Institution: Cardiff University

Unit of Assessment: A2

Title of case study: Safely reducing antibiotic prescriptions to help contain antibiotic resistance.

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

Research by Cardiff University is contributing to initiatives within the NHS and across Europe to safely reduce unnecessary antibiotic prescribing and thus help contain antimicrobial resistant bacteria. Our researchers conducted observational studies of prescribing patterns linked to local resistance data and qualitative research with GPs and patients on their perceptions of acute respiratory tract infections and antibiotic use and resistance. This enabled the Cardiff team to develop clinician training and patient education resources (covering issues such as communication skills, point of care testing, and typical duration of infections) to reduce unnecessary prescribing. Our trials proved these interventions were effective, at times cutting prescribing by as much as two-thirds. Our research has provided the basis for new clinical guidelines, antibiotic stewardship initiatives and policies, and educational tools for clinicians and patients that are being used in the UK and internationally.

2. Underpinning research (indicative maximum 500 words)

Antibiotic prescribing practices and perceptions

Cardiff University researchers, including Chris Butler (Clinical Fellow, 1993; Professor of Primary Care Medicine, 2001-present), Nick Francis (Clinical Lecturer, 2003-2010; Senior Clinical Research Fellow, 2010-present), Fiona Wood (Lecturer, 2003-2013; Senior Lecturer 2013-present), Kerry Hood (Senior Lecturer 2002-2007; Reader, 2007-2009, Professor, 2009-present), Frank Dunstan (Professor of Medical Statistics, 2002-present) and Stephen Rollnick (Research Fellow, 1993; Professor of Healthcare Communication, 2013-present), have developed and evaluated effective, evidence-based tools which improve the clinical management of respiratory tract infections (RTIs) and help to reduce inappropriate antibiotic use.

Butler and Rollnick provided the earliest insights into clinicians' and patients' perspectives on why antibiotics were prescribed for sore throats [3.1]. This research, published in the British Medical Journal (BMJ) in 1998, revealed several drivers for inappropriate prescribing, including GP perceptions that community antibiotic prescribing was incidental to resistance ('resistance is not a problem in my practice') and a lack of tools to support clinicians to change their prescribing habits.

Butler, Dunstan and colleagues then produced the first ever evidence that showed antibiotic use was linked to antibiotic resistance at a local (practice) level. Analysing data from urine samples submitted by Welsh GPs, they found that antibiotic resistance was common in primary care; patients infected with resistant strains were sicker for longer and consumed more healthcare resources compared to patients infected with bacteria sensitive to antibiotic treatment. The research also revealed that reducing antibiotic prescribing was associated with reduced resistance at the general practice level [3.2].

In 2003 and 2006 Butler and Francis produced new data on the normal illness course of upper RTIs in children and acute sore throat in adults. This data is used to help set realistic expectations about likely illness course. Butler, Francis, Wood and colleagues also conducted qualitative research to describe the perceptions of both general practitioners (GPs) and the general public regarding antibiotic use and resistance, including interviews with GPs about their rationale for using broad-spectrum antibiotics (which generally cause greater 'collateral damage') and parents about their information needs regarding their child's RTI.

Butler (as a work package leader), supported by others from Cardiff, played a central role in the EU-funded FP6 project 'Genomics to combat resistance to antibiotics in Community-acquired lower respiratory tract infections in Europe' which ran from 2006 to 2011. This project provided evidence that there is 'unhelpful' variation in the antibiotic prescribing practices of doctors between 14 European sites. The project has produced the most reliable data so far on the prognostic value of signs, symptoms and point of care testing for RTIs in primary care [3.3], as well as trial data on the effectiveness of antibiotics in adults with acute cough [3.4].

Evaluation of tools

From 2005-2011 the Cardiff team collated the insights from their empirical investigations. Informed by complementary research strengths in motivational interviewing, shared decision making, and other behaviour change theories, the team developed a set of communication skills strategies to help clinicians adopt a non-prescribing approach while enhancing patient empowerment and maintaining patient satisfaction. Output from this work included a communications skills training programme [3.3], a blended learning package (http://www.stemmingthetide.org/) [3.6], and interactive patient information booklets, supported by online clinician training, for children (www.whenshouldiworry.com) [3.5] and adults [3.7] with RTIs.

The team also led or played a central role in four major trials of the tools developed by the research. The tools under investigation included 'blended learning' (combining multi-media and interactive learning), enhanced communication skills training, point of care testing, and interactive booklets. The trials demonstrated statistically significant, clinically important, safe, and acceptable reductions in antibiotic prescribing through use of the tools [3.3, 3.5-3.7]. The paper describing the blended learning (STAR) study was one of six papers internationally shortlisted for the BMJ Research Paper of the Year Award 2013.

