, with outcomes assessed using objective measures. The AVSU has undertaken seminal research that identified the best quality of life instruments for outcome assessment in IC, which are now recommended by international reporting standards. The Hull unit demonstrated clinical and cost effectiveness of supervised exercise programmes (SEP), compared with invasive revascularisation, stimulating a global revolution in IC management with the National Institute for Health and Care Excellence now recommending SEP as the first-line intervention.</p>		
2. Underpinning research		
<p>Historically, intermittent claudication (IC) was managed conservatively or by invasive revascularisation (angioplasty or bypass surgery). Objective measures of organ perfusion such as ankle pressures or treadmill walking distances were used to assess disease progression and treatment effectiveness. The Academic Vascular Surgical Unit (AVSU), led by Professor Ian Chetter, has worked for over 2 decades to:</p> <ol style="list-style-type: none"> ensure patient-reported quality of life (QoL) outcomes are prioritised and regarded as the standard for outcome assessment in both clinical practice and new clinical trials (2.1) and; provide conclusive evidence to support the use of supervised exercise programmes (SEP) as the global, first-line, intervention for claudication rather than invasive revascularization (2.2) <p>Furthermore, the work of the AVSU has underpinned international reporting standards, clinical guidelines and associated training, and has led to significant patient benefit.</p>		
Key research findings		
2.1 Identification of the most appropriate generic and disease specific QoL instruments for patients with IC		
<p>Based on a long-standing programme of research in Hull, the team found the Short Form 36 and EuroQoL instruments were the most appropriate <i>generic</i> QoL tools in terms of validity, reliability and responsiveness for use with patients suffering with IC [1]. Research findings demonstrated that the correlation between clinical indicators of disease severity and QoL was not sufficiently close to assume that changes in the clinical indicators resulted in reciprocal changes in QoL, and</p>		

thus it was concluded that QoL must be analysed independently [2]. The 2003 systematic review by the AVSU [1] also highlighted that disease-specific instruments for patients with claudication had undergone very limited evaluation. A subsequent prospective cohort study of 70 claudicants, identified the VascuQoL tool as the most appropriate disease-specific QoL instrument for this patient group [3].

2.2 Demonstration that supervised exercise programmes (SEP) were more effective at management of IC compared with surgical interventions.

Using both the generic and disease-specific outcome measures, the AVSU demonstrated in a non-randomised, controlled, trial of 70 claudicants, that SEP was both clinically- and cost-effective compared with conservative medical therapy and that the disease-specific, VascuQoL tool was again the most powerful [4]. In 2010, the AVSU published early outcomes from the first adequately powered (n=178), randomized, controlled, trial comparing SEP, angioplasty (a commonly used surgical intervention) and SEP plus angioplasty. Based on clinical and QoL changes at 3 months, it was concluded that SEP should be the primary treatment for claudicants and that angioplasty should always be preceded by a SEP [5]. The AVSU's subsequent work, including long term follow-up of this cohort, health economic analysis and Cochrane systematic review has confirmed the original conclusions and also identified the supplementary benefits of SEP in terms of general physical activity, balance and reduction in falls risk [6].

Our studies have identified that the "Achilles heel" of SEP is patient uptake, which can be as low as 25%. Qualitative research from the AVSU has identified the 3-month duration of the intervention as a frequently cited reason for non-participation. To address these issues, the AVSU is currently investigating the acceptability, efficacy and patient perceptions of a concentrated, short duration (6 weeks), anaerobic, high intensity SEP funded by an NIHR RfPB grant (£149,292) to ensure maximum patient benefit.

