

<p>Institution: University of Bristol</p>
<p>Unit of Assessment: 3</p>
<p>Title of case study: Millions of people worldwide, and leading companies, benefit from novel approach to developing and evaluating products designed to protect against tooth-wear and dentine hypersensitivity.</p>
<p>1. Summary of the impact (indicative maximum 100 words) Dentine hypersensitivity manifests as daily, transient, arresting tooth pain in 40% of adults. Pain is caused by toothbrush abrasion and dietary acid erosion, which combine to wear teeth, expose dentine and open dentine tubules.</p> <p>For 20 years, Bristol's Dental Clinical Trials Unit has worked in partnership with industrial sponsors to develop a dental model to evaluate products designed to protect teeth from erosion and abrasion, and to test whether new toothpastes block dentine tubules, thereby reducing pain from sensitive teeth. This model is used by researchers worldwide and is the "gold standard". New toothpastes launched by GSK, Colgate, Unilever and P&G between 2008 and 2013, tested with the dental model, demonstrably reduce dentine hypersensitivity. These toothpastes are sold in advanced and emerging markets in over 100 countries, with sales of £5bn in 2012.</p>
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>The Bristol Dental Clinical Trials Unit (CTU) developed the intra-oral appliance model [1] initially to investigate the aetiological factors of dentine hypersensitivity (DH), abrasion and erosion on human tooth samples retained in the mouth. The model enabled the development of low-erosive, low-abrasive products to protect teeth and the evaluation of toothpastes for their acid-resistant occlusion ability to treat DH and reduce pain. DH's global prevalence is growing as more people retain healthy teeth for life and increasingly consume "healthy" yet erosive diets, eliciting frequent DH episodes as tooth-wear opens dentine tubules. A partnership was formed between the CTU and industry to address this issue using the Bristol model.</p> <p>In 1994, pioneering CTU research led by Professor Addy (1994-2007) and supported by Dr West (Lecturer, 1994-2004; Senior Lecturer 2004-2009) developed the intra-oral appliance model allowing human tooth samples to be retained in volunteers' mouths. The model permits samples to be tested clinically rather than in the laboratory [1]. Historically, laboratory testing produced indicative results but could not replicate the mouth's complex intra-oral environment. This was a major obstacle to assessing product effectiveness.</p> <p>The original upper appliance [1] proved it was possible to differentiate degrees of tooth erosion from acidic drinks, leading to the development and marketing of Ribena ToothKind [2] between 1994 and 2000, demonstrating the model's reproducibility [7]. This was the first acidic drink proven to have reduced erosive potential compared to marketed competitors [2]. A series of clinical studies followed, improving the stability and taste of the drink by varying calcium and phosphate, whilst maintaining low erosive properties. The methodology was audited independently, with the product gaining British Dental Association approval. Proof of concept of the model was achieved. Following the development of Ribena ToothKind, carbonated and sports drinks were modified and evaluated in the model, with positive results. Erosion of deciduous teeth was compared to adult teeth, the former being more susceptible. The next step in the strategy (2003-2004 [8]) was to investigate the protective effects of toothpastes against tooth erosion. The results using the model were very positive.</p> <p>Professor West commenced leadership of the CTU in 2007 (Senior Lecturer 2004-2009; Professor 2009-present) with a series of clinical studies (2007-2010 [9]) identifying low-abrasive toothpastes which did not open dentine tubules on application [3] and new pastes which protected teeth from erosive dietary challenge [4]. The appliance was improved, allowing multiple-sample positioning in upper [4] and lower dental [3] appliances. New designs permitted more samples to be retained in the mouth, with removal and replacement at any point in the study for treatment and measurement [3, 4]. This allowed the CTU and sponsors to develop low-abrasive pastes and toothpastes affording erosion resistance to teeth.</p>

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A further research programme led by Professor West using the dental model in clinical studies (2009-2012 [10]), developed and confirmed new desensitising toothpastes which blocked open dentine tubules more effectively than control toothpastes [5]. Following the success of toothpaste occlusion technologies using the dental model [5], these desensitising toothpaste products were subsequently evaluated in randomised control trials and gave immediate and prolonged pain relief from DH [6].

