

**Impact case study (REF3b)**

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| <b>Institution:</b> King's College London   |
| <b>Unit of Assessment:</b> UoA3 - Dental  |
| <b>Title of case study:</b> Oral Disease Severity Scoring Systems: a reliable objective assessment for monitoring and improving patient care  |
| <p><b>1. Summary of the impact</b></p> <p>Researchers from King's College London (KCL) designed and trialled a series of Oral Mucosal Disease Severity Scoring Systems (ODSS) that are now used routinely in clinical assessment of both serious and common oral diseases. They have changed clinical practice and significantly improved patient care and quality of life. For example, using ODSS has changed the first line treatment for orofacial granulomatosis from drugs to diet control, optimising treatment and definition of disease phenotypes. ODSS has achieved national and international impacts by providing objective evidence for the efficacy of treatments and is now incorporated into international guidelines of good practice and core training for oral medicine specialists.</p>  |
| <p><b>2. Underpinning research</b></p> <p>Oral inflammatory diseases can be painful, even life-threatening, and are frequently associated with concomitant disease in extraoral sites. Previously treatment was hampered by lack of objective measures of disease severity. Research at King's College London (KCL) defined a series of oral disease severity scoring systems (ODSS) for specific conditions that provide quantitative and reproducible measures of disease. Since both oral and extraoral sites are present in many diseases, multiple disciplines collaborated in the research, engaging the Departments of Oral Medicine, Dermatology, Rheumatology and Gastroenterology at KCL and Guy's and St Thomas' NHS Foundation Trust (GSTT). Led by Prof Stephen Challacombe (1989-present, Professor of Oral Medicine), the team engaged Dr Jane Setterfield (2001-present, Reader in Dermatology in Relation to Oral Disease), Dr Michael Escudier (1993-present, Senior Lecturer in Oral Medicine /Honorary Consultant), Dr Richard Cook (2004-present, Senior Lecturer/ Honorary Consultant) and Dr Penelope Shirlaw (Consultant in Oral Medicine, GSTT 2003-present).</p> <p><b>Recurrent Aphthous Stomatitis (RAS)</b></p> <p>RAS, characterized by spontaneous emergence of more than two bouts of oral ulcers a year, was the first focus for exploring the feasibility of developing ODSS. Integrating clinical experience and previously published studies, KCL researchers developed a system assigning a numerical score to each of six ulcer characteristics: size, number, duration, ulcer-free period, pain and mucosal site. Different sites (14 in total) in the oral cavity were grouped as non-keratinised (7 sites, score of 1 for each site) and keratinised or specialised (7 sites, score of 2 for each site). Scoring sites in this manner contributed to distinguishing major and minor RAS subtypes. Scores for each characteristic were allocated a maximum value that allowed for identification of a more serious condition but did not give undue weight to any single value in the overall score. For initial validation of the system, 20 RAS patients were assessed and scored blindly by two different clinicians. The system was then further validated by assessing another 223 RAS patients. While used clinically for a number of years, the work on this ODSS and the scoring system was published in 2013 (Tappuni AR, et al. 2013).</p> <p><b>Mucous Membrane Pemphigoid (MMP) and More</b></p> <p>Based on the RAS success, a similar approach focused on scoring both oral and extraoral sites of MMP, an autoimmune blistering disease frequently associated with scarring of involved sites, demonstrating that more severe MMP is associated with dual circulating IgG and IgA autoantibodies (Setterfield J, et al. Br J Dermatol, 1998). Subsequently the oral component of the scoring system was expanded and modified to measure severity of pemphigus vulgaris (a severe blistering disorder of the skin and mucous membranes) and oral lichen planus (a chronic autoimmune disease of the lining of the mouth frequently affecting extraoral sites including hair, skin, nails and genitalia). Disease severity was scored at each of 17 sites in the oral cavity on the basis of site score (0-2, absence or extent of lesions) coupled with an activity score (0-3, ranging from no lesion to ulceration). As before, scoring was validated in multidisciplinary clinic patients (Escudier M, et al. 2007). The scoring system was further modified to assess disease severity in orofacial granulomatosis (a rare chronic inflammatory disease presenting with sometimes severe</p> |

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and disfiguring lip swelling) by scoring of additional sites (for a total of 20 sites) with scores for lip swelling (White A, et al. 2006).

