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| Institution: Sheffield Hallam University | | |
| Unit of Assessment: UOA24 - Sport and Exercise Sciences, Leisure and Tourism | | |
| Title of case study: Lifestyle Changes to Improve Outcomes in People Living With and Beyond Cancer | | |
| Period when the underpinning research was undertaken: 2000 - 2020 | | |
| 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: |
| Professor Liam Bourke | Professor of Cancer Research | 2007-2010 and 2014-present |
| Dr Helen Crank | Reader | 2002-2019 |
| Dr Rebecca Turner | Research Fellow | 2018-present |
| Dr Sophie Reale | Research Fellow | 2018-present |
| Liam Humphries | Research Fellow | 2006-present |
| Professor John Saxton | Reader | 2000-2010 |
| Period when the claimed impact occurred: August 2013 - July 2020 | | |
| Is this case study continued from a case study submitted in 2014? No | | |

1. Summary of the impact

Research undertaken at Sheffield Hallam University on optimising cancer-specific outcomes through lifestyle and exercise interventions has underpinned international clinical guidelines for cancer patients and survivors. New standards of clinical best practice have been established, based on the research, which have been endorsed by the European Association of Urology (EAU), the European Association of Radiotherapy and Oncology (ESTRO), the European Society of Urogenital Radiology (ESUR) and the International Society of Geriatric Oncology (ISOG). The research has also influenced national guidance in a number of countries. It has shaped practice internationally, changing clinical approaches and impacting on the quality of life of patients. It has also led to the establishment of a new exercise rehabilitation service for cancer survivors, as well as specialist cancer care and exercise training programmes for exercise and health care professionals.

2. Underpinning research

Cancer survivors suffer substantial, chronic and debilitating impacts on health outcomes and quality of life. This includes (*inter alia*) depression, anxiety, increased CVD risk, increased fracture risk, functional declines, adverse body composition changes, lymphedema, cognitive impairment, sexual dysfunction, loss of muscle strength and even suicidal intent. There has been a growing appreciation of the potential benefits of lifestyle changes for people diagnosed with cancer, but there are few high quality randomised controlled trials (RCT) that demonstrate any impact on clinically relevant outcomes or outcomes that are meaningful to survivors.

At Sheffield Hallam University a dedicated research team led by Professor Liam Bourke design, develop and lead multi-centre clinical trials evaluating the impacts of lifestyle changes and complex behavioural interventions in cancer populations. Our studies are implicitly designed to improve cancer-specific outcomes for patients, ranging from cancer-specific quality of life, cancer-related fatigue, combating the adverse effects of primary cancer treatments and even improved cancer progression outcomes. Our work has been recognised in national awards - in 2017 Professor Bourke won the inaugural patient involvement in research prize from Cancer Research UK. Our group actively partners through grant awards with other co-applicants at institutions such as University College London Hospitals, Barts Medical School and the Universities of Leeds, Sheffield, York and Bristol.

Impact is at the heart of our research design. One of our key strengths is in the 'real-world' applicability of our work. Studies of lifestyle changes in cancer populations often suffer from a

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highly problematic lack of generalisability, leading to critical problems with implementation and impact due to non-representative study cohorts (i.e. excluding patients with realistic co-morbidity profiles and recruiting cohorts who are already physically active to trials). This is further compounded by powering studies and developing interventions around outcomes with little or no clinical relevance. Our studies at Sheffield Hallam have purposefully been designed to address these methodological weaknesses in the field in terms of optimising our study cohort inclusivity, identifying clinically relevant outcomes to test, and embedding our interventions into NHS clinical practice. We generate research that is applicable to both 'real-world' patients and 'real-world' clinical practice.

Prostate and breast cancer make up the two largest survivorship groups in the UK - our research has been targeted at these two groups specifically to maximise real world impact.