3. References to the research

1. Mehta T, Venkata Subramaniam A, Chetter I, McCollum P. Disease-specific quality of life assessment in intermittent claudication: review. *Eur J Vasc Endovasc Surg.* 2003 Mar;25(3):202-8
2. Mazari FA, Carradice D, Rahman MN, Khan JA, Mockford K, Mehta T, McCollum PT, Chetter IC. An analysis of relationship between quality of life indices and clinical improvement following intervention in patients with intermittent claudication due to femoropopliteal disease. *J Vasc Surg.* 2010 Jul;52(1):77-84.
3. Mehta T, Venkata Subramaniam A, Chetter I, McCollum P. Assessing the validity and responsiveness of disease-specific quality of life instruments in intermittent claudication. *Eur J Vasc Endovasc Surg.* 2006 Jan;31(1):46-52.
4. Lee HL, Mehta T, Ray B, Heng MS, McCollum PT, Chetter IC. A non-randomised controlled trial of the clinical and cost effectiveness of a Supervised Exercise Programme for claudication. *Eur J Vasc Endovasc Surg.* 2007 Feb;33(2):202-7
5. Mazari FA, Khan JA, Carradice D, Samuel N, Abdul Rahman MN, Gulati S, Lee HL, Mehta TA, McCollum PT, Chetter IC. Randomized clinical trial of percutaneous transluminal angioplasty, supervised exercise and combined treatment for intermittent claudication due to femoropopliteal arterial disease. *Br J Surg.* 2012 Jan;99(1):39-48
6. Lane R, Harwood A, Watson L, Leng GC. Exercise for intermittent claudication. *Cochrane Database Syst Rev.* 2017 Dec 26;12:CD000990.

Grants

The AVSU has been awarded almost £8 million in national and international peer reviewed funding for research into claudication, exercise and peripheral arterial disease, including the following major awards:

- George Davies Early Career award (P Coughlin) 2014 £150,000
- NIHR HTA Bypass v Angioplasty in Severe Ischaemia of the Leg (BASIL-2) trial – co-applicant with Prof A Bradbury (Birmingham); 2014 – 2023; £2,024,094
- NIHR HTA Balloon vs Stenting in Severe Ischaemia of the Leg (BASIL-3) trial; co-applicant

with Prof A Bradbury (Birmingham); 2015-2021; £1,938,633

- NIHR HTA Multiple Interventions for Diabetic Foot Ulcer Treatment (MIDFUT) trial; co-applicant with Mr D Russell (Leeds); 2017-2022; £1,787,716
- NIHR EME Does Neuromuscular Electrical Stimulation Improve the Absolute Walking Distance in Patients with Intermittent Claudication (NESIC) compared to best available treatment? A Multicentre Randomised Controlled Study; co-applicant with Prof A Davies (London); 2017-2021; £1,073,008
- NIHR **Senior Investigator** (Prof I Chetter) 2018-2023; £75,000
- NIHR RfPB High Intensity Interval Training In pATiEnts with intermittent claudication (INITIATE) study; **Chief Investigator** Prof I Chetter; 2019-2021; £149,292

Since 2014, members of the AVSU have won the Vascular Society of Great Britain and Ireland's Sol Cohen Prize on 2 occasions and the Richard Wood Prize once. Prof Chetter is the Royal College of Surgeons of England, National Research Speciality Vascular Lead, as well as being the current Chair of the Vascular Society of Great Britain and Ireland's Research Committee.

4. Details of the impact

Based on the research from the AVSU at Hull there has been an international step-change in both the assessment of outcomes and the shift to non-interventional management of IC. This has resulted in significant benefits for patients, practitioners and health care institutions alike. Specifically, there has been a significant change to using patient-focused outcomes as a measure of treatment for IC (**4.1**); widespread adoption of SEP as a non-invasive treatment alternative for IC management (**4.2**); and incorporation of SEP into multiple national and international training guidelines (**4.3**).