Oral dryness (hyposalivation) can significantly affect nutrition and psychological well-being and lead to tooth decay and other oral infections. In collaboration with Professor Gordon Proctor (1985-present, Professor of Salivary Biology), saliva flow and mucosal wetness at four sites in the oral cavity were measured in 100 patients with oral dryness and in 50 healthy subjects (Osailan S, et al. 2011). These measurements were correlated with a series of signs – including frothy saliva, a mirror sticking to the tongue and/or buccal mucosa, loss of tongue papillae and active or recently restored cervical caries – that can be easily applied in the clinic to produce a clinical oral dryness score. Each feature scores 1 with a high total score indicating increased oral dryness severity. Reproducibility of the scale was demonstrated by close agreement of scores from 20 patients with oral dryness determined independently by three clinicians (Osailan S, et al. 2012).

### 3. References to the research

Escudier M, Ahmed N, Shirlaw P, Setterfield J, Tappuni A, Black MM, Challacombe SJ. A scoring system for mucosal disease severity with special reference to oral lichen planus. *Br J Dermatol* 2007;157(4):765-70. Doi: 10.1111/j.1365-2133.2007.08106.x (16 Scopus citations)

Osailan SM, Pramanik R, Shirodaria S, Challacombe SJ, proctor GB. Investigating the relationship between hyposalivation and mucosal wetness. *Oral Diseases* 2011;17:109-14. Doi: 10.1111/j.1601-0825.2010.01715.x (6 Scopus citations)

Osailan SM, Pramanik R, Shirlaw P, Proctor GB, Challacombe SJ. Clinical assessment of oral dryness: development of a scoring system related to salivary flow and mucosal wetness. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012;114(5):597-603. Doi: 10.1016/j.oooo.2012.05.009 (2 Scopus citations)

Setterfield J, Shirlaw PJ, Kerr-Muir M, Neill S, Bhogal BS, Morgan P, Tilling K, Challacombe SJ, Black MM. Mucous membrane pemphigoid: a dual circulating antibody response with IgG and IgA signifies a more severe and persistent disease. *Br J Dermatol* 1998;138:602-10. Doi: 10.1046/j.1365-2133.1998.02168.x (70 Scopus citations)

Tappuni AR, Kovacevic T, Shirlaw PJ, Challacombe SJ. Clinical assessment of disease severity in recurrent aphthous stomatitis. *J Oral Pathol Med* 2013;42(8):635-41. Doi: 10.1111/jop.12059. (0 Scopus citations: recent publication) (n.b. First author is currently at Queen Mary, University of London having moved there in 2009. The work described in this paper was performed wholly at KCL and completed in 2005.)

White A, Nunes C, Escudier M, Lomer MCE, Barnard K, Shirlaw P, Challacombe SJ, Sanderson JD. Improvement in orofacial granulomatosis on a cinnamon- and benzoate-free diet. *Inflamm Bowel Dis* 2006;12(6):508-14. Doi: 10.1097/00054725-200606000-00011 (29 Scopus citations)

#### Research Funding:

- 2005-9. PIs: Challacombe SJ, Proctor G, Marriot C. Understanding the dry mouth. GlaxoSmithKline, £300,000
- 2008-9. Sanderson J (PI), Challacombe SJ, Spencer J. The difficult problem of oral Crohn's disease: a unique pathological entity in IBD? National Association for Colitis and Crohn's Disease, £ 57,975.
- 2009-10. PI: Setterfield J. Major award to support translational research initiatives. NIHR Biomedical Research Centre for Ophthalmology, £53.483

### 4. Details of the impact

Research at King's College London (KCL) to assign numerical values to clinical signs has led to development of oral disease severity scoring systems (ODSS) that provide objective measures of disease severity for recurrent aphthous stomatitis (RAS), mucous membrane pemphigoid (MMP), pemphigus vulgaris, oral lichen planus (OLP), orofacial granulomatosis (OFG) and oral dryness.

