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| <p>Institution: University College London</p> |
| <p>Unit of Assessment: 3A - Allied Health Professions, Dentistry, Nursing and Pharmacy: Dentistry</p> |
| <p>Title of case study: Development of new guidelines for antibiotic prophylaxis for dental procedures in patients at risk of infective endocarditis</p> |
| <p>1. Summary of the impact</p> <p>Infective endocarditis (IE) is a rare but life-threatening disorder that may arise as a consequence of bacteraemia following invasive procedures such as those of dentistry. Research at the UCL Eastman Dental Institute has detailed the dental causes, prevalence and character of bacteraemia following dental procedures and demonstrated that everyday oral health activities are more likely to be a cause of bacteraemia than invasive dentistry. The research outcomes informed 2008 NICE guidelines that recommended that antibiotic prophylaxis solely to prevent IE should not be given to people at risk of IE undergoing dental and non-dental procedures. This has since caused a 78.6% fall in related antibiotic prescribing, a cost-saving of approximately £4m to the NHS in England and will reduce the threats of fatal anaphylaxis and antibiotic resistance.</p> <p>2. Underpinning research</p> <p>Infective endocarditis (IE) is a rare disorder but with significant morbidity and mortality. Oral streptococci may cause approximately 48% of confirmed cases of endocarditis. Until 2008, it was standard practice to give antibiotic prophylaxis to at-risk patients prior to certain dental procedures to reduce the risk of IE. The number of patients affected was approximately 130,000 per year. However, there was no strong evidence to support this practice, and some researchers questioned its effectiveness. This uncertainty led to a programme of research at the UCL Eastman Dental Institute (UCL EDI) to understand the processes involved.</p> <p>A review by Roberts [1] concluded that everyday procedures such as clenching and tooth-cleaning are more likely to cause IE than single invasive dental procedures and that the benefit of antibiotic prophylaxis prior to dental treatment was questionable.</p> <p>Roberts, Lucas, Spratt and Wilson thus undertook a programme of work from the late 1990s onwards to understand the events that lead to bacteraemia and to determine its prevalence and intensity. They established that simple dental procedures (rubber dam placement, use of fast or slow drills, placement of simple restorations and orthodontic therapy) induced bacteraemia [2, 3, 4]. A study subsequently demonstrated that bacteraemia was as likely to develop as a consequence of tooth brushing at home as from cleaning or scaling by a dental professional [5]; indeed tooth-brushing was found to be an important factor in cumulative dental bacteraemia and that over one year, bacteraemia due to tooth-brushing was many millions of times greater than a single dental extraction [6]. A later study of a cohort of 500 children to determine the duration, prevalence and intensity of bacteraemia following dental extractions demonstrated that bacteraemia could be detected after 10 seconds and up to about 11 minutes following extraction and that a rich microbiota was present in blood with 42 different taxa being characterised.</p> <p>Roberts subsequently co-authored a Cochrane review on antibiotics for the prophylaxis of bacterial endocarditis in dentistry [7] in which it was concluded that there was no evidence as to whether penicillin prophylaxis is effective or ineffective against bacterial endocarditis in people at risk of endocarditis who are about to undergo an invasive dental procedure. Indeed the review demonstrated that there was a lack of evidence to support the previously published guidelines.</p> <p>The experimental evidence of the Eastman group and the literature review subsequently served to underpin the development of NICE guidelines for the use of antibiotic prophylaxis for invasive dental (and other) procedures.</p> <p>Researchers at UCL EDI who contributed to this work included: Professor Graham Roberts (Head</p> |

of Paediatric Dentistry); Dr Victoria Lucas (Senior Clinical Lecturer); Professor Mike Wilson (Head of Microbiology); Dr David Spratt (Reader in Microbial Ecology); Ruth Holt (Senior Lecturer); Dr Aviva Petrie (Senior Lecturer in Statistics); Roger Davis (Consultant and Honorary Senior Lecturer in Special Care Dentistry).

3. References to the research

- [1] Roberts GJ. Dentists Are Innocent! "Everyday" Bacteremia Is the Real Culprit: A Review and Assessment of the Evidence That Dental Surgical Procedures Are a Principal Cause of Bacterial Endocarditis in Children. *Pediatr Cardiol.* 1999 Sept-Oct;20(5):317-25. Copy available.
- [2] Roberts GJ, Gardner P, Longhurst P, Black A, Lucas VS. Intensity of bacteraemia associated with conservative dental procedures in children. *BDJ.* 2000 Jan;188:95-8. Copy available.
- [3] Roberts GJ, Lucas VS, Omar J. Bacterial endocarditis and orthodontics. *J R Coll Surg Edinb.* 2000 Jun;45(3):141-5. Copy available.
- [4] Lucas VS, Omar J, Vieira A, Roberts GJ. The relationship between odontogenic bacteraemia and orthodontic treatment procedures. *Eur J Orth.* 2002;24:293-301.
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4. Details of the impact