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

Note: All Cardiff researchers in **bold**

Key References

1. Butler CC, **Rollnick S**, **Pill R**, **Maggs-Rapport F, Stott N**. Understanding the culture of prescribing: Qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. British Medical Journal. 1998;317(7159):637-42. doi: http://dx.doi.org/10.1136/bmj.317.7159.637
2. **Butler CC**, **Dunstan F**, **Heginbothom M, Mason B, Roberts Z, Hillier S**, et al. Containing antibiotic resistance: decreased antibiotic-resistant coliform urinary tract infections with reduction in antibiotic prescribing by general practices. The British Journal of General Practice. 2007;57(543):785-92 http://www.ncbi.nlm.nih.gov/pubmed/17925135
3. Cals JW, **Butler CC**, Hopstaken RM, **Hood K**, Dinant GJ. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. BMJ. 2009;338:b1374 doi: http://dx.doi.org/10.1136/bmj.b1374
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5. **Francis NA**, **Butler CC**, **Hood K**, **Simpson S**, **Wood F**, **Nuttall J**. Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial. BMJ. 2009;339:b2885 doi: http://dx.doi.org/10.1136/bmj.b2885
6. **Butler CC**, **Simpson SA**, **Dunstan F**, **Rollnick S**, Cohen D, **Gillespie D**, et al. Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. BMJ. 2012;344:d8173. doi: http://dx.doi.org/10.1136/bmj.d8173
7. Little P, Stuart B, **Francis N**, Douglas E, Tonkin-Crine S, Anthierens S, Cals JW, Melbye H, Santer M, Moore M, Coenen S, **Butler C**, **Hood K**, **Kelly M**, Godycki-Cwirko M, Mierzecki A, Torres A, Llor C, Davies M, Mullee M, O'Reilly G, van der Velden A, Geraghty AW, Goossens H, Verheij T, Yardley L; on behalf of the GRACE consortium. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. Lancet. 2013 Oct 5;382(9899):1175-1182. doi: http://dx.doi.org/10.1016/S0140-6736(13)60994-0 Epub 2013 Jul 31.

Key funding

SAVIT Study: The effect of intranasal sodium cromoglycate on symptoms of suspected acute viral URTI in children. **Butler**. MRC (1999-2000). £98,012. www.controlled-trials.com/ISRCTN21562211/

The link between antibiotic prescribing and resistance in the community: definition, dynamics, and influences. Howard, **Palmer**, Magee, **Dunstan** (2000-2003). NHS Wales Office of Research and Development for Health and Social Care. £199,713.

Antibiotic Resistance in Community Urinary Tract Infection. **Palmer**, **Butler**, **Dunstan**. Wellcome Trust (2002-2005). £271,9320.
The development and evaluation of an interactive leaflet for children with acute respiratory tract infections. **Butler**, **Simpson**, **Hood**, **Francis**. MRC (2005-2009). £307,860.
STAR: Stemming the Tide of Antimicrobial Resistance. **Butler**, **Evans**, **Hood**, **Simpson**, **Palmer**, **Rollnick**, **Dunstan**. MRC (2006-2009). £509,753.
GRACE: Genomics to combat resistance against antibiotics in community-acquired lower respiratory tract infections in Europe. **Butler**, **Hood**. EC FP6 project (2006-2011). Total project grant €11.5 million; £804,740 to Cardiff University.

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

The findings and recommendations of the Cardiff research team have provided the basis for new educational materials, training programmes and other decision management tools used by clinicians in the UK and abroad. The Cardiff research has also informed new clinical guidelines in the UK and elsewhere on the management of RTI. The widespread dissemination of Cardiff's research is helping to improve antibiotic stewardship across Europe. Our four trials (see Section 3) all demonstrated the effectiveness of different tools to reduce antibiotic prescribing. The reductions ranged from 32% to 67% in trial participants and a 4.2% reduction in overall antibiotic prescribing (and a 5.5% reduction in antibiotic dispensing costs) over a one-year period at the whole general practice level. This equates to a saving of £830 per annum for an average sized UK general practice. Given the widespread adoption of Cardiff's tools and training in NHS initiatives to reduce GP antibiotic prescribing (see below), if 50% of all UK GP practices achieved just half of the average savings observed in the trials, the direct costs savings across the country since publication of the NICE guidelines would total £9 million.

Guidelines

The NICE guidelines on managing acute RTI were published in 2009 and were distributed to all GPs in the UK. They highlighted the importance of eliciting patient expectations; GPs are encouraged to achieve a shared understanding regarding the management and treatment of the infection. This recommendation stems directly from the Cardiff research, which is cited in the NICE publication [5.1]. Aspects of Cardiff's research have also informed a revision of the Dutch national guidelines on RTIs [5.4].

Patient educational materials

In 2009 the Cardiff team published the results of a trial revealing that use of the interactive booklet for children about RTIs, which was developed by the Cardiff team, resulted in a two-thirds reduction in antibiotic use [3.5, see 'What this study adds' summary, p7]. The results were picked up by the UK medical media, including Pulse, Healthcare Today and Onmedica; the publicity stimulated widespread uptake of the booklet around the UK. The booklet has been available for purchase at the Royal College of GPs bookshop since 2010. Over 90,000 copies have been purchased by or sent to general practices since 2009. In September 2009, for example, NHS Forth Valley highlighted the 'When Should I Worry?' booklet as a potential aid to management of self-limiting upper respiratory infections through the Whole System Working initiative in 2009-10. 27,000 copies of the booklet have been distributed to practices to date [5.2]. In 2012, Welsh Government sent 30,000 copies to all general practices in Wales as part of European Antibiotic Awareness Day activities [5.3].