Prostate Cancer

Our 2013 RCT of lifestyle changes (exercise training and tailored diet advice) in men with advanced prostate cancer on long-term androgen deprivation therapy (ADT) [R1] was the first in the world to demonstrate that not only could such an intervention improve both cancer-specific quality of life (FACT-P) and cancer-specific fatigue (FACT-F), but also that the magnitude of impact exceeded the thresholds for clinically meaningful effects (FACT-P mean difference: 8.9 points; $p = 0.001$, FACT-F mean difference: 5.3 points; $p < 0.001$). The trial was purposefully designed to maximise 'real-world' applicability by recruiting non-active participants (reflective of the larger patient population) who also suffered from multiple morbidities (CVD, metabolic dysfunction, joint pathologies) and also including men with metastatic disease. Further, men with advanced prostate cancer on ADT are at high risk of CVD (strokes, heart attacks, sudden cardiac death). Our analysis was the first in the world to report that such lifestyle changes improve arterial health [R2], assessed using a novel ultrasound technique: flow mediated dilatation (FMD). Changes in FMD seen in this study translated to a clinically significant risk reduction of 29% fewer adverse cardiovascular events. Qualitative analysis of patient reported impacts [R3] confirmed quantitative findings from the trial, and also revealed that the intervention was successful in reducing anxiety around treatment and fear of disease progression/recurrence - one of the most common and typically intractable causes of distress in cancer survivors.

Breast Cancer

Our 2007 RCT [R4] was again specifically designed to be inclusive in its recruited cohort and was designed and powered to improve important clinically relevant outcomes. The tailored exercise intervention successfully improved cancer-specific quality of life (as determined through the Functional Assessment of Cancer Therapy - General (FACT-G) method), and the magnitude of impact exceeded the threshold for clinically meaningful effects (FACT-G mean difference, 9.8 units; $p = .004$). Further, in an RCT combining healthy eating and tailored exercise programme, we reported clinically important reductions in depressive symptom scores and a normalisation of hypothalamic-pituitary-adrenal (HPA) axis regulation for survivors in the early recovery phase, up to 18 months after breast cancer treatment. [R5]

To facilitate integration in clinical practice and optimise clinical benefits, we have gone further. Looking across all cancers, our 2018 Cochrane review highlighted how behavioural interventions should be designed and tailored to maximise adherence to prescribed exercise. Identification of key behaviour change techniques supports robust and meaningful behavioural change, longer term maintenance and provides enduring patient benefit. [R6]

3. References to the research

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- R1.** Bourke L, Gilbert S, Hooper R, Steed L, Joshi M, Catto J, Saxton J, Rosario D (2013). Lifestyle Changes for Improving Disease Specific Quality of Life in Sedentary Men on Long Term Androgen Deprivation Therapy for Advanced Prostate Cancer. A Randomised Controlled Trial. *European Urology*, 65(5):865-72.
<https://doi.org/10.1016/j.eururo.2013.09.040>

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- R2. Gilbert S, Tew G, Fairhurst C, Bourke L, Saxton J, Winter EM, Rosario D (2016). Effects of a Lifestyle Intervention on Endothelial Function in Men on Long-Term Androgen Deprivation Therapy for Prostate Cancer. *British Journal of Cancer*, 114:401-8. <https://doi.org/10.1038/bjc.2015.479>
- R3. Bourke L, Sohanpal R, Nanton R, Crank H, Rosario D, Saxton J (2012). A Qualitative Study Evaluating Experiences of a Lifestyle Intervention in Men with Prostate Cancer Undergoing Androgen Suppression Therapy. *Trials*, 13, 208. <https://doi.org/10.1186/1745-6215-13-208>
- R4. Daley AJ, Crank H, Saxton JM, Mutrie N, Coleman R, Roalfe A (2007). Randomized Trial of Exercise Therapy in Women Treated for Breast Cancer. *Journal of Clinical Oncology*, 25(13): 1713-21. <https://doi.org/10.1200/jco.2006.09.5083>
- R5. Saxton JM, Scott EJ, Daley AJ, Woodroffe M, Mutrie N, Crank H, Powers HJ, Coleman RE (2014). Effects of an Exercise and Hypocaloric Healthy Eating Intervention on Indices of Psychological Health Status, Hypothalamic-Pituitary-Adrenal Axis Regulation and Immune Function After Early-Stage Breast Cancer: A Randomised Controlled Trial. *Breast Cancer Research*, 16, R39. <https://doi.org/10.1186/bcr3643>
- R6. Turner RR, Steed L, Quirk H, Greasley RU, Saxton JM, Taylor SJ, Thaha MA, Bourke L (2018). Interventions for Promoting Habitual Exercise in People Living with and Beyond Cancer. *Cochrane Database of Systematic Reviews* 2018, 9. <https://doi.org/10.1002/14651858.CD010192.pub3>

All articles were rigorously peer-reviewed prior to publication in leading journals in the field.