The research described above provided substantial evidence to challenge the existing guidelines on antibiotic prophylaxis (typically in the UK 3g of amoxicillin or 600mg of clindamycin) prior to a relevant procedure). Roberts was co-opted onto the NICE Guideline Development Group as adviser on this topic. In 2008, NICE issued Clinical Guideline 64, *Prophylaxis against infective endocarditis [a]*. The work of the Roberts group was influential in this document and 7 papers were cited at 16 points throughout the document. The guidelines recommended that antibiotic prophylaxis used solely to prevent IE should not be given to people at risk of IE undergoing dental and non-dental procedures. Four points were highlighted that underpinned this recommendation and work by the Roberts group was used to support 3 of these:

- there is no consistent association between having an interventional procedure, dental or non-dental, and the development of IE (cites reference [1])
- regular tooth brushing almost certainly presents a greater risk of IE than a single dental procedure because of repetitive exposure to bacteraemia with oral flora (cites references [5] and [6])
- the clinical effectiveness of antibiotic prophylaxis is not proven (cites reference [7])
- antibiotic prophylaxis against IE for dental procedures may lead to a greater number of deaths through fatal anaphylaxis than a strategy of no antibiotic prophylaxis, and is not cost effective.

Impact case study (REF3b)

As a consequence of the NICE guidelines, there has been a demonstrable change in clinical practice, with a resulting decrease in antibiotic prescribing for dental procedures and infective endocarditis. A review in 2011 revealed that prescriptions in England reduced by 79% in the two years after guidelines were issued with no increase in the rate of infective endocarditis [b]. A review of dental prescribing in Wales also reported that dental prescriptions for amoxicillin 3g sachets and clindamycin capsules decreased sharply after the publication of the NICE guidelines in 2008 [c]. Overall this represents a reduction of over half a million doses over a five-year period for the two countries. The reduction of unnecessary antibiotic prescribing has three key impacts: (i) improved patient safety through reduced adverse reactions to antibiotics; (ii) a cost-saving to the NHS through lower wastage; (iii) a reduction in antibiotic use helping to prevent an increase in antibiotic resistance in the community.

Improved patient safety: The guidelines discuss anaphylaxis as one of the reasons for their recommendation. It has been estimated that approximately 20 individuals per million patients who receive a dose of penicillin suffer a fatal anaphylactic reaction [d]. Approximately 500,000 doses have been avoided and an estimated 10 lives likely to have been saved and countless episodes of anaphylaxis avoided (in the UK alone).

Cost-savings to the NHS: Prior to the guidelines, approximately 129,000 doses were prescribed per year and this reduced to 27,504 doses per year in the two years after the guidelines were issued. This represents a reduction of over half a million doses over the five years and a consequent saving of approximately £4m in prescription fees (calculated from data in [b]).

A reduction in antibiotic use: As detailed above, approximately 500,000 fewer doses of antibiotics were prescribed to patients in the period. The inappropriate and overuse of antibiotics in the past has provided an extremely strong selective pressure for bacteria to evolve and acquire a myriad of different resistance mechanisms. As highlighted by the Chief Medical Officer of England, bacterial resistance to antimicrobials now represents one of the most urgent problems facing public health and modern healthcare. Once antibiotics become ineffective, increases in morbidity and premature mortality will follow.

Changes in international guidelines: The research described above has also had an impact on guidelines around the world, which have been reviewed and modified using evidence generated by the UCL EDI team. Roberts was acknowledged as an international expert by the American Heart Association in 2007 prior to his work with NICE and six papers by the Roberts group were used to support their recommendations. The research also informed the 2008 American Academy of Pediatric Dentistry guidelines for antibiotic prophylaxis for dental patients at risk of infection [e] and the 2009 European Society of Cardiology Guidelines on the prevention, diagnosis, and treatment of infective endocarditis [f] leading to a change in their clinical recommendations. Other international bodies have used the above guidelines to inform their own national recommendations. For example, in Australia, national guidelines twice reference work by Roberts and colleagues [g].

5. Sources to corroborate the impact

- [a] NICE guidance. CG064 c against infective endocarditis. 2008: <http://guidance.nice.org.uk/CG64/Guidance/pdf/English> (Appendices, including references, here: <http://guidance.nice.org.uk/index.jsp?action=download&o=40042>)
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- [e] American Academy on Pediatric Dentistry Clinical Affairs Committee; American Academy on Pediatric Dentistry Council on Clinical Affairs. Guideline on antibiotic prophylaxis for dental patients at risk for infection. *Pediatr Dent*. 2008-2009;30(7 Suppl):215-8.
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- [f] Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, Moreillon P, de Jesus Antunes M, Thilen U, Lekakis J, Lengyel M, Müller L, Naber CK, Nihoyannopoulos P, Moritz A, Zamorano JL; ESC Committee for Practice Guidelines. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J*. 2009 Oct;30(19):2369-413. <http://dx.doi.org/10.1093/eurheartj/ehp285>
- [g] Daly CG, Currie BJ, Jeyasingham MS, Moulds RF, Smith JA, Strathmore NF, Street AC, Goss AN. A change of heart: the new infective endocarditis prophylaxis guidelines. *Aust Dent J*. 2008 Sep;53(3):196-200; quiz 297. <http://dx.doi.org/10.1111/j.1834-7819.2008.00049.x>.