THE FREE FOUNDATION

CENTRE FOR CONFLICT WOUND RESEARCH

Annual Report

Year 1

Sep 2018 – Aug 2019

Scar Free Foundation Centre for Conflict Wound Research (SFF-CfCWR)

Title of Grant Projects:

University Hospitals Birmingham (UHBFT) and University of Birmingham (UoB)

1) **SMOOTH** - a prospective intra-patient Single-blinded randomised trial to examine the Mechanistic basis of fractiOnal ablative carbOn dioxide laser Therapy in treating adult burns and/or trauma patients with Hypertrophic scarring *(Prof Naiem Moiemen)*
2) **DeScar** - first in human clinical trial of a bioactive dressing designed to prevent scarring of skin burns *(Prof Liam Grover)*
3) **CfCWR Programme Grant** (*Prof Naiem Moiemen: Director)*

Centre for Appearance Research, University of the West of England, Bristol (UWE)

4) **UNITS** - Understanding Needs and Interventions for the Treatment of Scarring: The psychosocial impact of conflict-related disfigurement *(Prof Diana Harcourt & Dr Heidi Williamson)*

Length of funding: September 2018 – August 2021 (3 years)

INTRODUCTION

The Scar Free Foundation Centre for Conflict Wound Research (SFF-CfCWR) at Queen Elizabeth Hospital Birmingham (QEHB) commenced in September 2018 and is a partnership with the University of Birmingham (UoB), the Centre for Appearance Research (CAR, University of the West of England), and the CASEVAC[1] injured veterans club. It is our aspiration to generate a national and international network of clinical and academic research with the common goal of improving the lives of patients living with scarring and developing approaches to prevent scarring.

The principal aim of the Centre is to reduce and eventually eradicate the impact of scarring and related loss of function amongst Armed Forces personnel who sustain critical injuries during their deployment, as well as civilians injured in conflict or terrorism incidents. It will achieve this by supporting a nationally relevant programme of biological and clinical research under three strategic themes:

- Acute wound care and diagnosis – development of therapies and diagnostic tools that are appropriate for treating acute injuries sustained in austere conflict environments, where risks of contamination, extremes of temperature, and transportability are all factors.
- The biology of scarring – to better inform new treatments by advancing our understanding of how the body heals and protects itself following the types of trauma that are likely in future conflicts, including chemical, burn, and complex blast injury.
- Life-long scar impact, revision, and rehabilitation – improvement of therapies for seriously injured Armed Forces personnel and veterans to reduce and correct scars, and to promote resilience to the psychological impact of their injuries.

The SFF-CfCWR has been created around four core programmes with other affiliated projects that support the vision and objectives of the centre:

<u>CORE BIRMINGHAM PROJECTS:</u>

1. **Improving Scar Therapies**. This work package will have two elements:
    a. Prevention of scarring.
    DeScar - first in human clinical trial of a bioactive dressing designed to prevent scarring of skin burns. DeScar will begin patient recruitment in 2020.
    b. Treatment of existing scars.
    SMOOTH - a prospective intra-patient Single-blinded randomised trial to examine the Mechanistic basis of fractiOnal ablative carbOn dioxide laser Therapy in treating adult burns and/or trauma patients with Hypertrophic scarring. SMOOTH will begin patient recruitment later in 2019.

<u>AFFILIATED BIRMINGHAM PROJECTS:</u>

2. **Improving Scar Assessment**: BOSS-2 (Burn Objective Scar Scale project) - a prospective study to examine the validity of a panel of objective burn scar measurement tools. This project will: (1) Allow validation of the global burn objective scar score, identified in BOSS-1 study; (2) Correlate objective versus subjective measures; (3) Assess the acceptability of the global scar score with clinicians and patients. Grant application submitted to SFF – awaiting outcome Jan 2020.

[1] The CASEVAC Club formed in 2017 and is a members only club for those seriously wounded in combat during recent conflicts in Iraq and Afghanistan. The CASEVAC Club was created in the image of the Guinea Pig Club, formed by downed WW2 aircrew who experienced serious burns and subsequently contributed to the development of plastic surgery.

3. **Scarring Biology:** SIFTI-2 - this activity is based on an ongoing prospective longitudinal observational study, currently underway at UHB, Birmingham Children's Hospital (BCH) and St Andrew's Centre for Burns in Chelmsford. SIFTI-2 aims to investigate biomarkers of scarring following severe burn injury and is collecting repeat samples of blood, urine and skin biopsies over a 1-year period, providing a valuable biobank for future research projects within the SFF-CfCWR and the scar research community more broadly. As of 26/11/2019, 92 patients have been recruited plus 5 healthy child volunteers. We are working towards opening a site in Guangzhou in China.

CORE UNIVERSITY OF WEST OF ENGLAND (UWE) PROJECT:

4. **Identifying Effective Psychosocial Interventions** – the Understanding the Needs and Interventions for the Treatment of Scarring (UNITS) study is being run at the Centre for Appearance Research (CAR) at University of the West of England, Bristol with support of the CASEVAC injured veterans group. This research aims to investigate the psychosocial impact of appearance-altering injuries (e.g. blast injuries resulting in scarring and limb loss, scarring from burns or gunshot wounds) sustained during operational deployment or field training on UK military personnel, ex-service personnel, and their families. This research has a specific focus of understanding how issues and concerns surrounding body image, self-esteem, identity and overall adjustment to an altered appearance, may affect psychosocial wellbeing. The overall objective of this project is to determine how to adapt existing civilian interventions and/or develop new interventions tailored to the needs of the Armed Forces community to help support adjustment and psychosocial wellbeing.

A - THE PROJECTS

Section 1 – Research

1.a. Technical Summary
SMOOTH

Equipment procurement and staff appointment and training: In January 2019 the laser equipment in QEHB was upgraded to allow for a standardised protocol across both sites. The calibration and purchasing of auxiliary equipment to cover both sites was finalised in June 2019; delivered in September and training undertaken in October.

Site initiation visit for QEHB was completed on 21st October 2019. The relevant study documents were finalised the same month.

Two Clinical Research Fellows, Miss Krupali Patel and Mr Tarek Hassouna, were appointed in March and April 2019 respectively. They have undertaken Good Clinical Practice (GCP), research and clinical trial methodology training. Two band 6 research nurses (one with a clinical background in Burns) were assigned to support the study as co-lead nurses.

Laboratory: the laboratory protocol has been finalised, with some adjustments for the Swansea site, and the team have also planned out a logistic mechanism for sample transportation between the two trial sites. The team have optimised the immunohistochemistry (IHC) staining protocols for cellular and molecular markers of immune cells, skin specific cells and senescent cells. For feedback on the pathohistology readouts, they have also set up a collaboration with a clinical dermatologist, Dr Claudia Roberts, for obtaining clinical opinions of these samples. The team have now allocated a designated space for storing formalin fixed and paraffin embedded biopsy samples inside a Good Clinical Practice (GCP) compliant lab in the UoB research laboratory at QEHB. All subsequent biopsies from the SIFTI-2 and SMOOTH trials will be stored here. Biopsy samples from SMOOTH will additionally be frozen in a format suitable for RNAseq single cell analysis and stored at -80C.

Protocol Development: Study design and protocol development has been a continuous process in collaboration with the clinical teams in Birmingham and Swansea, and was finalised in agreement with all the PIs (Principal Investigators) on 18th June 2019.

IRAS, HRA and contracting: All essential patient documents were finalised following a consultation meeting with the PPI group and CASEVAC club on 7th June 2019. Application for Research Ethics Committee (REC) and Health Research Authority (HRA) approval was submitted via the Integrated Research Application System (IRAS). On 30th July 2019, a favourable opinion was obtained from REC; HRA approval granted 6th September 2019.

A meeting with the R&D Head of Governance (UHB – the sponsor) was held on 21st October 2019 to facilitate Trust approval. However, further amendment to patient information sheets and protocol was required to conform to the General Data Protection Regulation (GDPR) prior to approval. The amendments through IRAS were submitted to R&D Head of Governance for approval on 1st November 2019. On 19th November 2019 R&D trust approval was obtained, followed by a meeting on 25th November 2019 to discuss strategies to begin recruitment.

Trial recruitment**:** In preparation for the opening of the study in Swansea, an initial meeting in Morriston Hospital in August 2019 took place, to discuss any needs for the site to facilitate recruitment. The aim is to begin recruitment on 6th December 2019.