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

- [1] West, N., Maxwell, A., Hughes, J., Parker, D., Newcombe, R. & Addy, M. (1998) 'A method to measure clinical erosion: the effect of orange juice consumption on erosion of enamel', *Journal of Dentistry*, 26 (4): 329-335. [http://dx.doi.org/10.1016/S0300-5712\(97\)00025-0](http://dx.doi.org/10.1016/S0300-5712(97)00025-0)
- [2] Hughes, J., West, N., Parker, D., Newcombe, R. & Addy, M. (1999) 'Development and evaluation of a low erosive blackcurrant juice drink 3. Final drink and concentrate, formulae comparisons in situ and overview of the concept', *Journal of Dentistry*, 27 (5): 345-350.* [http://dx.doi.org/10.1016/S0300-5712\(98\)00068-2](http://dx.doi.org/10.1016/S0300-5712(98)00068-2).
- [3] Macdonald, E., North, A., Maggio, B., Sufi, F., Mason, S., Moore, C., Addy, M. & West, N. (2010) 'Clinical study investigating abrasive effects of three toothpastes and water in an in situ model', *Journal of Dentistry*, 38 (6): 509-516. <http://dx.doi.org/10.1016/j.jdent.2010.03.007>.
- [4] Hooper, S., Newcombe, R., Faller, R., Eversole, S., Addy, M. & West, N. (2007) 'The protective effects of toothpaste against erosion by orange juice: Studies in situ and in vitro', *Journal of Dentistry*, 35 (6): 476-481.* <http://dx.doi.org/10.1016/j.jdent.2007.01.003> Listed in REF2
- [5] Seong, J., Macdonald, E., Newcombe, R., Davies, M., Jones, S., Johnson, S. & West, N. (2013) 'In situ randomised trial to investigate the occluding properties of two desensitising toothpastes on dentine after subsequent acid challenge', *Clinical Oral Investigations*, 17 (1): 195-203.* <http://dx.doi.org/10.1007/s00784-012-0683-7>.
- [6] West, N., Newcombe, R., Hughes, N., Mason, S., Maggio, B., Sufi, F. & Claydon, N. (2013) 'A 3-day randomised clinical study investigating the efficacy of two toothpastes, designed to occlude dentine tubules, for the treatment of dentine hypersensitivity', *Journal of Dentistry*, 41 (2): 187-194. <http://dx.doi.org/10.1016/j.jdent.2012.11.007> Listed in REF2

GRANTS

- [7] Addy and West (1996-1999) *Erosion by soft acidic drinks programme*, GlaxoSmithKline, £231,500.
- [8] Addy and West (2003) *Protective effects of toothpaste on tooth erosion*, Procter & Gamble, £67,000.
- [9] West and Addy (2005-2009) *Protective effects of toothpaste on teeth exposed to toothwear*, GlaxoSmithKline, £842,377.
- [10] West (2009-2012) *Occlusion of dentine tubules programme*, GlaxoSmithKline, £909,020.

4. Details of the impact (indicative maximum 750 words)**Link between research and impact**

The CTU model was the first intra-oral model to measure tooth-wear [1], with development and refinement [2, 3, 4, 5] revolutionising research methodologies on reduction of tooth-wear, and the first to measure intra-oral tubule occlusion. In 2010, world dental leaders were invited to a DH symposium in Geneva, with the consensus being that in situ erosion models with an intra-oral acidic challenge are the ideal [a]. Unilever commented that "the CTU developed an intra-oral appliance retaining human tooth tissue which was a breakthrough novel technology in this area" [b].

This research has enabled new desensitising toothpastes with proven efficacy in DH pain reduction to be licensed. GlaxoSmithKline (Rapid Relief, Repair and Protect, Pronamel) [c], Procter and Gamble (Oral B Pro Expert/Health) [d] and Colgate Palmolive (Pro Relief) launched products between 2008 and 2012, having tested toothpastes using the intra-oral model. The Bristol methodology has helped to protect teeth from tooth-wear and reduce pain from DH worldwide.