4.1 A paradigm shift to patient-focused outcomes in recent and ongoing trials

Research from Hull has underpinned a number of international guidelines that now recommend the use of both generic and disease-specific QoL outcome measures to assess efficacy of intervention in IC (**Evidence 1**). Furthermore, our research supported the prioritization of the generic and disease-specific outcome measures in the guidelines update for the management of peripheral arterial disease in 2015 (**Evidence 2**). Additionally, Prof Chetter was/is a member of the **Trial Management Groups for 3 recently completed/ongoing National Institute of Health Research (NIHR) trials which have all incorporated patient-focused outcome measures**. The NIHR HTA "*Bypass v Angioplasty in Severe Ischaemia of the Leg*" (BASIL 2) (completed with 345 participants) and BASIL3 (Ongoing until May 2021 with recruitment aimed at 477 participants) trials include generic (EuroQol 5D, Short Form12) and disease-specific (VascuQol, (**Evidence 3i, ii**)). The completed NIHR EME "*Does Neuromuscular Electrical Stimulation Improve the Absolute Walking Distance in Patients with Intermittent Claudication*" (NESIC) trial (192 participants) includes generic (EQ5D, Short Form 36) and disease specific (intermittent claudication questionnaire) as outcome measures (**Evidence 3iii**).

4.2 Widespread uptake of SEP as first line intervention for IC

Hull's research is an essential component of the National Institute for Health and Care Excellence (NICE) clinical guidelines 147 (Diagnosis and management of peripheral arterial disease) which recommend that SEP should be offered as first-line intervention for all patients with IC, replacing angioplasty that should only be offered if a SEP has not produced satisfactory symptomatic improvement (**Evidence 4**). **Patients that have received SEP report that they are able to walk much "further without experiencing pain" (Evidence 5i) and that their "quality of life has improved considerably" (Evidence 5ii)**. International guidelines in North America, proposed jointly by the American Heart Association and American College of Cardiology (**Evidence 6**) and Europe (**Evidence 1**) advocate the same treatment plans again based on Hull's published work.

During the ongoing coronavirus pandemic the Circulation Foundation, the UK's only national peripheral arterial disease charity, recognized the AVSU's longstanding expertise in the area of SEP research, and asked the unit to produce a booklet detailing home-based SEP for patients in isolation (**Evidence 7i**). Ms Rachel Bell, Chair of the Circulation Foundation stated, "... the research undertaken in Hull by Prof Chetter's team has a huge impact upon our work and is incredibly beneficial to the mission of our charity" (**Evidence 7ii**).

4.3 Impacts on healthcare practitioner training and service providers

The UK Specialty Advisory Committee for Vascular Surgical Training has, since 2018, included SEP as the first line therapy for IC into the recent additions of the UK curricula for training vascular surgeons, nurses and podiatrists, thus all new trainees in the breadth of disciplines involved in treating IC are implementing the practice defined by Hull's work (**Evidence 8i, ii, iii**). The Vascular Society of Great Britain & Ireland (VSGBI) produced a document entitled "*The provision of services for patients with vascular disease 2018*", which sets out the principles by which a vascular service should deliver optimal patient care in the UK. This publication was based on the research from the AVSU in Hull and advocates offering SEP to all patients with IC (**Evidence 9**). The Past-president of the VSGBI states that the AVSU's work on SEP has "*revolutionized the thinking of practitioners and available treatment methods*" (**Evidence 10**). **The new training regimens are cost-effective and represent a non-invasive alternative not previously available**. Research from Hull highlighted the huge variability in the provision of SEP for IC, which may only be provided by as few as 42% of UK vascular units. As a result of these findings in 2018 NICE released a Quality statement identifying the provision of SEP for IC as a high priority area for quality improvement across the UK (**Evidence 11**). Furthermore, the training has been adopted across Europe as this fulfills the current best-practice guidelines (**Evidence 12**).