DeScar

Equipment procurement and staff appointment and training: All staff appointments have been made. No procurement of large equipment is required at this stage and we are coordinating quotes and updated costs for future manufacturing stages.

Manufacturing: A testing procedure to check that the decorin in the dressing is functional prior to release of product to the clinical trial site has been validated at UoB. Between March and September 2019, we re-explored industry standard methods of sterilising the dressings and tests showed the dressings were still active overall, but further validation work is required to look at homogeneity of performance. We have finalised the panel of quality control test required fully characterise the dressings prior to release, transferred the methods to the manufacturer who are now validating those methods for use by their own staff.

Regulatory: A package of work we believe will address the additional requirements stated by the MHRA is in progress with a contract research organisation. The team reprofiled other resources to procure this additional toxicology package. Data collection is ongoing, and we have commissioned this in phased approach – will determine whether decorin reaches the bloodstream first before sanctioning the typically standard systemic toxicology tests. Current data suggests, although this is yet to be confirmed officially, that the systemic toxicity risk is relatively low.

The sensitivity of the tests developed to detect decorin in blood should enable us to justify whether any measured variations in decorin in the blood stream are natural variations or linked to exposure to the synthetic decorin delivered at the wound site. Our agreed strategy is to have the Scientific Advisory meeting based on a more complete data body in order to get the most definitive outcomes and routes towards trial.

The Investigational Medicinal Product Dossier (IMPD) is currently being compiled and we have been continuously gathering documentation for the MHRA Scientific Advisory meeting. The IMPD and Investigator's Brochure (IB) will be produced upon delivery of the pre-clinical toxicity testing results. Information from these documents will feed into the protocol and other documents for the regulatory package.

Protocol Development: The protocol is now in late draft. Regular meetings with the technical team and a meeting with the Manchester animal studies team have refined trial design and highlighted aspects of trial methodology requiring further development. Outcomes need to be finalised, namely which wound healing assessment methods to utilise.

Patient information sheets, consent forms and key documents required for internal approval have been drafted.

The Schedule of Events Cost Attribution Template (SoECAT) has been drafted and discussed with Clinical Research Network (CRN) representatives. This will be completed once the outcomes have been finalised.

IRAS, HRA and contracting: A project ID has been created on the Integrated Research Application System (IRAS) and populated with the project information. Project details will be updated upon finalisation of the protocol before an application for Research Ethics Committee (REC) and Health Research Authority (HRA) approval is submitted. Once the protocol is finalised, contract discussions with the R&D department at UHB will begin.

UNITS

The UNITS study started in September 2018. Work has since focused on a gap analysis (which includes a literature review (study 1)), a qualitative interview study (study 2) and the development of a quantitative study (study 3). An additional interview study, of health professionals, has also been carried out as part of the gap analysis. The gap analysis has been completed, including a systematic approach to reviewing published and grey literature as well as engaging key stakeholders. This review identified only four relevant papers, of which three were from the USA and one from Turkey - indicating there is only limited research in the field internationally, and no previous research examining this topic in the UK. A report of the literature review has been prepared for submission to the academic journal 'Social Science and Medicine'.

The qualitative study to interview veterans with appearance-altering conflict-related injuries received ethical approval from the UWE Research Ethics Committee (REC) in March 2019. Twenty veterans with altered appearances were recruited and interviewed by August 2019, meaning the target sample size was reached within year 1. These 20 veteran interviews have been transcribed and analysed. The results from this analysis have been finalised amongst the UNITS team and are being shared with the study Advisory Groups. Briefly, this analysis identified seven master themes which broadly represent the challenges the veterans experienced regarding their appearance since their injury, the mechanisms that enable them to cope and manage these challenges, and their experiences and perceptions of support, and barriers to accessing it. Two additional themes were not directly related to the veterans' appearance, but were important in the context of their injury experiences and recovery. The first is the broad context of the injury including their physical recovery, the impact of their physical recovery on their mental health, the support they received formally and informally, and the change to their lives, especially family roles. The second is the military-specific context including the formal military support they received, the role of the military ethos of hardiness and strength, the coinciding experience of transition to civilian life, valuing physical fitness, and having received state-of-the-art medical care. The additional study, interviewing health professionals involved in providing support to military veterans with appearance-altering injuries has been completed (details below). Papers on the results from these interviews are being prepared for submission and peer review in academic journals. These results have informed the development of the data collection material for study 3 (a survey of 200 military personnel and 200 civilians, all with an altered appearance as a result of a traumatic injury).

In addition, 13 family members (seven spouses and six parents) have been recruited and interviewed, and interviews have been transcribed. One more interview with a spouse has been scheduled. Recruitment for this section of the study is ongoing, and six interviews are remaining.

An application to the Ministry of Defence Research Ethics Committee (MODREC) was submitted in October 2019 for the recruitment of currently serving personnel and their families. The application was reviewed and approved by the Royal Air Force (RAF) Scientific Assessment Committee (SAC) in November 2019 and by the MODREC review board (subject to minor edits) in January 2020.

The design and materials for study 3 (a survey of military veterans and serving personnel with altered appearances due to conflict-related injuries and civilians who have sustained appearance-altering traumatic injuries) have been drafted. An application for ethical approval for this study was submitted to the UWE REC in December 2019, and approved in January 2020. The survey will be finalised when the full results of study 2 are available, and final ethics approval will be given when the definitive survey is made available to the UWE REC.

Multiple Public and Patient Involvement (PPI) engagements have been conducted over the last year, informing the development and conduct of the project. A Veteran Advisory Group was formed and

met in February 2019 where they reviewed the materials for study 2 (interview study). This group will meet for the second time in February 2020. An additional PPI event was held in March 2019 at QEH Birmingham including further review of recruitment materials by representatives from the CASEVAC Club. A family advisory group has been formed and will meet for the first time in February 2020. All PPI activities have been documented including all recommendations, outcomes and impact. The steering committee, chaired by Dr Chris Pawson (Head of Psychology, UWE, Bristol) has met three times to date (October 2018, April 2019, October 2019) and provided very useful insights and feedback regarding recruitment and data collection, dissemination, and impact. The next steering committee meeting takes place on 6th March 2020.

1.b. Difficulties Faced

SMOOTH

Delay in Clinical Research Fellow recruitment contributed to loss in momentum in protocol and study outline development until their appointment in March/ April 2019, which then enabled the necessary push towards achieving the milestones set for the delivery of the study.

DeScar

Key documentation in relation to the regulatory submission relate to the IMPD and IB which in turn require pre-clinical studies to be completed and the manufacturing process to be finalised. This work is complex and the timing/ delivery of data is subject to change. A major difficulty the technical team faced were large differences of opinion in the appropriate animal models and study design for our additional work package requested by the MHRA across different CROs and specialist toxicology consultants. This was compounded by the avoidance from many to give a clear ruling on how to proceed and instead only present options. In the end, the technical team took on board all views and developed their own package designed to tackle the most fundamental risks first in a phased approach to make best use of time and money. Getting to this point incurred a significant delay but we are now working with a very proactive CRO to deliver the required toxicology package.

A regulatory package cannot be submitted without these key documents and therefore the final submission and ultimate approval/ initiation of study recruitment is dependent on the above work package and the availability of the product for clinical use. These issues are out of our control so to mitigate them, the technical, clinical and trial teams meet weekly to discuss progress and monitor timelines. The aim is to have everything for the regulatory package in late draft by the time the pre-clinical testing results are expected so that these can feed straight into the relevant documents without delaying submission of the regulatory package.

We experienced a delay in supplying manufactured product to the CRO due i) staff turnover at the CMO (the new staff then need training to use out quality control tests) and, ii) a proposed shut down on the room we intended to use for a manufacturing run. This did impact our timelines for some of the toxicology work but mitigated in part by agreeing with our CRO to run the parts of the toxicology programme requiring the decorin only. To avoid significant weekly financial penalties for delay of work due to animal housing and welfare costs, we had to reschedule the work although the elements focusing on the decorin itself are almost complete regardless of the delays.

