Institution: University of Warwick

Unit of Assessment: UOA2 - Public Health, Health Services and Primary Care

Title of case study: Improving outcomes from sudden cardiac arrest

Period when the underpinning research was undertaken: 1 January 2013- 31 December 2018

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 Gavin Perkins	Professor	01/03/2007- present
Professor Jerry Nolan	Professor	1/12/2018- present
Dr Joyce Yeung	Associate Clinical Professor	27/03/2017- present
Professor Anne-Marie Slowther	Professor	01/02/2006- 30/09/20
Dr Kirstie Haywood	Principal Research Fellow	30/11/2004- present

Period when the claimed impact occurred: 1 August 2013- 31 December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact (indicative maximum 100 words)

Sudden cardiac arrest kills 4,000,000 people each year. Research from the University of Warwick shaped, informed and supported implementation of: NHS policy (2017), the NHS Long Term Plan (2019), the mandatory introduction of CPR training in schools from 2020, national media campaigns and a new GBP3,000,000 defibrillator network (from 2019) to improve public access. These initiatives have increased bystander CPR and lives saved. The Warwick-led Out-of-Hospital Cardiac Arrest Outcome (OHCAO) registry has been specifically identified as contributing to the national strategy. Warwick led randomised trials evaluating mechanical chest compression devices (2015) and drug treatments during cardiac arrest (2019) led to changes in international resuscitation guidelines across Europe, America, Australasia and Asia. Placing the patient at the centre of Warwick's work led to the development of Core Outcome Set for Cardiac Arrest (COSCA) adopted by the International Liaison Committee on Resuscitation (2018). Warwick's research informed the Recommended Summary Plan for Emergency Care and Treatment (ReSPECT) which has been adopted by over 150 NHS Trusts since 2017 and improved patient centred care.

2. Underpinning research (indicative maximum 500 words)

Out of Hospital Cardiac Arrest Outcomes and community defibrillator use

Research from Warwick Medical School (2014-present) has identified that 27,000 people die each year from sudden cardiac arrest in the UK. It found gaps in the community response to cardiac arrest with only one in two people receiving bystander cardiopulmonary resuscitation (CPR) and less than one in forty receiving public access defibrillation [3.1]. Subsequent research in collaboration with the British Heart Foundation (BHF) identified a lack of knowledge about where defibrillators are located and their readiness for use, and suggested a national public access defibrillator network could reduce barriers to their use [3.2], revealing substantial opportunities to enhance the community response to cardiac arrest and better outcomes for patients.

Mechanical CPR use

High quality CPR is critical for achieving the best outcomes from cardiac arrest. The PARAMEDIC1, multi-centre, cluster randomised trial, sought to determine if using a mechanical chest compression device was clinically superior and cost effective compared to standard CPR. Launched in 2010 across 4 NHS Ambulance Services, the award winning trial (International

Society Clinical Trials 2016) found no difference in survival outcomes and marginally worse neurological outcomes associated with mechanical CPR [3.3]. The cost effectiveness evaluation, from the perspective of NHS and personal social services, was dominated by manual CPR, as the mechanical CPR group had poorer health outcomes and incurred higher health and social care costs.

Drug treatment in cardiac arrest

Despite the use of drug therapy for over 100 years in the treatment for cardiac arrest there was no evidence that their use improved long term outcomes. Warwick led the world's largest drug clinical trial in cardiac arrest (2014-2017). The PARAMEDIC2 trial provided definitive evidence that adrenaline is highly effective at restarting the heart (odds ratio 3.59 (3.14- 4.12)) and improved 30 day survival 3.2% versus 2.4% (OR 1.47 (1.09- 1.97)). While economic modelling showed that adrenaline was highly unlikely to be cost effective when examined from a within trial perspective or extrapolating to a lifetime horizon, including the economic benefits from organ donation in non-survivors brought the incremental cost effectiveness ratio within the range typically supported by healthcare systems [3.4].

Core Outcome Set for Cardiac Arrest (COSCA)

The reported heterogeneity in outcome assessment and reporting guidance were key triggers for the development of the Core Outcome Set for Cardiac Arrest consensus work (COSCA), (2015-2018) [3.5] led by Haywood and Perkins in international collaboration with researchers, clinicians, patients and the public. This important core outcome set, accepted by the international research community, set about to improve consistency of reporting and analysis of cardiac arrest effectiveness trials, paving the way for consistent and unambiguous narrative in cardiac arrest research. For the first time, this research highlighted the importance of favourable neurological outcome and health related quality of life from the patients and public perspective.