Similarly, in response to Public Health England's "Getting It Right First Time (GIRFT)" programme highlighting lack of timely access to services for patients with peripheral arterial disease (**Evidence 13**) the Vascular Society of Great Britain and Ireland produced a Quality Improvement Framework(QIF) in 2019 aimed at providing a best practice clinical care pathway for peripheral arterial disease. This QIF includes a target of >90% UK vascular units to provide commissioned SEP within 1 hour travel time for patients with IC (**Evidence 14**)

5. Sources to corroborate the impact

Evidence 1. European Society of Cardiology/European Society of Vascular Surgery Guideline on the Diagnosis and Treatment of Peripheral Arterial Disease. Eur J Vasc Endovasc Surg. 2018; 55: 305-68

Evidence 2. An Update on Methods for Revascularization and Expansion of the TASC Lesion Classification to Include Below-the-Knee Arteries: A Supplement to the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). The TASC Steering Committee, Michael R Jaff. Vascular Medicine 20; 5 465-478

Evidence 3. Trials using assessment of outcomes and non-interventional management of IC.

i. BASIL-2 Trial Investigators. Bypass versus angio plasty in severe ischaemia of the leg - 2 (BASIL-2) trial: study protocol for a randomised controlled trial. Trials. 2016 Jan 6;17:11.

ii. BASIL-3 Collaborative Group. BAloon versus Stenting in severe Ischaemia of the Leg-3 (BASIL-3): study protocol for a randomised controlled trial. Trials. 2017 May 19;18(1):224.

iii. Lawton R et al. . A multicenter randomized controlled study to evaluate whether neuromuscular electrical stimulation improves the absolute walking distance in patients with intermittent claudication compared with best available treatment. J Vasc Surg. 2019 May;69(5): 1567-1573.

Evidence 4. NICE Clinical guideline 147. Lower limb peripheral arterial disease; diagnosis and management. Published November 2019. www.nice.org.uk/guidance/cg147/evidence/full-guideline-pdf-186865023

Evidence 5i Testimonial. Patient A.

Evidence 5ii Testimonial. Patient B.

Evidence 6. 2016 AHA/ACC Guideline on Management of Patients with Lower Extremity Peripheral Arterial Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.

<https://doi.org/10.1161/CIR.0000000000000470>.

Evidence 7i. <https://www.circulationfoundation.org.uk/news/covid-19-special-configure>

Evidence 7ii. Testimonial. Chair of Circulation Foundation

Evidence 8. Training curricula promoting SEP as first line treatment for Intermittent Claudication

i. Intercollegiate Surgical Curriculum Programme - Vascular Surgery Curriculum

https://www.gmc-uk.org/-/media/documents/vascular-inc_trauma-tig-approved-jul-17_pdf-72509215.pdf

ii. Society of Vascular Nurses – Advanced Vascular Nurse Competencies

<https://www.svn.org.uk/wp-content/uploads/2014/12/SVN-advanced-compet-final-version.pdf>

iii. College of Podiatry; <https://cop.org.uk/api/documentlibrary/download?documentId=280>

Evidence 9. The Provision of Services for patients with Vascular Disease 2018

<https://www.vascularsociety.org.uk/userfiles/pages/files/Document%20Library/VS%202018%20Final.pdf>

Evidence 10. Testimonial. Immediate Past-President of the Vascular Society of Great Britain and Ireland

Evidence 11. Quality statement from NICE www.nice.org.uk/guidance/qs52/chapter/Quality-statement-3-Supervised-exercise-programmes

Evidence 12. European adoption of curricula

https://uemsvascular.com/wpsite/wp-content/uploads/2017/10/2.6_Syllabus_FEBVS-1.pdf

Evidence 13 GIRFT

https://gettingitrightfirsttime.co.uk/wp-content/uploads/2018/02/GIRFT_Vascular_Surgery_Report-March_2018.pdf

Evidence 14 PAD QIF

[https://www.vascularsociety.org.uk/userfiles/pages/files/Newsletters/PAD%20QIF%20April%202019\(1\).pdf](https://www.vascularsociety.org.uk/userfiles/pages/files/Newsletters/PAD%20QIF%20April%202019(1).pdf)