UNITS

The main difficulty to date has been navigating the MODREC application for study 2, specifically in terms of (a) establishing the best approach to identifying, inviting and recruiting eligible currently serving military personnel and (b) identifying and connecting to an MOD sponsor to support our application. The research team made multiple attempts to talk to relevant MOD officials including serving military personnel and civil servant MOD employees but found themselves being passed between various personnel and departments in their attempts. This created a delay in (a) finalising

the recruitment method and (b) connecting with a potential sponsor, meaning the MODREC application was submitted eight months behind schedule. This delay has now been resolved with a very supportive sponsor (Helen Helliwell, Director Armed Forces People Policy, MOD) being identified and a robust recruitment method finalised with support from MOD statistics. Since the submission of the MODREC application in October 2019, it has been reviewed and approved by the RAF SAC and the MODREC review board, both of whom have commented on the quality of the application, the rigor of the proposed study, and the detailed risk protocol. Recruitment of eligible currently serving military personnel and their families will commence shortly.

1.c. Project Progress Update

SMOOTH

The trial was due to open at the end of September however due to changes in the Head of Governance at UHB there were delays, which will push back timelines in year 2.

However a meeting on 25th November 2019, helped to strategise how to compensate for the delay by optimising a populated waiting list of potential participants who have verbally agreed in principle and would be suitable to be recruited to the trial in the coming 4 – 6 months.

DeScar

The project has overrun due to the aforementioned delays in pre-clinical testing which were out of our control, the time has been used to develop regulatory and internal documentation ready to be updated and submitted for approval when the results are available. While incurring a delay due to pre-clinical data gathering, we partly mitigated future risk in MHRA engagement by going to the MHRA with data rather than ask for verification for a study design. This gives us the stronger position of arguing a case to be permitted to apply for phase 1 clinical trial based on fact rather than assumptions and hypothetical go/no-go points. In parallel, we have continued as planned with quality control validation and this, along with the clinical protocol development, is feeding into the MHRA Scientific Advisory briefing document and IMPD as planned.

UNITS

The project is currently running to schedule across most aspects except for the recruitment and inclusion of currently serving military personnel and their families in study 2, as described above in section 1.B. Although the submission of the MODREC ethics application was delayed by eight months, the actual delay to the study is less since this forms just one of three aspects of study 2 (interviews with veterans, family members, and serving personnel). There will be a delay of one to three months of the completion of all aspects of study 2, but we do not envisage that this will impact on the overall timeline since our design enables us to progress with the other aspects of the project in the meantime. The project is therefore still running to schedule, despite this delay. Now that the study team have navigated the MODREC process and are connected with personnel who are willing and able to assist with the recruitment and act as a sponsor, we do not envisage the same delay occurring for the submission of MODREC approval for study 3 (to recruit serving military personnel into the survey).

1.d. Lay Summary

SMOOTH

Following approval of the grant application to conduct the trial, a study timeline across 3 years was drafted to plan various steps/parts of the study to help keep the running of the trial as smooth and efficient as possible. These steps are referred to as milestones. The study will be run at hospitals in Birmingham and Swansea.

Milestone 1: Equipment procurement and staff appointment and training: In January 2019, the laser equipment for treatment was upgraded at QEHB. In June 2019, the different types of devices needed for scar assessment were checked, calibrated and ordered for use across both sites. The devices arrived in September 2019.

In March and April 2019, two Clinical Research Fellows were appointed to help with the delivery of the study. Following completion of GCP (Good Clinical Practice) training, they received education in clinical trial and research methodologies and publication writing. In addition, from August 2019, two band 6 nurses were assigned as lead research nurses to support the study.

Milestone 2: Protocol development: From September 2018, during the first year, time has been spent developing the protocol in collaboration with the clinical teams in Birmingham and Swansea.

The study protocol, which demonstrates what the study aims to achieve and how it will be done, was finalised following discussions with the principal investigators (PIs).

Milestone 3: IRAS, HRA and contracting: Essential documents relating to the trial were drafted with meetings with the Patient and Public Involvement (PPI) group and the CASEVAC club on 7th June 2019. These documents are largely for patients participating in the study including patient information sheets and patient consent forms.

After incorporating the PPI comments on the patient information sheets, the application for ethical approval was submitted in July 2019 via the IRAS (Integrated Research Application System) application process. The SMOOTH study gained preliminary ethical (HRA approval) on 6th September 2019. The Birmingham team obtained R&D Trust (the study 'sponsor') approval from UHB on the 19th November 2019.

Milestone 4: Trial Recruitment: In preparation for the opening of the study in Swansea in year 2, an initial meeting at Moriston Hospital, occurred on 30th August 2019, to allow for both clinical and research teams (including the laboratory and administration staff) to meet, establish rapport, discuss logistics, collaborate on any improvements and highlight any specific needs for their site (e.g. procurement of equipment, need for staffing, allocation of roles/duties, communication across both sites). This visit was well received and found to be productive.

The Birmingham site, at the Queen Elizabeth Hospital Birmingham (QEHB), had their site initiation visit on 21st October 2019, with positive feedback. During this meeting; the study background, reason for doing the study, design, objectives, delivery of the study and delegation of duties were discussed.

Formal device training at the Birmingham site was delivered on 22nd October 2019, to the Research Fellows and nurses responsible for conducting both objective and subjective scar assessments.

A meeting was held on 25th November discussing strategies to begin recruitment of participants and ensuring all team members are on board. We aim to begin recruitment on 6th December 2019. Patients that meet the eligibility criteria for the study have already been identified and have agreed in principle to participate in the trial.

DeScar

The milestone within this period was the 'preparation of all documents to be submitted to the MHRA' (Medicines and Healthcare Products Regulatory Agency). The MHRA are the UK body for reviewing and authorising applications to run clinical trials in the UK and the supply of new

medicines and medical devices to the UK market. The purpose of the work leading to this milestone was to engage with the MHRA for a 'Scientific Advisory meeting' in order to seek confirmation that the safety and performance data created to date, any plans for further data and the design of the clinical trial, would be considered sufficient for a safe and robust clinical trial in humans to be carried out. Seeking the MHRA's view in this meeting would either provide more confidence in our application for a clinical trial to be approved or identify areas requiring additional thought. Such meetings are therefore very good opportunities to reduce the level of risk in projects. However, there is a limit to the number of times a meeting can be held about the same product. Therefore, there is a balance to be found between attempting to seek early confidence from the MHRA based on less data and using time to generate enough robust data so that the MHRA can make a more informed decision.

Updates on this project can be grouped into three categories:

- pre-clinical safety (i.e. building a body of data on the safety of the product before entering humans),
- manufacturing – specifically, 'optimising and validating' a process (i.e. making it as good as possible and showing the process accurately produces what it is supposed to) that can be certified as supplying a clinical-grade product fit for human use,
- clinical trial documentation – clinical design, protocol for how participants will be engaged and treated etc.

Pre-clinical: The MHRA had previously ruled that data on the safety of the decorin from the field was insufficient to fully support our application for a phase 1 clinical trial. This is partly because the data was based around a product designed for a different use. At the time, the lack of clinical experience with decorin prompted the MHRA to take a conservative approach and requested us to prove key exposure risks were acceptable. In order to progress to trial, we needed to collect our own data pre-clinical package on the safety of our decorin skin dressing. Such studies are typically very expensive and take months to commission and complete.

Designing what could be considered to be a sensible pre-clinical study design to address the MHRA's points was considerably more difficult and time consuming than anticipated. Different professional companies who carry out pre-clinical testing (CROs – contract research organisations) have different views on experimental set up and implementation and, as we have found, very rarely tell you exactly what to do. Typically, clients are given 'guidance' on a variety of options with the disclaimer that the client should seek confirmation from the MHRA.

In the end, we confirmed a package of toxicology work between ourselves, three CROs and our external regulatory advisor that we believe would address the additional requirements stated by the MHRA. Overall, our agreed strategy is to have Scientific Advisory meeting based on a more complete body of data rather than plans in order to get the ultimate outcomes and routes towards trial. We raised some funding to pay for some of this additional work and studies are ongoing.

Manufacturing: A testing procedure to check that the decorin in the dressing is functional prior to release of product to the clinical trial site has been validated at UoB. We have finalised the panel of quality control test required fully characterise the dressings prior to release to the clinic, transferred the methods to the manufacturer who are now validating those methods for use by their own staff. The people ultimately responsible for making and releasing the dressings must be properly trained in order to be qualified to pass or reject product before being sent for use in the clinic.

Trial documents and documents for MHRA Advisory meeting: All the documents needed for the regulatory package are in late draft, work having started on them in 2018. The trial has been

discussed at trial management meetings held throughout 2019 and all changes have been documented in the minutes and subsequently used to update all the relevant documents. All draft documents will be completed once the results of the animal studies are available next year, expected April 2020.