ReSPECT

Resuscitation is not universally successful and it is important to consider CPR decisions in the context of broader care and treatment. Warwick-led research (2016) synthesised key evidence from the published literature, qualitatively evaluated clinicians and patients view on resuscitation decisions and explored approaches to implementation in the NHS [3.6]. The research found variation and sub-optimal practice. Linking Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) to overall treatment plans improved clarity about goals of care, aided communication and reduced harms and informed the development of a new national approach to emergency care and treatment planning with guidance.

3. References to the research (indicative maximum of six references)

[3.1] Hawkes C, Booth S, Ji C, Brace-McDonnell SJ, Whittington A, Mapstone J, **Cooke MW,** Deakin CD, Gale CP, Fothergill R, Nolan JP, Rees N, Soar J, Siriwardena AN, **Brown TP, Perkins GD**; (2017) OHCAO collaborators. Epidemiology and outcomes from out-of-hospital cardiac arrests in England. Resuscitation.;110:133-140. doi: 10.1016/j.resuscitation.2016.10.030
[3.2] Arvanitis T, Deakin C, Deanfield J, Docherty M, **Khan MO**, Lambaise P, **Keung S, Perkins G**, **Smith C**. (2015) BHF National Public Access Defibrillator Feasibility Study (Confidential report)
[3.3] Gates S, Lall R, Quinn T, Deakin CD, **Cooke MW, Horton J, Lamb SE**, **Slowther AM**, Woollard M, Carson A, **Smyth M**, Wilson K, Parcell G, Rosser A, Whitfield R, Williams A, Jones R, Pocock H, Brock N, Black JJ, Wright J, Han K, Shaw G, Blair L, Marti J, Hulme C, McCabe C, Nikolova S, Ferreira Z, **Perkins GD**, (2017) Prehospital randomised assessment of a mechanical compression device in out-of-hospital cardiac arrest (PARAMEDIC): a pragmatic, cluster randomised trial and economic evaluation. Health Technol Assess. ;21(11):1-176 doi:10.3310/hta21110
Awarded International Clinical Trial of the Year Award 2016
[3.4] Perkins GD, **Ji C,** Deakin CD, Quinn T, **Nolan JP**, **Scomparin C**, **Regan S**, Long J, **Slowther A**, Pocock H, Black JJM, Moore F, Fothergill RT, Rees N, O'Shea L, Docherty M, Gunson I, Han K, Charlton K, Finn J, **Petrou S**, **Stallard N**, **Gates S**, **Lall R**; (2018)

PARAMEDIC2 Collaborators. A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest. N Engl J Med. 23;379(8):711-721. doi:10.1056/NEJMoa1806842 [Altmetric score 2993,17th highest in history of NEJM]
[3.5] Whitehead, L, **Perkins, G.D**., Clarey, A and **Haywood, K.L.** (2013) A systematic review of the outcomes reported in cardiac arrest clinical trials: the need for a core outcome set. Resuscitation, 88 (Supplement 1). pp. 150-7. doi:10.1016/j.resuscitation.2013.08.129
[3.6] Perkins GD, **Griffiths F**, **Slowther AM**, George R, **Fritz Z**, Satherley P, Williams B, **Waugh N, Cooke MW, Chambers S, Mockford C, Freeman K**, **Grove A**, Field R, **Owen S**, Clarke B, **Court R, Hawkes C**. (2016) Do-not-attempt-cardiopulmonary-resuscitation decisions: an evidence synthesis. Southampton (UK): NIHR Journals Library, Health Services and Delivery Research, 4 (11). doi:10.3310/hsdr04110

Grants

PI Gavin Perkins, Epidemiology and Outcome of Out of Hospital Cardiac Arrest, British Heart Foundation, 1/10/2018 to 30/09/2023, GBP809,984
PI Gavin Perkins, Epidemiology and Outcome of Out of Hospital Cardiac Arrest Resuscitation Council (UK), 1/04/2015 to 31/03/2018, GBP100,217
PI Professor Simon Gates Co-PI Gavin Perkins, Prehospital Randomised Assessment of a Mechanical Compression Device in out of Hospital Cardiac Arrest (PARAMEDIC): a pragmatic cluster randomised trial and economic evaluation, NIHR HTA, 07/37/69, 01/06/2009 to 01/07/2015, GBP2,037,709
PI Gavin Perkins, Prehospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug administration In Cardiac arrest (PARAMEDIC2), NIHR HTA, 12/127/126, 01/03/2014 to 01/08/2019, GBP2,751,276.78
PI Gavin Perkins, Evaluation of the Recommended Summary Plan for Emergency Care and Treatment. NIHR HS&DR 15/15/09, 1/11/2016 to 01/10/2020, GBP 795,327.36
PI Gavin Perkins, Do not attempt cardiopulmonary resuscitation (DNACPR) decisions, NIHR HSDR, 12/5001/55, 01/06/2013 to 01/09/2014, GBP182,637.17