4. Details of the impact

Our research has generated the following impacts for cancer patients, survivors and health care professionals:

Underpinning International and National Cancer Guidelines

Prostate cancer is the most frequently diagnosed cancer among men in over one-half (105 of 185) of the countries of the world: Australia, Northern and Western Europe representing the highest age standardised rate per 100,000 people. According to the European Commission, around 1.3 million citizens of the European Union are estimated to have had a prostate cancer diagnosis in the last five years [E.1]. In 2016, the Chair of the European Prostate Cancer Clinical Guidelines committee requested Professor Bourke lead the addition of an entirely new chapter to their international guidance, centred around the adverse effects of cancer treatments and maintaining/improving quality of life for men with prostate cancer. Lifestyle recommendations had previously not been part of the clinical guidance. Sheffield Hallam research studies in prostate cancer formed the cornerstone of the new European recommendation, written in the guidelines, to "Offer men on androgen deprivation therapy, 12 weeks of supervised (by trained exercise specialists) combined aerobic and resistance exercise" [E.2].

This research-based recommendation has featured in these international guidelines, endorsed by the European Association of Urology (EAU), European Association of Radiotherapy and Oncology (ESTRO), European Society of Urogenital Radiology (ESUR) and the International Society of Geriatric Oncology (ISOG), since 2017 [E.2]. These guidelines are accessed approximately 200,000 times per year by health care professionals working and treating men with prostate cancer in Europe [E.3]. Inclusion in these guidelines has directly elevated what is considered 'best care' for men, in terms of optimising cancer-specific quality of life and reducing cancer-specific fatigue.

Our research has also shaped national policy in Germany, appearing in the 'Guideline Program in Oncology' of the Working Group of the Scientific Medical Societies in Germany (AWMF), the German Cancer Society (DKG) and the German Cancer Aid (DKH). [E.4]

In addition, research reports from our trials in both breast and prostate cancer has been cited in the Clinical Oncology Society of Australia's 'Position Statement' on exercise and cancer care,

highlighting that exercise needs to be embedded in standard oncology practice and include referrals to accredited exercise professionals. [E.5]

Our Cochrane review behavioural outcomes have been cited and used to shape the most recent practice guideline update from the American Cancer Society. This oncology practice guidance highlighted that behaviour change issues are a critical impediment to meaningful change and better patient outcomes. Our Cochrane findings directly address this problem and provide solutions - facilitating integration of lifestyle programmes in cancer management plans. [E.6]

Changing Clinical Practice and Providing Patient Benefit

Following inclusion in these guidelines, our research has been widely adopted and changed clinical approaches.

"As a direct result of the...evidence base generated from SHU research outputs, from 2018 we have been able to re-examine and reform our care pathways within STH urology to optimise the provision of cancer treatment for all men with advanced prostate disease. This involves now embedding entirely new pathways of lifestyle and behavioural support in standard care for patients after training provided by SHU research staff to urologists, oncologists and clinical nurse specialists working in our NHS service. Men on ADT can now be provided with disease specific tailored referrals to exercise for up to 12 months. We regularly hear from men in clinic how beneficial such provision has been to them."

- Professor Derek Rosario, Consultant Urological Surgeon,
Sheffield Teaching Hospitals NHS Trust [E.7]

"We have learnt increasingly how important exercise is to outcomes following treatment for breast cancer. I now routinely recommend exercise to patients as one of the things they can do...to reduce the risk of recurrence."

- Rebecca Roylance, Consultant Medical Oncologist,
University College London Hospitals [E.7]

"SHU [research] helps us to be more informed practitioners and benefits clinically important outcomes for our patients. As a direct result of the cancer research led by SHU (such the STAMINA trial and the Active Everyday project) our clinical practice has improved - we have been able to provide substantive and evidence-based referrals for people living with and beyond cancer."