UNITS

UNITS is a three-year project aimed at understanding the psychosocial experiences and support needs of military personnel, veterans, and their families, affected by conflict-related appearance altering injuries (e.g. scars from blast injuries or gunshot wounds). UNITS comprises four studies:

1. Gap Analysis – to identify existing literature and research in this specific field.
2. Interview study - including one-to-one interviews with 20 injured currently serving personnel, 20 injured veterans and 20 spouses/parents of an injured service person or veteran.
3. Questionnaire study – involving 200 military personnel/veterans with appearance-altering injuries and 200 civilians with appearance-altering injuries in order to examine how the experiences and challenges facing military personnel and veterans are similar or different to those facing civilians.
4. Intervention and support material development – using the information and knowledge gathered from studies 1, 2, and 3 we will either adapt existing materials and interventions designed to support civilians with appearance-altering injuries, or develop new materials and interventions to provide support specifically for the psychological and social challenges military personnel, veterans, and their families may face as a consequence of their appearance-altering injury.

The UNITS project started in October 2018. Since then work has focused on conducting the gap analysis (study 1), the interview study (study 2) and the development of the questionnaire study (study 3). During this time key milestones have been reached.

Gap Analysis:

The gap analysis has been completed. This involved using online academic databases and general search engines such as Google to search for literature and research relevant to the topic of the psychological and social impact of military conflict-related appearance-altering injuries. As well as the online search, the research team made connections with relevant service providers, such as BLESMA, Help for Heroes, and Style for Soldiers, and with other academics in the field of military research and appearance research, to seek additional literature and build relationships with other researchers, service providers, and health professionals working with this specific group of military personnel and veterans.

Section 2 – Dissemination

2.a. Dissemination Undertaken

Both the DeScar and SMOOTH teams have outlined that no dissemination activities have been undertaken within the September 2018 – August 2019 reporting window, due to the projects currently both being in early stages.

UNITS

Date	Event	Presentation type and title
21st November 2018	UWE Health and Social Sciences Departmental Away Day	Oral presentation: An introduction and overview of the UNITS study
14th March 2019	King's College London Veteran Mental Health Conference	Poster presentation: The psychosocial impact of deployment-

		related appearance-altering injuries: How should we support military service personnel, veterans and their families?
1st April 2019	UWE Heath and Social Sciences Department Newsletter	Written article: UNITS Overview
16th May 2019	Scar Free Foundation Conflict Wound Research Symposium	Oral presentation: Addressing the psychosocial support needs of military personnel, and their families, affected by scarring: where next?
19th June 2019	University of California, Los Angeles (UCLA) Division of Population Behavioural Health, Stress, Trauma and Resilience Seminar Series.	Oral Presentation: Understanding needs and interventions for the treatment of scarring: the psychosocial impact of conflict-related disfigurement.
11th July 2019	Blast Injury Conference	Oral Presentation: Blast injuries and the psychosocial adjustment to an altered appearance: Exploring how best to support the Armed Forces community

In addition, abstracts for presentations on the veteran interviews (study 2) and health professional interviews have been accepted for the Appearance Matters 9 conference (July 2020). Abstracts have also been submitted to the British Psychological Society Division of Health Psychology (DHP) conference (June 2020; details of acceptance awaited). The veteran interview study has also been submitted to the annual convention of the American Psychological Association Division 19 (Society for Military Psychology) (August 2020).

2.b. PPI/Public Engagement Activities Undertaken

PPI meetings have been held at key points along the project timeline in the last 12 months to inform the design of both studies and the participant recruitment process. A PPI meeting took place with the **SMOOTH** project team, members of the CASEVAC Club, a patient who had received the laser therapy and his partner during HRH The Duke of Sussex's visit to the Centre in March 2019. The former patient and his wife discussed their own experiences of the laser treatment and answered questions from the CASEVAC representatives on acceptability of the treatment (e.g. pain), potential negative effects (e.g. psychological/PTSD), implications for daily life (e.g. limited sun exposure, worrying about partner) and aftercare (e.g. regular application of topical creams). A second PPI meeting was held to look at the recruitment materials, patient information sheets and consent process in June 2019. Early drafts of the documents were discussed and reviewed by the PPI group members and suggestions were subsequently incorporated into the documents and their advice taken on board to encourage patient recruitment, participation and understanding of the study.

A PPI meeting was held for the **DeScar** project in June 2019 and Clinical Research Fellow Tarek Hassouna discussed the project with the group. The group talked about the recruitment process in detail, reviewed and amended the patient information materials to make them more acceptable to patients. A further meeting was held with DeScar Researcher Richard Williams, PPI/E Lead Laura Nice and the PPI group to discuss and reflect on the impact of involvement on the project so far. During this meeting the group co-developed a model to capture this impact of PPI resulting in a co-produced poster highlighting the 'Impact of Patient and Public Involvement along the Product Development Pathway'. This poster was co-presented at the Patient Reported Outcomes Conference

in June 2019 with Laura Nice, a member of our PPI group and her carer. Successful public engagement and social media promotion of the poster has resulted in an enquiry from the BMJ (British Medical Journal), who have asked us to submit an article for journal publication. A BMJ Opinion piece is in development, with a further paper documenting the impact of PPI towards the end of the project planned.

Further project-specific PPI meetings are planned for the duration of both projects to discuss the study design (e.g. schedule of assessments), ongoing recruitment (e.g. any possible problems), results, implications of the findings for patients/their families, writing dissemination materials and innovative ways to share the results with different audiences

UNITS

Two veterans (one of whom is a member of the CASEVAC Club) who have sustained appearance-altering conflict injuries were consulted during the development of the application for funding of the UNITS study, which was shaped as a result of their suggestions and feedback. Since the study began in October 2018, multiple Public and Patient Involvement (PPI) engagements have been conducted, helping to inform the ongoing development and conduct of the project. Specifically:

The Veteran Advisory Group:

An advisory group including two veterans who have sustained combat injuries that resulted in a change to their appearance was formed in January 2019. The research team connected with one of these veterans via the CASEVAC club and with the other via BLESMA. Both veterans are male and were injured during deployments to Afghanistan.

To date, there has been one in-person meeting of the Veteran Advisory Group, in February 2019. The aim of this meeting was to clarify the purpose of the advisory group and discuss how the group will run and the expectations of the veterans, the expectations of the group facilitators (MK and VW of the research team), including issues of confidentiality, and to review the method and materials for the conduct of study 2 (the interview study). The meeting was voice recorded with the express permission of the veterans, to ensure the two facilitators could focus on running the group and not missing any important comments or feedback from the veterans. The veterans had been provided with the advisory group and study materials in advance of the meeting, so that they had time to review and consider any feedback at their leisure. The facilitators aimed to create a safe and informal space for the veterans to share their thoughts and feedback on the method and materials of study 2.

Two forms were designed to capture and record the feedback from the veterans for each item discussed. The form also provided a space to record the actions to be taken as a result of the feedback, the outcome of the action and the impact.

The feedback from the veterans specifically about the recruitment and data collection materials were very useful and led to the editing of the participant information sheet, the study advert, and the study invitation. The veterans agreed to take a second look at the edited materials following the group, which provided an opportunity to check that the edits met the veterans' expectations and to demonstrate the value and impact of their involvement.

The next advisory group is planned for February 8th 2020, where the same approach will be taken for gathering their input into the materials for study 3 (the survey).

The CASEVAC Club Workshop:
A workshop event was held at QEH, Birmingham in March 2019, attended by six veterans and two family members from the CASEVAC club. The materials previously reviewed by the veteran advisory group were considered in this workshop, which also involved a discussion about recruitment, particularly of family members. This workshop provided a safe and informal space for feedback, which was recorded following the same procedures as used for the veteran advisory group.

The Family Advisory Group:
A family advisory group has been formed including one mother and one spouse of combat-injured veterans with appearance-altering injuries. The research team were able to connect to the mother via a family-specific service charity (Ripple Pond) and to the spouse via the CASEVAC Club. The group will meet for the first time in February 2020.

Mock interview and interview schedule review:
Prior to the commencement of the veteran interviews in study 2, a mock interview was conducted with a member of staff in the UWE Wellbeing team who is an ex-service person and has previously worked with injured service personnel. The mock interview helped the researcher conducting the interviews (MK) to become familiar and comfortable with the interview schedule that had been developed and to check with a veteran if the language used and questions being asked were suitable.