4. Details of the impact (indicative maximum 750 words)

NHS Long Term Plan milestone to improve outcomes from cardiac arrests

Through Perkins' membership of NHS England Community Resuscitation Steering Committee and working closely with the National Clinical Director for Cardiovascular Disease, Warwick research on poor bystander CPR and automated external defibrillator use directly informed the NHS Long Term Plan (2019) recommendation 3.71 and associated milestone to "work with our partners to improve community first response and build defibrillator networks to improve survival from out of hospital cardiac arrest." Warwick research contributes to the delivery of this milestone to save lives of people sustaining a cardiac arrest, and is estimated to save up to 4,000 lives annually by 2028 [5.1].

Funded by the British Heart Foundation (BHF) and Resuscitation Council UK, the Warwick-led OHCAO Registry is specifically identified as contributing to the national strategy: "More effective mapping of data on incidence will help direct community initiatives to areas where they are most needed, with the British Heart Foundation's national Outcomes Registry allowing us to track survival rates and target unwarranted variation" [5.1].

Perkins contributed to the development of the Resuscitation to Recovery National Framework (2017). Supported by 20 professional organisations, the Framework identifies a number of interventions including the improvement of public awareness cardiac arrest and use of CPR and public access defibrillators and recommends that: "Data should be submitted to the national Out-of-Hospital Cardiac Arrest Outcomes (OHCAO) Registry so that performance and progress towards improved survival rates can be monitored and unwarranted variation can be addressed; appropriate local resources must be allocated for these audit purposes" [5.2]. These interventions have facilitated the integration of the OHCAO registry Out-of-Hospital Cardiac Arrest outcome data as part of the National Ambulance Quality Indicator Programme, enabling continuous quality improvement by all NHS Ambulance Services through monthly reports.

Enhancing the uptake of cardiopulmonary resuscitation
Working with charities (BHF, Resuscitation Council UK, St John Ambulance), Warwick's research underpinned major national media campaigns to promote communities learning CPR and enabled the Resuscitation Council UK and BHF to produce a compelling case to the Department for Education for the mandatory introduction of CPR training in schools. A requirement to teach CPR is now part of the national curriculum in England (2020). In the last 5 years 6,800,000 people have been taught CPR as a result of these initiatives [5.3]. As members of the International Liaison Committee on Resuscitation, Warwick researchers contributed to establishing the World Restart a Heart Initiative, which has trained over 15,000,000 people in how to perform CPR in the last 3 years. Together these initiatives have seen "the rate of bystander CPR in the community has increased from 57% (2014) to 69% (2019), leading to an additional estimated 1000 lives being saved" (NHS England) [5.4].

After highlighting the low rates of public access defibrillator use and potential additional number of lives that could be saved, if uptake increased, Perkins worked with charities to explore barriers and facilitators to their use which led to the development of new national signage from 2017 to facilitate defibrillator use which is used widely on automated external defibrillators around the UK with records showing over 8000 downloads [5.3, 5.5]. In addition Warwick research underpinned the BHF and Microsoft investment of more than GBP3,000,000 to build a national defibrillator network – the Circuit. Launched in 2019, the Circuit is active across 30% of NHS Ambulance Services with plans to roll out across the UK by spring 2021 [5.3].

Changes to international resuscitation guidance
Through participation in the International Liaison Committee on Resuscitation (ILCOR) (Perkins (Co-Chair), Couper, Yeung, Smyth, Nolan) Warwick's primary research and meta-analysis on mechanical chest compression devices led to recommendations against mechanical CPR use and informed resuscitation guidelines across Europe, America, Australasia and Asia [5.6]. Warwick's collaboration with Health Technology Wales to undertake a technology appraisal also recommended against mechanical CPR use [5.7]. A National Institute for Health Research report identified that the research led by Warwick has the potential to save the NHS up to GBP40,000,000 in technology spend [5.8]. Working with ILCOR, Warwick research led to an accelerated review of drug therapy guidelines for cardiac arrest and the first strong recommendation for the use of drugs in cardiac arrest which has been implemented in to international clinical practice guidelines. ILCOR Co-Chair, Robert Neumar stated: "We calculated that for every 1000 people treated with adrenaline an additional 10 lives will be saved*"* [5.9].