Nature and extent of the impact

Since the introduction of the model [1], it has been employed by many research groups worldwide

Impact case study (REF3b)

[e, f] and has had a huge impact on the evaluation of products for tooth-wear and tubule occlusion. The model permits products that are effective in the laboratory to be tested in real-world conditions to determine whether the theoretical results translate into real effects. Best-practice product-testing now consists of laboratory testing, clinical testing using the model and randomised control trial human pain studies, correlating methodologies to strengthen the significance of the observed results [5, 6].

Photographs of teeth showing occluded dentine tubules, taken following research using the model, feature in promotional and educational guidance for the public and dental professionals, as well as in sponsor' in-house training. Television advertisements use graphics illustrating occluded tubules to explain the physical effect of the toothpastes and pain reduction. The sponsor companies use this literature worldwide.

Professor West was invited to speak at 22 international symposia on DH between 2007 and 2013 for GSK (18 symposia [c]), P&G and Colgate-Palmolive and is on advisory groups for GSK [c] and P&G. She was a keynote speaker at the launch of desensitising toothpastes developed using the CTU intra-oral model for Repair and Protect and Rapid Relief (GSK), Pro-Relief (Colgate) and Oral B Pro Expert (P&G).

Industrial development benefits of the impact

Researchers now have the ability to develop products quickly and test them in a reliable and consistent way to show dentine tubule occlusion. The model has been adopted globally and used by sponsors such as GSK [c], P&G [d], Colgate and Unilever [b] at international research sites. GSK comments that "following this methodological development and understanding, the Bristol Clinical Trials Unit intra-oral appliance for in situ clinical trials, is now routinely used to assess the ability of toothpastes to block open dentine tubules" [c]. Professor West has been influential in changing industrial practice in product development, resulting in the recent successful launch and high global sales of desensitising toothpastes, affecting millions of people worldwide [b, c, d, g, h, i]. In Europe, over 40% of the population experience tooth-wear and DH [j]. These new toothpastes address this problem.

Commercial benefits of the impact to industry

Research on DH using the model, has underpinned science-led global marketing with high sales of Sensodyne toothpastes for GSK (Rapid Relief, Pronamel and Repair and Protect) to relieve DH pain [c]. GSK desensitising toothpastes are available in over 100 countries with a turnover in 2011/2012 of £1.7bn, making relief from sensitive teeth available to a global population [c, g, h]. GSK has recently relaunched Ribena ToothKind as Ribena Light, with low-erosive drinks sales worth £1bn in 2011. Sensodyne Rapid Relief was launched in 2010 and Sensodyne Repair & Protect in 2011. The latter has attracted almost 2.3m households and is worth £15.7m of the UK sensitive-toothpaste market [h]. It achieved a 4% share of the total toothpaste market and became the number one selling toothpaste in the first 16 weeks of sales [h]. Sensodyne product sales rose by 16% in 2011 and 13% in 2012, with strong growth in emerging markets such as Africa, China and India. Similarly, Lucozade and Ribena sales were up by 10% in 2011 [g]. In 2012, Sensodyne Repair and Protect became GSK's first billion-dollar brand [g]. Repair & Protect was awarded Product of The Year for 2013. Product of the Year is the world's largest independent, consumer-voted award for product innovation [h].

Similarly, the CTU's work with P&G (2007-2010) led to the marketing of an occluding product, Oral B Pro Expert/Health – a desensitising paste with the ability to protect tooth tissue from erosive acid challenge and block dentine tubules [d, i]. P&G have the second-leading brand in desensitising toothpaste, with a 20% share of the market, again benefiting millions of people worldwide [d,i].

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

- [a] Shellis RP, ed. *Methodology and Models in Erosion Research Workshop*, Zürich, April 2010. Caries Research 2011; Supplement Issue: Vol. 45, Supplement 1. 45-46.
<http://content.karger.com/ProdukteDB/produkte.asp?Aktion=Ausgabe&Ausgabe=255064&ProduktNr=224219>. *Caries Res* 2011;45(suppl 1):45–46 (DOI:10.1159/000325971)
This Supplement contains review articles reporting the consensus of the 2010 Dental Erosion methodology workshop, confirming the intra-oral appliance described in this impact statement

with intra-orally challenge, as the best way to assess tooth wear. Pages 45-46.