Recruitment video for study 3:
In response to a suggestion from our PPI members, a short video has been made (including a CASEVAC Club member) to help promote study 3 (the survey) to potential participants.

2.c. Public domain/AMRC Open Research Platform Publishing Plans
SMOOTH
In compliance with the condition of the REC favourable opinion requiring all clinical trials to be registered on a publicly accessible database, within six weeks of recruiting the first research participant at the latest, the study will be registered at the ClinicalTrials.gov database.

Protocol publication is currently being drafted for submission to an appropriate journal such as *BMJ Open* or *Trials*. The draft will be updated following approval of the amended protocol.

Upon completion of the trial, findings will be published accordingly, and a thorough dissemination plan developed. Locally, results will be disseminated through PPI meetings and the Annual Research Showcase held at the Queen Elizabeth Hospital Birmingham. National and international dissemination will be through project updates and news articles on relevant websites e.g. SFF-CfCWR and Scar Free Foundation; attendance at CASEVAC meetings; conference presentations e.g. British Burns Association; charity newsletters; social media.

DeScar
The clinical trial will be registered on the International Standard Randomised Controlled Trial Number (ISRCTN) registry database as well as EudraCT trial and ClinGov databases. We plan to submit the protocol for publication in a peer reviewed journal. Once the trial has completed recruitment and follow-up, the results will be submitted for publication to a high impact, peer reviewed journal. We will submit the paper for publication, regardless of the outcome.

UNITS

A minimum of three papers will be submitted to open access peer reviewed journals (e.g. Social Science and Medicine, Military Behavioural Health, Military Psychology, BMJ Open, Body Image) reporting the findings from the literature review within the gap analysis (study 1), military, veteran and family interviews (study 2), the health professional interviews, and the comparative questionnaire study (study 3). In addition, a lay summary of the research findings from the military and veteran interviews, family interviews, and questionnaire study will be written and shared with all participants who express an interest in receiving it, and with relevant military and veteran service providers including those who assisted with recruitment.

2.d. Expected Academic, Economic and Societal Impacts of the Research

SMOOTH

Academic Impact: Laser therapy is yet to prove its clinical efficacy in scar management. Improved understanding of the mechanisms that mediate scar reduction with laser treatment, combined with standardised assessment of scarring and rigorous randomised control trial design, will enable better treatment design for laser treatment of hypertrophic scars. The SMOOTH study will interrogate laser therapy with a range of outcome measures helping in "the development of evidence based standard protocols" for scar treatment and will crucially address a gap in the mechanistic understanding of laser therapy in the treatment of mature hypertrophic scarring. Serial clinical and histologic assessment will allow us to examine and correlate clinical changes in mature scars in response to laser therapy with molecular and cellular changes in the scar and surrounding tissue.

This study will enable us to optimise the use of laser therapy in scar patients and move closer towards scar free healing.

Economic and societal impact: The yield of the SMOOTH study to society and the economic benefits are multifaceted. Burn injury is the fourth most common type of trauma after road traffic accidents, falls and interpersonal intentional injury. In 2004 it was estimated that worldwide 11 million people suffered fire-related burn injury with 265,000 deaths annually. Burns are also one of the leading causes of disability-adjusted life-years lost. Crucially, up to 90% of the patients who survive a burn injury suffer significant, predominantly hypertrophic scarring. These injuries can vary in size and depth and can have a significant impact on the rest of a patient's life. Following large burns patients may be in hospital receiving treatment for several months. During this time patients will have undergone surgery and received skin grafts to repair their damaged skin; these along with the original burn injury can frequently result in significant scarring.

Scarring not only impacts on a person's appearance but also on their psychological recovery. Symptomatic and physical scars can therefore have a significant impact on a patient's lifestyle, their independence in daily activities (washing or dressing), and ability to work.

Although there have been advances in non-invasive techniques used in series or combination (e.g. massage, pressure garments, steroid injections, etc.) the need for more invasive procedures such as surgery are necessary. These treatments are not only limited in their effectiveness but they are also costly, invasive, painful and for patients who have already had lengthy periods of in-hospital admission and under gone multiple theatre trips this is often daunting and less preferable option.

The effect of laser treatment will be measured through objective scar assessment which not only quantifies the physical characteristics of the scar but crucially assesses the patients perspective through subjective questionnaires measuring the impact of the treatment on their quality of life. This less invasive therapy can be offered as a day procedure under local anaesthesia, reducing the

cost to services, improving patient well-being with fewer in-hospital procedures, reduced length of hospital stay and follow up appointments with the team.

DeScar

Academic Impact: Physicochemical measures of scarring will then allow basic scientists to explore how wound healing at the molecular level propagates to the macroscale in patients. The impact on basic science research in scarring will be a drive to develop tools to measure and quantify metabolic and cellular activity in scars so that treatments can be tailored to the individual. This should create new fields of scar research and open more opportunities of academic degrees.

Societal Impact: Ultimately the goal of the project will be to develop a dressing that ameliorates problematic scarring that can cause both psychological and physical difficulties throughout a patient's lifetime.

Economic Impact: This technology will undoubtedly save the NHS and other healthcare delivery systems money due to reduced staff-time and the avoidance of additional hospital stays. On average each major burns patient costs the NHS/Healthcare Provider £150,000 and by reducing the need for long-term treatment, we would hope to significantly reduce this figure. The socioeconomic impact of this is likely to be significant across a number of clinical indications. We have previously indicated the burden of skin burns (4 million people in the developed world of which 70% are children), similarly the platform technologies will likely impact the treatment of other conditions where scarring is an issue.

UNITS

This research will provide academic impact by adding to the current limited research evidence about the impact of changes to appearance as a result of combat injures on the psychosocial wellbeing of serving military personnel, veterans, and their families.

It has potential to impact on the work of current service providers for physically injured military personnel, veterans and their families, by providing information about the potential psychosocial challenges related specifically to adjusting to looking different following their injury and how best to support those who may need it.

This research will result in the development of materials/interventions intended to offer support to military personnel affected by an altered appearance. The effectiveness of these materials will be the subject of further funding applications. The evaluated materials have potential for considerable, measurable impact on the lives of military personnel and veterans affected by conflict injuries and their families by enabling access to evidence-based interventions and support materials. We will collect evidence of impact through data on the take-up and use of such resources, and testimonials from key stakeholders including support organisations and beneficiaries.

Section 3 – Staffing

3.a. Staffing Changes/ Issues

Two clinical research fellows (CRFs) were appointed earlier this year: Krupali Patel (commenced in March 2019) and Tarek Hassouna (commenced in April 2019) who are supporting SMOOTH and DeScar, respectively.

SMOOTH

In August 2019, a charge research nurse with a clinical background in Burns was assigned as lead research nurse for the study. In addition, another charge research nurse from the delivery team was

assigned to support the study as co-lead nurse to ensure that sufficient support to the study is provided.

DeScar
There have been some staffing changes since September 2018 but there have been no issues. Following the departure of Amrita Athwal from the D3B team, Abigail Clutterbuck-James was appointed senior trial coordinator for DeScar in February 2019. Sara Trevitt joined the trial in August 2019 as trial coordinator, replacing Jennifer Keely.

UNITS
Victoria Williams (Research Associate) was employed for 80% FTE whilst completing her MSc Health Psychology at UWE, Bristol, for which she completed a dissertation linked to the UNITS study. Since completing her MSc she has returned to 100% FTE on the UNITS study.

There have been no other staffing changes or issues with staffing in the past year.

3.b. Collaborations with Other Labs/Research Teams
SMOOTH
The trial protocol was developed in collaboration between the Birmingham and Swansea clinical teams. The collaboration with Swansea team has allowed for their expertise in laser scar management of patients to be shared with the Birmingham team. Discussions helped formulate a more robust trial protocol in order to avoid the design flaws of previous randomised trials.

Established collaborations have been further strengthened with Professor Janet Lord's team at the Institute of Inflammation and Ageing, UoB to identify novel technology associated with tissue regeneration, scarring and markers of senescence.

The study has also opened up collaboration with Institute of Applied Health Research and the Centre for Patient Reported Outcomes Research, UoB with Dr Anita Slade's team to allow for validation of the BBSIP (Brisbane Burn Scar Impact Profile).

DeScar
Within the preceding Wellcome Trust-funded project, we collaborated with University of Manchester and a specialist burns pre-clinical research team to complete a pilot efficacy pig model study. Although this study was completed some time ago, insights are still coming out from the deep array of samples taken. The findings will continue to inform on relevant measures of healing progress and help refine the protocol.