Responding to COVID-19, researchers from Warwick undertook a rapid review of science related to performing resuscitation in a patient suspected to have COVID-19. The findings informed global recommendations for how to safely perform CPR in this setting [5.10].

Involvement of patients improving outcomes from cardiac arrest trials
The patient centred Core Outcome Set for Cardiac Arrest (COSCA) developed by Warwick was adopted by ILCOR in 2018. "Warwick's work integrated the patient's voice in to prioritizing outcomes from cardiac arrest creating an international collaboration involving patients for the first time in international resuscitation guideline development" [5.9]. The core outcome set for cardiac arrest, is internationally endorsed and now used globally to prioritise the most important outcomes in cardiac arrest trials capturing patient priorities [5.9].

NHS and patient benefit from implementation of ReSPECT
In 2014, Warwick's systematic review of resuscitation decisions was presented to more than 100 patients, clinicians (multidisciplinary and multiprofessional), healthcare commissioners and regulators at the Royal Society of Medicine. A Working Group representing patient, clinician, commissioners, charities and policy makers developed a new approach. Warwick's mixed methods programme informed the development of the Recommended Summary Plan for Emergency Care and Treatment (ReSPECT), with guidance from the British Medical Association, the Resuscitation Council UK and the Royal College of Nursing. The ReSPECT

programme has been rolled out to over 150 NHS Trusts since February 2017 [5.11]. Audits and qualitative research has shown that patients and the NHS benefit from greater patient involvement in decision making about future emergency treatments and the adopting trusts have reported a reduction in complaints associated with CPR discussions. The Royal College of Physicians recommended in 2018 that Physicians "consider using a structured tool, such as the ReSPECT process, to support conversations and documentation" and "promotes the use of the ReSPECT process to support advance care planning" [5.12].

5. Sources to corroborate the impact (indicative maximum of 10 references)

[5.1] The NHS Long Term Plan. (January 2019) - Recommendation 3.71 and associated milestone- NHS England. https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf
[5.2] Resuscitation Council (UK). Resuscitation to Recovery: A National Framework to improve care of people with out-of-hospital cardiac arrest (OHCA) in England 2017 https://www.resus.org.uk/publications/resuscitation-to-recovery/
[5.3] Written statement, Director of Health Innovation Programmes, British Heart Foundation
[5.4] Written statement, Emeritus National Clinical Director for Heart Disease, NHS England (2013-19)
[5.5] Association of Ambulance Chief Executives launch of the new defibrillator location signage https://aace.org.uk/news/new-public-access-defibrillator-pad-signs-launched/
[5.6] European Resuscitation Council Guidelines for resuscitation (2015), https://cprguidelines.eu/ , American Heart Association Guidelines Update for CPR and Emergency Cardiovascular Care (2015) 132(suppl 2):S436–S443 https://www.ahajournals.org/doi/full/10.1161/CIR.0000000000000260 and Resuscitation council UK guidelines https://www.resus.org.uk/resuscitation-guidelines/adult-advanced-life-support/ recommend that automated mechanical chest compression devices
[5.7] Health Technology Wales: Mechanical Chest Compression https://www.healthtechnology.wales/reports-guidance/mechanical-chest-compression/
[5.8] NIHR Themed Review: Care at the scene https://evidence.nihr.ac.uk/themedreview/care-at-the-scene-research-for-ambulance-services/ (p21)
[5.9] Written statement, ILCOR
[5.10] Perkins GD, Morley PT, Nolan JP, Soar J, Berg K, Olasveengen T, Wyckoff M, Greif R, Singletary N, Castren M, de Caen A, Wang T, Escalante R, Merchant RM, Hazinski M, Kloeck D, Heriot G, Couper K, Neumar R.(2020) International Liaison Committee on Resuscitation: COVID-19 consensus on science, treatment recommendations and task force insights. Jun;151:145-147. doi: 10.1016/j.resuscitation.2020.04.035. and Couper, K, Taylor-Phillips, S, Grove, A, Freeman, K, Osokogu, O, Court, R, Mehrabian, A, Morley PT, Nolan JP, Soar, J, Perkins, GD (2020) COVID-19 in cardiac arrest and infection risk to rescuers: A systematic review, Resuscitation, doi: 10.1016/j.resuscitation.2020.04.022.
[5.11] Amended Emergency Care Treatment Plans (ReSPECT) informed by Warwick research https://www.resus.org.uk/respect/
[5.12] RCP guidance: "talking about dying" 2018 https://www.rcplondon.ac.uk/projects/outputs/talking-about-dying-how-begin-honest-conversations-about-what-lies-ahead and Description of some of the impacts of Respect. https://www.bmj.com/content/356/bmj.j876