- [b] Letter of support from Unilever, Global Clinical Leader Oral Care, Unilever R&D, Bebington, Wirral, UK. *This letter confirms the successful use of the model by Unilever in collaboration with Professor West's research group to develop toothpastes that protect against tooth wear and reduce the pain of dentine hypersensitivity, with global market sales.*
- [c] Letter of support from GSK, Medical Director Consumer Health Care, Weybridge, Surrey, UK. *This letter confirms the successful use of the model by GSK in collaboration with Professor West's research group to develop toothpastes and provides examples of these, together with an overview of their global market sales. It also confirms that Professor West is an international researcher in toothwear and dentine hypersensitivity frequently speaking in the international forum and advising GSK in advisory groups.*
- [d] Letter of support from P&G, Clinical Director, P&G, Oral Care Clinical Operation, P&G, Mason Business Centre, 8700 Mason-Montgomery Rd, Mason, OH 45040, USA. *This letter confirms that P&G has collaborated with Professor West and used the intra-oral model to successfully develop toothpastes that protect against tooth wear. Examples of toothpastes developed using this model, and sales figures for these are provided.*
- [e] Olley, R., Pilecki, P., Hughes, N., Jeffery, P., Austin, R., Moazzez, R., Bartlett, D (2012). An in situ study investigating dentine tubule occlusion of dentifrices following acid challenge. *Journal of Dentistry* 40 (7): 585–593. <http://dx.doi.org/10.1016/j.jdent.2012.03.008> *This article published by an independent UK group supports the use of the Bristol intra-oral appliance for dentine hypersensitivity research by other research groups.*
- [f] Schlueter, N., Klimek, J. & Ganss, C.(2009) 'Efficacy of an Experimental Tin-F-Containing Solution in Erosive Tissue Loss in Enamel and Dentine in situ', *Caries Research*, 43 (6): 415-421. <http://www.karger.com/Article/FullText/252974> *This article published by an independent group based in Germany supports the use of the Bristol intra-oral appliance for tooth wear research by other research groups.*
- [g] GlaxoSmithKline Annual Reports 2011, 2012. <http://www.gsk.com/content/dam/gsk/globals/documents/pdf/GSK-Annual-Report-2011.pdf> (pp 24,55,68) <http://www.gsk.com/content/dam/gsk/globals/documents/pdf/GSK-Annual-Report-2012.pdf> (pp 12,27,39). *These reports demonstrate growing toothpaste sales in Oral Healthcare, and identify the Sensodyne Sensitivity Toothpaste range developed using the model, performing strongly, driven by the launch of Sensodyne Repair & Protect. See brochure pages 24, 55, 68 and 12, 27, 39 of the 2011 and 2012 reports, respectively.*
- [h] Sensodyne announces toothpaste 'Product of the Year 2013' winner. <http://www.talkingretail.com/products/product-news/sensodyne-announces-toothpaste-product-of-the-year-2013-win> *This article gives sales figures for Sensodyne Repair & Protect, developed using the model, and reports that it won Product of the Year, the world's largest independent consumer voted award for product innovation 2013.*
- [i] P&G Annual Report 2012. *This report demonstrates P&G are number two in global market share position in Oral Healthcare, and identify increase in sales in 2012 with expansion of the Oral B Pro Expert/Health sensitivity toothpaste range developed using the model. See brochure pages 27 and 35.*
- [j] West, N., Sanz, M., Lussi, A., Bartlett, D., Bouchard, P. & Bourgeois, D. (2013) 'Prevalence of dentine hypersensitivity and study of associated factors: a European population-based cross-sectional study'. *Journal of Dentistry* 41(10):841-851. <http://dx.doi.org/10.1016/j.jdent.2013.07.017>. *This article demonstrates a high incidence of dentine hypersensitivity in young European adults, over 40%, supporting the need for the development of toothpastes that are better at reducing toothwear and pain from sensitive teeth. The intra-oral model will continue to provide impact as it is used in studies to test the efficacy of such toothpastes.*