UNITS
Since starting this project and as a result of networking opportunities (including the Scar Free Foundation Conflict Injury Symposium (May 2019)) we have developed links with researchers and clinicians, nationally and internationally.

Dr Keeling has submitted an application in collaboration with Dr Natalie Hammond (sociologist, Manchester Metropolitan University) to the British Academy/Leverhulme small grants scheme to fund an exploratory study specifically focussing on the psychosocial impact of genital injury project.

Dr Dominic Murphy (Clinical Psychologist, Combat Stress), is acting as external validator for the analysis of interview data collected in study 2.

Dr Keeling was awarded UWE's Vice Chancellor Early Career Researcher award in 2019. This prestigious accolade is funding a 12-month study of the impact of an altered appearance due to conflict injury on intimate relationships. The interviews and gap analysis in the UNITS study identified this as an important topic, warranting a dedicated study in its own right. This project (led by Dr Keeling) is being conducted by Dr Nick Sharratt, Senior Research Fellow with experience of researching intimacy and visible difference/altered appearance.

In addition, teams at Stanford Hall, and Dr David Sarwer (clinical psychologist, Temple University, Philadelphia, USA) are keen to be kept updated on the progress of the UNITS study and are interested in future collaborative projects.

Section 4 – Future plans

4.a. Further Funding Plans

SMOOTH

We expect the results from the trial will provide us with sufficient data to design a future full scale multi-centre RCT and apply to the NIHR-HTA (Health Assessment Technology) programme. In addition the mechanistic understanding of scar laser therapy could open up opportunities to work with industry on potential anti-scarring candidates in combination with laser therapy.

DeScar

IMP development and pre-clinical testing are delaying the submission of the regulatory package and consequently the trial start date. Currently, the trial is predicted to start in October 2020. Based on the maximum estimated recruitment rate of 5 patients per month, last patient last visit will be February 2022. This 6 month extension beyond the end of current funding in August 2021 can be absorbed by the unit. However, if the trial runs at recruitment rate of 2 patients per month (minimum predicted recruitment rate) then last patient last visit will be August 2022 and further funding will be needed. Timelines will be reviewed once the trial is open and recruiting and a more accurate estimation of trial duration can be obtained. If the trial is proven to be safe we will look to apply for funding from NIHR for a multicentre study.

UNITS

As per the original research proposal, grant applications for further funding to trial any adapted materials and/or to develop and trial new interventions will be made in the final year of the study.

In addition, our findings to date point to the need for further research, particularly in relation to genital injuries, intimacy and relationships, and the experiences and possible support needs of children of military personnel with altered appearance as a result of conflict-related injuries. We are keen to pursue these areas in the future, along with other potential studies that may be identified during the remainder of the current funding.

4.b. Changes to the Investigation Plans

SMOOTH

Delay in recruitment will have an impact on achieving the initial proposed recruitment milestone. However, measures have been put in place to shorten the recruitment period. There is potential for changes in year 2 and 3.

DeScar

As previously mentioned, factors external to the clinical trial have delayed the preparation and submission of the regulatory package. However, once the preclinical work has been completed, we expect to update the trial documents and submit regulatory package relatively quickly. Once the trial

has opened to recruitment, the plan of investigation will continue as originally planned including 6 month follow-up of patients.

UNITS
There are no changes to the plan of investigation.

4.c. Research or Staffing Issues in the Upcoming Year
The DeScar and SMOOTH teams both outline that none are envisaged.

UNITS
James Kiff is leaving UWE at the end of February 2020 and will be employed as a clinical psychologist within the Outlook Disfigurement Support Unit at North Bristol NHS Trust. This new post is only 80% FTE, and he will therefore continue his input into the UNITS study, funded by UWE's matched funding. We do not envisage any other research or staffing issues in the upcoming year.

B - THE PROGRAMME

The table below illustrates status on milestones set out for the core programmes supporting the Centre. This core programme is run by the Birmingham based programme management team.

CfCWR Programme Milestones Status

No.	Description	Timeframe	Status
1	**Director post** - Roles/ responsibilities for Director/ co Director defined - Search Committee for succession planning	Sep – Oct 18 Jan – Dec 19	**Complete**
2	**Management** - Establishment and set up of management meetings - Advisory Group held	Sep – Nov 18 Jun – Sep 19	**Complete** **Delayed by funders to Feb 2020**
3	**Reporting** - Interim report submitted - Annual report submitted	Mar 19 Sept 19	**Complete (June and September 2019)** **Delayed by funders to Dec 2019**
4	**Symposium / Grant Call** - Date and venue finalised - Programme/ grant call agreed - Symposium organisation - Symposium held - Grant process (submission to award) – via SFF	 Nov 18 Jan 19 Jan – May 19 May 19 Aug 19 – Jul 20	 **All complete** **Ongoing by SFF**
5	**SFF CfCWR Dissemination event** - Year 2 - Year 3	May 20 May 21	***Not live yet***
6	**Build academic capacity** - MSc/PhD registration (1 per year: 3 total) - With support of UoB clinical academic office appoint new ACFs/ clinical lecturers (2019 – 2021: 3 total)	Sep 21 Sep 21	**I MSc ongoing; I PhD registration in year 2; 2 others in line** **In progress**

7	**Collaborations** - Establish new collaborations with other academic (from bench to bedside)/ pharma/ NGOs/ international organisations (3-4 per year: 9 total)	Sep 21	**Complete for year one**
8	**Grants** - Submissions: 1 in year 1 2 in year 2 3 in year 3 - Awards (up to £500K)	 Sep 18 – Aug 19 Sep 19 – Aug 20 Sep 20 – Aug 21 Sep 21	**On track**
9	**Conferences** Invited speaker (2/year) Presentations: 4 in year 2 6 in year 3	 Sep 19 – Aug 20 Sep 20 – Aug 21	**On track** ***Not live yet***
10	**Publications** 2 in year 1 4 in year 2 6 in year 3	 Sep 18 – Aug 19 Sep 19 – Aug 20 Sep 20 – Aug 21	**On track**
11	**New translational research projects (from basic science) - 1/ year** 1 in year 1 1 in year 2 1 in year 3	 Sep 18 – Aug 19 Sep 19 – Aug 20 Sep 20 – Aug 21	**On track**
12	**Improving veteran/patient outcomes (care)** - Guidelines to Scar Management - Developed Standard Set of Scar Assessment Tools - Establish a national comprehensive Scar Management Service (military/civilian) - A hub for pharma to test new interventions	 Sep 21 Sep 21 Sep 21 Sep 21	 ***Not live yet***

1. Director post

Since September 2018 Professor Naiem Moiemen has been the Director of the SFF-CfCWR until a permanent Chair in Wound Healing Research (Institute of Inflammation and Ageing, UoB) and Centre Director has been recruited. The vacancy was advertised through September and October 2019, but unfortunately no suitable candidates applied. Therefore a new recruitment strategy is currently being developed and the post is back out to advert.

2. Management

All management meetings were arranged for September 2018 – August 2019 early in the reporting year.

Research Programme Management Meetings (RPMG)

The role of the RPMG is to oversee the delivery of the Programme and Birmingham projects. UWE attend RPMG meetings, to provide updates and discuss issues of relevance across the two sites, but are not managed by the Birmingham management team. The RPMG meets quarterly and is chaired by the Centre's Director. This operational group report locally to the Management Executive Group (MEG).

Management Executive Group (MEG)

The MEG provides the strategic direction, priorities and objectives for the Programme and Birmingham projects. The MEG is co-Chaired by the Dean of Medicine (UoB) and Executive Director of Delivery (UHB) under Birmingham Health Partners. The MEG will meet 6 monthly to oversee the functioning of the Centre and will include representation from UHB/ UoB/ Royal Centre for Defence Medicine (RCDM) and other key stakeholders.

Advisory Group

In consultation with the SFF the Centre will have an annual External Advisory Group meeting to provide: strategic oversight; ensure the activity of the research work streams reflects the strategic direction of the centre; ensure the SFF-CfCWR's obligations to its key stakeholders are met; and add value to, and promote the success of the SFF-CfCWR. The Advisory Group was delayed by SFF and will be held in Feb 2020.

3. Reporting

The SFF-CfCWR provided update reports to SFF as requested, for the Board of Trustees and Research Council, in June and September 2019. The annual report was revised by SFF to a submission date in December 2019.