- Professor Diana Greenfield - Clinical Academic Lead, Nursing and Consultant Nurse in
Specialised Cancer Services, Sheffield Teaching Hospitals NHS Trust [E.7]

"For once it was something positive that we could offer to patients."

- Dr Serena Hilman, Consultant Clinical Oncologist, Weston Area NHS Trust [E.7]

This has particularly impacted the quality of life for men with advanced disease, reducing adverse effects of cancer such as fatigue, and mitigating the increased risk of CVD these men are subject to because of their androgen deprivation therapy.

"It's made a complete difference to my life in general, my head you know, everything. I look forward to everything."

- Advanced prostate cancer patient [E.7]

Providing a Dedicated Exercise Rehabilitation Service for Cancer Survivors

In the UK, providing effective exercise rehabilitation schemes are, according to the joint NHS England and Cancer Research UK strategy document 'Achieving World-Class Cancer Outcomes, 2015-20', "vital in minimising consequences of treatment and improving quality of life for someone with cancer". To this end, our research outputs from RCTs have led to a partnership with the national cancer charity Macmillan Cancer Support, to provide a dedicated exercise rehabilitation service for cancer survivors referred from regional NHS Trusts. Since January 2015, this new service - 'Active Everyday' has accommodated 386 referrals into the service, supporting survivors of breast, prostate, bladder, cervical, colo-rectal, pancreatic, head and neck, kidney, lung, uterine and haematological cancers. Concomitant improvements in cancer-specific fatigue, quality of life and physical activity have been reported up to 6 months after baseline. 30 specialist regional

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cancer professionals have also been trained to provide these services and cancer has now been added to the regional NHS rehabilitation referral programme. [E.8]

Upskilling Exercise and Health Care Professionals

From national publicity generated through our Cancer Research UK prostate cancer study PANTERA [E.9], in 2018 the team secured a 5-year partnership with Nuffield Health as part of an NIHR funded programme grant (STAMINA) [E.10]. Through this programme we are working with Nuffield to train up to 25 of their fitness centres to facilitate national roll-out of oncology-specific lifestyle services for men with prostate cancer - training approximately 125 of their staff to provide specialised prostate cancer lifestyle programmes.

In addition to this, approximately 150 NHS health care professionals from 25 NHS prostate cancer care teams are being trained in exercise and behavioural support techniques (from our 2018 Cochrane review) to deliver the new EAU best standard of care for men with advanced prostate cancer on ADT. Such services were not available anywhere in the country before our research. This programme provides new nationally accredited qualifications for exercise and health care professionals. Further, it provides bespoke 'sign-off for exercise programmes' (currently a major barrier to access any available referral schemes) that will be applicable not only to other cancer services, but more widely across other NHS chronic conditions.

5. Sources to corroborate the impact

- E.1. Global Cancer Statistics 2018: <https://doi.org/10.3322/caac.21492>
- E.2. European Association of Urology Prostate Cancer Guidelines (reference at 8.3.2.1): <https://uroweb.org/guideline/prostate-cancer>
- E.3. Email from Karin Plass, Manager of EAU Guidelines Office, confirming approximately 800,000 downloads between 2017-20
- E.4. German Guideline Program in Oncology: <https://www.awmf.org/leitlinien/detail/II/032-034OL.html> and <https://www.awmf.org/leitlinien/detail/II/032-009OL.html>
- E.5. Clinical Oncology Society of Australia Position Statement: <https://www.cosa.org.au/media/332488/cosa-position-statement-v4-web-final.pdf>
- E.6. Exercise is Medicine in Oncology: Engaging Clinicians to Help Patients Move Through Cancer: <https://doi.org/10.3322/caac.21579>
- E.7. Compiled testimony emails
- E.8. Achieving World-Class Cancer Outcomes and Macmillan Active Everyday reports
- E.9. Regular Exercise May Stop Prostate Cancer Spreading, Mirror Newspaper (2015): <http://www.mirror.co.uk/lifestyle/health/regular-exercise-stop-prostate-cancer-7124029>
- E.10. NIHR-Funded Study Investigates How Exercise Can Tackle Side Effects of Prostate Cancer Treatment (2018): <https://www.nihr.ac.uk/news/new-nihr-funded-study-investigates-how-exercise-can-tackle-side-effects-of-prostate-cancer-treatment/9502>