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Routine use of ODSS in clinics has provided quantitative and reproducible measures of disease. In contrast to more descriptive approaches, disease progression can be objectively measured and the efficacy of treatments monitored.

**Scoring Systems in Clinical Use at GSTT:** The RAS scoring system has been used in the multidisciplinary clinic at Guy's and St Thomas' NHS Foundation Trust (GSTT) over the last 10 years and the other scoring systems were quickly adopted as they developed. All of the systems are available for free download by clinicians from the GSTT website (Oral Medicine section) (1). GSTT has also trained a number of UK healthcare professionals in the use of ODSS in their clinical practice including Specialist Registrars in Oral Medicine, Dermatology and Gastroenterology. ODSS training is also incorporated into KCL's MSc in Clinical Dermatology for medical graduates wishing to specialise in dermatology.

**Scoring Systems in Clinical Use in UK:** ODSS have been adopted for use at various UK locations and adapted to suit an even further range of patients. For instance, since 2009, both Birmingham and Midland Eye Centre (2a) and St Paul's Eye Unit at Royal Liverpool University Hospital, have been using an adapted MMP scoring system for ophthalmologists who may encounter this problem (2b). The latter published a comparison of this and other scoring systems that widely cites Escudier M 2007 and Setterfield J 1998. Glasgow Dental Hospital uses a modified form of the OLP scoring system (2c). ODSS are also embedded within the templates of the SALUD package, a comprehensive dental information management system developed in Dublin, Ireland by the company Two-Ten Health. This system is being installed in several Dental Schools and Hospitals in the UK, including KCL and GSTT, as part of the National Programme for IT (2d).

**Scoring Systems in Clinical Use Internationally:** As well as in the UK, SALUD is used in dental schools and hospitals in North America, Europe, Asia and Australia (3a). Since 2011, ODSS have been included in the European Association for Oral Medicine (EAOM) guidelines for good practice and can be downloaded from the EAOM website (members section). Guidelines, written by Setterfield J, cite Escudier M 2007 and Tappuni A 2005 (OLP) as well as Osailan SM 2011 and 2012 (Oral Dryness) (3b). ODSS for OFG is used regularly in Oral Medicine Clinics in the Zagreb University Hospital, Croatia while OLP scoring is used in trials both in Zagreb and in the Copenhagen University Hospital, Denmark(3c)

**Scoring Systems in Clinical Trials:** ODSS have been essential in numerous clinical trials and studies to assess the efficacy of treatments. For instance, the oral dryness score was used in a clinical trial funded by GSK to compare new and established saliva substitutes (4a). The MMP severity scoring system is currently in use in a multicentre international research study coordinated by Moorfields Eye Hospital, 'Autoantigen & genetic determinants of disease in mucous membrane pemphigoid' (4b).

ODSS have additionally been utilised in a number of clinic-based trials investigating treatments for oral inflammatory diseases. For instance, the RAS scoring system was used by The London School of Medicine and Dentistry at Queen Mary University of London to show a significant decrease in severity and pain scores following 3 months of topical steroids (4c, which cites Escudier 2007 and Osailan 2012). In a St John's Institute of Dermatology and Department of Gastroenterology at GSTT clinical study, ODSS were used to demonstrate significant improvement in disease severity following treatment of patients with recalcitrant ulcerative OLP (4d, which cites Escudier 2007). In another study, by the Diabetes and Nutritional Sciences Division at KCL, ODSS were used to show significant improvement in patients with OFG following a low phenolic acid diet (4d, which cites White A, et al. 2006). More nuanced findings on the efficacy of anti-TNF- $\alpha$  treatment were shown with ODSS in a clinical trial at the Department of Gastroenterology at GSTT, where short term improvement was evident in those refractory to other treatments (4f, including White 2006) (4).