4. Symposium / Grant Call

The Scar Free Foundation (SFF) Conflict Wound Research Symposium took place at the University of Birmingham Medical School on the 16th and 17th of May, 2019. The aim of this event was to aid in setting a research agenda for conflict wound research over the next decade. The Symposium was attended by 84 researchers, clinicians, military veterans from the CASEVAC Club and senior armed forces personnel from the UK and the USA, along with representatives from military support charities.

The research priorities that came from the symposium are:

Theme 1: Acute wound care and diagnosis

Development of therapies and diagnostic tools that are appropriate for treating acute injuries sustained in austere conflict environments, where risks of contamination, extremes of temperature, and transportability are all factors.

- What tools or protocols could be developed to assist the objective assessment, rapid diagnosis and categorisation of conflict wounds?
- What steps can be taken to mitigate secondary injury prior to casualty recovery from conflict zones, for example tools to aid the detection of sepsis?
- What treatments, such as 'magic ingredient' wound dressings, should be developed for use in austere conflict and humanitarian environments?

- Considering the possible nature and environment of future conflicts, which models would best inform acute wound care research?

Theme 2: The biology of scarring

- What is the best suite of models to investigate high energy complex injuries?
- How can we make the best use of humans as models including being prepared for future conflict/events?
- What can we learn from other fields either for therapeutics or the understanding/monitoring of biology, for example imaging and bioengineering?
- What work should be undertaken to develop our understanding of the wound bio-membrane?
- How can we understand the long-term effects of relevant injuries for example accelerated ageing and the influence of psychology on biology?

Theme 3: Life-long scar impact, revision and rehabilitation

Improvement of therapies for seriously injured armed forces personnel and veterans to reduce and correct scars, and to promote resilience to the psychological impact of their disfiguring injuries

- How do we ensure the best psychosocial outcomes for military personnel with conflict injuries that have altered their appearance, and their families?
- What is the physiological, life-long impact of limb amputation and prosthetic use?
- What is the role of physiotherapy and other treatments such as laser therapy in breaking down disabling, internal scar tissue and supporting return to function?

In September 2019, The Scar Free Foundation announced that later in the autumn, they will be launching a call for applications which address these vital areas. An initial £150,000 will be available to support pilot or feasibility studies, which have the potential to be developed into larger-scale research programmes with higher awards from the Foundation and other funders.
https://scarfree.org.uk/news/2019/media-release-conflict-wound-research-priorities-call-for-pilot-studies

5. SFF-CfCWR Dissemination event

This milestone is not live yet. The SFF-CfCWR will work with SFF in the coming months to plan and deliver this to schedule in 2020.

Dissemination is an ongoing priority with the Centre, with active communication activities and a busy visitor programme:

Visits and Tours September 2018 - August 2019

Visit/Tour	Date
HRH Countess of Wessex – official opening of SFF-CfCWR	November 2018
Mr Adam Reid, Academic Consultant Plastic Surgeon, Blond McIndoe Laboratories, University of Manchester	February 2019
HRH Duke of Sussex	March 2019
The Childwick Trust	May 2019
Steven Inman: Grants Manager, Armed Forces Covenant Fund Trust	June 2019
Dr James Fildes, Head of Ex-Vivo Lab in the Division of Infection, Immunity and Respiratory Research at the University of Manchester	August 2019

The huge highlight from the last year of our busy visitor's programme was the great honour of welcoming HRH The Countess of Wessex to officially open the Centre, followed a few months later

by a visit from HRH The Duke of Sussex. On both occasions, our visitors met with Centre staff and heard stories from members of the CASEVAC Club, who shared their own experiences of conflict wound injuries and their involvement in our research. Both visits garnered significant national press coverage, with its concomitant promotion of the SFF and the Centre itself.

5.b. Invited Lecture

The Centre warmly welcomed Professor Keith Harding from the Cardiff University School of Medicine and the Welsh Wound Innovation Centre to give a guest lecture in March 2019. Professor Harding talked to 'Wound Healing: An orphan Academic and Clinical challenge?' and his lecture was very well attended by staff within UoB and UHB and was held at the Institute for Translational Medicine.

5.c. Communications

As part of her broader role, Dr Karen Cooke acts as a communications lead for the SFF-CfCWR.

New Centre website

A bespoke website was designed by the SFF-CfCWR project management staff and built by a specialist UHB website team. The website was launched in July 2019. The website outlines, across Birmingham and UWE, the Centre's core projects, allied studies, the research and management teams, partners, collaborators, news stories and events, publications and public involvement content (including profiles on PPI contributors).

https://www.conflictwoundresearch.org.uk/

News Stories

The Centre staff actively seeks out stories and have reached out to the Centre for Appearance Research at UWE, to invite pieces from them too. The Centre links in effectively and frequently to the comms team at UHB, UoB and SFF.

Twitter

SFF-CfCWR had a twitter account but this closed in October 2019 as UHB moved towards one central research account. Our communications lead now tweets on UHB's account using #CfCWR, #SFF and @scarfreefoundation as appropriate.

6. Build academic capacity

Developing the next cadre of clinical academics is essential for the future success of the CfCWR. We appointed 2 clinical research fellows (Krupali Patel and Tarek Houssana); Tarek Houssana will register for a higher degree in the New Year. In addition we have appetite from a couple of junior trainee doctors in our research programme in the next year.

We also continue to work with the Birmingham Health Partners (BHP) Clinical Academic Training Office, led by Prof Lorraine Harper and with other University of Birmingham non clinical programmes to support additional projects aligned to the Centre.

7. Collaborations

7.a. Academic

Scar Alliance

The Scar Alliance brings together a national collaborative network of clinicians and academics with an interest in scar reduction research. The group's role is to identify areas of opportunity for collaboration and sharing of expertise and to identify key questions to address and apply for funding. Membership currently brings together key clinical and academic leads from Birmingham, Bristol,

Manchester, Chelmsford, East Grinstead, Oxford, UCL and The Royal Free, and Imperial College London. An international perspective is also garnered from Galveston, Texas. This group is facilitated and supported by SFF-CfCWR staff.

Previous monthly teleconferences (several held in the Sep 2018 - Aug 2019 time period) proved too burdensome for some of the members, so going forward the intention is to keep the activity of the Alliance mainly focussed on certain projects and applications. Going forward the Birmingham team will arrange twice yearly 'open' meetings, allowing for members to discuss any pertinent issues and share news and developments.

The foundations built by the Scar Alliance have enabled the application for a Wellcome Collaborative Award which has reached the final application round (see under 8 below). Also Scar Alliance members met in November 2019 and are planning to submit an application for a Wellcome Biomedical Resource and Technology Development Grants in January 2020.

Members of Conflict Wound Research Strategy Group

The Centre Director and Programme Manager are members of the Conflict Wound Research Strategy Group and have attended the Group's meetings in Sep 2018 and August 2019. This group is a joint initiative by The Scar Free Foundation, The Ministry of Defence and The CASEVAC Club. It is administered by The Scar Free Foundation and is chaired by the Chief of Defence People, currently Lt Gen Richard Nugee.

International

The SFF-CfCWR has close collaborative links with Professor Ronald G Tompkins, Harvard Medical School, Founding Director of the Centre for Surgery, Science & Bioengineering at Massachusetts General Hospital, USA who he has provided invaluable input into design of SIFT-1 and SIFTI-2 studies. Professor Tompkins has visited Birmingham several times in the reporting year and attended the Conflict Wound Research Symposium in May 2019. Professor Janet Lord visited his group in July and is planning to submit a grant application with Professor Tompkins in accelerated ageing. Also three UoB staff are going to his lab in December to learn their cell migration assays and a new way for measuring cell free DNA.

The Centre is also building on the long-established links between University of Birmingham and Sun Yat-sen University in Guangzhou in China. Professor Jun Wu is paving the way to set up the First Affiliated Hospital of Guangzhou Medical University, as an international site for the SIFTI-2 study.

In addition, the Centre has strong connections with the Shriner's Hospital in Galveston, Texas and the University of Texas Medical Branch, UTMB; Professor David Herndon, the Chief of Staff of the centre is the world leader in all aspects of burn care and Dr William Norbury, Associate Professor at UTMB, has an outstanding experience in state of the art laser modalities for the treatment of hypertrophic scarring. Dr Norbury is a member of the Scar Alliance.