Training clinicians

The evaluation of Cardiff's training package showed that communication skills training (to improve interactions with patients and enhance their experience) and the promotion of a point-of-care blood test, used alone or in combination, led to significant reductions in antibiotic prescribing. The results of this study led directly to a change in the Dutch national guidelines on lower respiratory tract infections; a training package on the updated guidelines was sent to 11,000 GPs [5.6] and made freely available online [5.4, 5.5]. The study also helped convince the Dutch health insurance system to pay for C-reactive protein (CRP) point of care testing [5.6].
Cardiff developed a blended learning package (e-learning, practice based outreach, experiential learning, and reflections) about antibiotic prescribing for RTIs. Research demonstrated this

approach reduced practice-level antibiotic prescribing, not just in those patients included in the trial. The Cardiff team's research, including the learning package, formed the basis of the Royal College of General Practitioners Managing Acute Respiratory Tract Infections (MARTI) course, which by December 2012 had been completed by over 4,300 clinical users and results in an average 24% increase in test scores between pre and post course evaluation [5.7]. A contract has just been signed where Cardiff's SME partners involved in the trial of the blended learning are investing £50,000 in further development and its commercialisation. Cardiff's research has influenced national and international antimicrobial stewardship programmes and campaigns. For example, Cardiff's interactive booklet for children and training in its use, and the MARTI module form part of the TARGET antibiotic toolkit [5.8], which was developed in 2012 by the Antimicrobial Stewardship in Primary Care collaboration (ASPIC) and has been accessed by more than 5,400 unique users since November 2012.

Public awareness and policy

The Cardiff team's development and trial of the blended learning package were picked up by local and national media. Articles in The Telegraph [5.9] and Professor Chris Butler's contributions to discussions on Radio 4's Women's Hour [5.10], Radio 4's Inside Health, and BBC Wales's Jason Mohammed Show all helped to disseminate the message about reducing antibiotic prescribing for RTIs to the general public. Butler, Francis and Stanton also advise the Health Protection Agency, the Department of Health, the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection, and the Welsh Antimicrobial Resistance Programme.

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

1. NICE clinical guideline on Respiratory Tract Infections, July 2008: www.nice.org.uk/nicemedia/pdf/CG69FullGuideline.pdf Corroborates the importance of Cardiff research in informing UK clinical guidelines. Cardiff research directly cited (pp.14, 88, 93).
2. Statement from Clinical Lead, NHS Forth Valley. Confirms the use and usefulness of the 'When should I worry?' interactive booklet developed by Cardiff in NHS Forth Valley.
3. Corroborative statement from Head of Welsh Antimicrobial Resistance Programme, Public Health Wales, about the use of the interactive booklet in Welsh General Practice.
4. Dutch Primary Care Guideline on Acute Cough 2013: http://nhg.artsennet.nl/kenniscentrum/k_richtlijnen/k_nhgstandaarden/Samenvattingskaartje-NHGStandaard/M78_svk.htm Confirms the influence of the Cardiff research in the updating of guidelines for training Dutch GPs. Cardiff research directly cited (Notes 18, 34, 37 and references). [Translated version saved as a pdf on 11/04/2013].
5. Educational website for Dutch GPs: http://www.acutehoest.nl/praktijk. Confirms Cardiff research as informing the education and training for Dutch GPs on antibiotic prescribing for respiratory tract infections. Cardiff research directly cited in Literature section. [Translated version saved as a pdf on 11/04/2013].
6. Corroborative statement from Assistant Professor, Maastricht University Medical Centre about the impact of the Cardiff research on Dutch clinical guidelines on lower respiratory tract infections and health insurance reimbursements.
7. RCGP online course - Managing Acute Respiratory Tract Infections http://elearning.rcgp.org.uk/course/info.php?id=17&nopopup=1 Confirms Cardiff research informed Royal College of General Practitioner guidance on patients presenting with acute ear pain, acute sore throat, sinusitis and acute cough. Cardiff research directly cited in References section. [Saved as a pdf on 11/04/2013].
8. RCGP TARGET antibiotic prescribing toolkit: http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit/training-resources.aspx. Corroborates the use of Cardiff research in the antibiotics training and resources for UK GPs. Cardiff research directly cited in 'Training Resources' and 'Patient information leaflet' http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit/patient-information-leaflets.aspx sections [Saved as a pdf on 11/04/2013].
9. 'GPs could prescribe 1.6m fewer antibiotics' *The Telegraph,* 09 Feb 2012. Article in The Telegraph reporting Cardiff research: www.telegraph.co.uk/health/healthnews/9071706/GPs-could-prescribe-1.6m-fewer-antibiotics.html [Saved as a pdf on 11/04/2013].
10. Woman's Hour, Radio 4, 16/08/2011. http://www.bbc.co.uk/programmes/b0135z1k Professor Butler provides expert comment on antibiotic resistance.

All documents, web pages, recordings and testimony available from HEI on request.