**A.S. Pharma Launch of Oral Dryness "Challacombe" Scale:** The Oral Dryness Scale (ODS) has also become part of the company A.S. Pharma's (part of CCMed group) educational and promotional material for their natural, mucin-based saliva substitute known as Saliva Orthana (5a).

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They use and promote the ODS (which they launched as the 'Challacombe Scale' in September 2011) as a means to assess dry mouth and determine treatment plans (5b,c). A.S. Pharma has widely distributed this scale to dental health professionals throughout the UK for adoption in clinical practice. It can be independently downloaded from their dedicated website. A Portuguese version of the scale is also available for download from the same website (5b). Translation of the scale was requested by Dr Jose Barbarosa Porto, President of the Brazilian Association of Dentistry for publication in the Brazilian Dental Journal. The ODS has been endorsed by the British Society of Dental Hygiene & Therapy as "easy to interpret and understand for the whole dental team" (5d).

### 5. Sources to corroborate the impact

1. Use of ODSS at GSTT
  - Oral medicine disease scoring systems: <http://www.guysandstthomas.nhs.uk/resources/our-services/dental/Disease-scoresheets-public-final230413.pdf>
  - Oral Medicine service: <http://www.guysandstthomas.nhs.uk/our-services/dental/specialties/oral-medicine/specialties.aspx>
2. Use of ODSS at other UK institutions
  - a. Letter confirming use from Queen Elizabeth Hospital and University of Birmingham
  - b. Reeves GMB, et al. Ocular and oral grading of mucous membrane pemphigoid. *Graefes Arch Clin Exp Ophthalmol* 2012;250:611-18. Doi: 10.1007/s00417-011-1853-z
  - c. Letter confirming use from Glasgow Dental Hospital.
  - d. SALUD screen grab shows overview plus OFG, dry mouth and OLP/MMP/PV score sheets
3. Use of ODSS internationally
  - a. SALUD website: [www.twotenhealth.com](http://www.twotenhealth.com)
  - b. Guidelines for OLP and Oral Dryness scoring downloaded from EAOM website
  - c. Letters confirming use from University of Zagreb and Department of Odontology, University of Copenhagen.
4. Use of ODSS in clinical trials to demonstrate efficacy of treatment
  - a. GlaxoSmithKline. 2007-9. Clinical trial comparing a new and established saliva substitute. Research Ethics Committee Reference: 06/Q0704/158. (£130.000) (Tappuni A, Challacombe SJ)
  - b. "Autoantigen & genetic determinants of disease in mucous membrane pemphigoid" funded by BMRC 045 NIHR Biomedical Research Centre for Ophthalmology Major Award to support translational research initiatives and the Special Trustees Moorfields Eye Hospital. Case Report Forms with oral scoring for MMP on page 9.
  - c. Tappuni AR, et al. Clinical assessment of disease severity in recurrent aphthous stomatitis. *J Oral Pathol Med* 2013;doi 10.1111/jop.12059. [Epub 2013 Mar 19]
  - d. Wee JS, et al. Efficacy of mycophenolate mofetil in severe mucocutaneous lichen planus: a retrospective review of 10 patients. *Br J Dermatol* 2012;167(1)36-43. Doi: 10.1111/j.1365-2133.2012.10882.x.
  - e. Campbell HE, et al. Development of a low phenolic diet for the management of orofacial granulomatosis. *J Hum Nutr Diet* 2013;doi:10.1111/jhn.12046.
  - f. Elliott T, et al. Experience with anti-TNF- therapy for orofacial granulomatosis. *J Oral Pathol Med* 2011; 40(1):14-9.
5. Oral Dryness (Challacombe) Scale
  - a. <http://www.aspharma.co.uk/index.htm>
  - b. <http://www.challacombescale.co.uk>
  - c. Dry mouth scale launched. *British Dental Journal* 211, 351 (2011): <http://www.nature.com/bdj/journal/v211/n8/full/sj.bdj.2011.884.html>
  - d. British Society of Dental Hygiene & Therapy endorsement: <http://www.thedentalweb.org/modules.php?name=NewsCentres&article=1&sid=3499>