7.b. Industry

In the last year we have been working with several small pharma companies (as below) to take forward industry collaborative trials alongside preliminary discussions with some other companies.

AIM ImmunoTech Inc

Discussions have continued with a US based company, AIM ImmunoTech Inc (previously Hemispherx Biopharma), to conduct 'A Phase I Study to Evaluate the Safety of Ampligen® on Immune Function and Clinical Recovery in Thermally Injured Patients' at UHB.

AIM ImmunoTech's Ampligen is recently approved in Argentina as the world's only approved therapeutic for the treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). The drug, which is an experimental therapeutic in the US, is currently in clinical trials for the treatment of multiple cancers (eight solid tumour types).

BioAegis Therapeutics

Discussions with US company, BioAegis, continue into 2019 about the design of possible future clinical trials using gelsolin in trauma and burns patients. Any trials would need to be externally funded as BioAegis are not large enough to directly fund, but the company would be prepared to provide the drug for the potential trials. The company are keen to proceed especially as a UoB led paper supporting the potential use of gelsolin in this context has just been published (Dinsdale *et al*., 2019; see under section 10).

The initial planned indication for BioAegis's gelsolin is severe community-acquired pneumonia, with the company planning to pursue other acute and chronic inflammatory and infectious conditions.

8. Grants

Awarded

Liam Grover (PI is Professor Dalby, University of Glasgow). EPSRC and SFI Centre for Doctoral Training in Engineered Tissues for Discovery, Industry and Medicine. Jul-2019 - Dec 2027. £7,013,579 (just under £3M to Birmingham). The lifETIME CDT will focus on the development of non-animal technologies (NATs) for use in drug development, toxicology and regenerative medicine.

Submitted

Tony Metcalfe, Paul Martin, Odhran Shelley *et al.* Understanding and Optimising Scar Free Healing in Skin. Application got through to full submission stage (deferred to February 2020's round) for a Wellcome Trust Collaborative Award. Funding sought will be up to £2.5M. The outcome/ shortlisting for interview is expected at the end of April 2020, with interviews if successful in late July 2020.

Naiem Moiemen, Jon Deeks, Alice Sitch et al. A prospective study to examine the validity of a panel of objective burn scar measurement tools (BOSS-2: Burn Objective Scar Scale project). Scar Free Foundation. £389,587 (Feb 2020 – Jan 2023). Awaiting final outcome Jan 2020.

9. Conferences

Invited speakers

None have been recorded that are directly relevant to the early work of the SFF-CfCWR presented here.

Attended:

19th Congress of the International Society for Burn Injuries. New Delhi, India. November 30 – December 4, 2018. Tony Metcalfe attended.

Presented:

Advances in Patient Reported Outcomes: Integration and Innovation. Leeds, UK June 2019. Laura Nice. Poster presentation. Decorin project (how PPI has helped the decorin project in terms of early insight into how to best work with patients in a future clinical trial).

Joint launch of Centre for Trauma Science Research (CTSR) and NIHR Surgical Reconstruction and Microbiology Research Centre (SRMRC) Showcase. 29th March 2019. Show and Tell. Best stand awarded to Burns Team: represented by Khaled Al-Tarrah, Krupali Patel and Liam Cato.

10. Publications

Although not direct outputs from the new SFF CfCWR projects the publications listed below are related to the previous SFF Burns research programme and build on the existing programme.

(i) Chimen M, Evryviadou A, Box CL, Harrison MJ, Hazeldine J, Dib LH. Appropriation of GPIbα from platelet-derived extracellular vesicles supports monocyte recruitment in systemic inflammation. Haematologica. 2019 Aug 29. pii: haematol.2018.215145. doi: 10.3324/haematol.2018.215145. [Epub ahead of print]
This work was funded by the Scar Free Foundation and NIHR-SRMRC.

(ii) Dinsdale RJ, Hazeldine J, Al Tarrah K, Hampson P, Devi A, Ermogenous C et al. Dysregulation of the actin scavenging system and inhibition of DNase activity following severe thermal injury. Br J Surg. 2019 Sep 10. doi: 10.1002/bjs.11310. [Epub ahead of print]
This work was funded by the Scar Free Foundation and NIHR-SRMRC.

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This study was funded by the Scar Free Foundation and the Wellcome Trust.

11. New translational research projects (from basic science)

DeScar:
Plans are underway for a PhD for Tarek Houssana using the same delivery platform but with a non-antibiotic anti-microbial which can be used in the battlefield to combat infection

SMOOTH:
Findings from the histologic study will inform translation research to influence senescence of dermal fibroblasts by repurposing drugs that are already in clinical use.

12. Improving veteran/patient outcomes (care)

Working with key stakeholders (SFF/ CASEVAC/ charities and PPI groups), via different communication channels, we strive to ensure the programme of research remains focussed on veteran/civilian patient outcomes.

The **SMOOTH** study will allow us to (1) develop evidence based standard protocols for scar treatment (laser therapy); (2) understand the mechanistic action behind laser therapy post treatment of hypertrophic scars; (3) develop new alternative/additive treatments to scar laser treatment.

The **DeScar** trial will lead to the development of a dressing that will reduce the chance/extent of scarring which will directly impact on the patient's future psychological and physical outcomes.

13. PPIE

Our Patient and Public Involvement/Engagement (PPI/E) activities at the Centre have been designed to ensure that people with lived experience of burn injuries and scarring play a key role in how our research is designed, carried out, disseminated and managed. PPI/E activity is supported by our PPI/E Lead, Laura Nice and fully costed into the work of the Centre. We align our PPI activity to the National Standards for Public Involvement (NIHR, 2019) and we remain committed to carrying out,

improving and promoting meaningful patient and public involvement throughout the Centre. In the last year this has been strengthened through active partnership with PPI/E communities nationally (e.g. invoDIRECT), regionally (e.g. as a member of PILAR: Public Involvement and Lay Accountability in Research and Innovation group) and locally (e.g. University Hospitals Birmingham Patient and Public Involvement in Research Strategy group).

We have an active PPI group at the Centre who meet regularly and all PPI contributors receive payment for time/expenses, an induction to the Centre and access to our 'buddy scheme' to support new members. Staff and PPI Contributors have access to bespoke resources (PPI 'Quick Guides' for researchers) and training opportunities. Our PPI/E Lead runs an 'Introduction to PPI' workshop for staff and members of the public. The materials have been co-produced and the presentation is co-delivered with a former burns patient and member of our PPI group (19/7/19 and 16/10/19).

We have appointed two PPI Contributors with lived experience of burn injuries and scarring to our Research Programme Management Group (RPMG). Lottie Pollak is a civilian group member and a Scar Free Foundation Ambassador and Josh Boggi is a military veteran and a member of the CASEVAC club who has recently joined us. Lottie and Josh participate in quarterly RPMG meetings to discuss the management and monitoring of the Centre's work. PPIE is a standing agenda item at RPMG as well as at our executive, project management and patient/public meetings.

Our PPI group members are central to our public engagement activities and help us communicate effectively to a wide audience. This has led to the development of a co-produced PPI section on our website, which includes details about PPI, how to get involved, biographies and quotes from our PPI Contributors explaining why the Centre is important and how the research conducted here has the potential to change lives:

"The establishment of the Centre is a massive step towards dealing with the aftermath of trauma. The things that are learnt will not only benefit those ravaged by conflict but the many others who have faced trauma, injury or other interventions that have left them wounded. I am one of the latter and have been living with scarring and other consequences for over 10 years. Now I am delighted to be part of a forward-thinking research group that aim to find solutions that will help all of us enjoy futures that will give us the greatest chance of fulfilment" (Lottie Pollak, PPI Contributor).

Our staff and PPI Contributors have been actively involved in public engagement activities to promote the work of the Centre. These have included 'Research Changes Lives' at Birmingham Central Library (27/10/18), Centre for Trauma Sciences and NIHR SRMRC joint Showcase 'Show & Tell' (26/3/19) and the 'Research Showcase' at Queen Elizabeth Hospital Birmingham (17/5/19). We also share regular news stories on our website, engage with the public on social media (e.g. Twitter) and promote our work at national/international conferences, allowing broader engagement with the clinical and scientific communities.

Work is also underway with colleagues at UWE to establish a unified approach to recording and measuring the potential impact of PPI across the Centre. A meeting was held with Laura Nice and the UWE team (27/8/19) and a template for recording PPI is in development.

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Disclaimer

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