Institution:
UNIVERSITY OF LIVERPOOL and LIVERPOOL SCHOOL OF TROPICAL MEDICINE

Unit of Assessment:
UA01 – Clinical Medicine

Title of case study:
The Liverpool Diabetic Eye Study has set the Standard for Screening for Sight-Threatening Diabetic Retinopathy in the UK and Europe.

1. Summary of the impact

The University of Liverpool (UoL) has provided pivotal evidence for the introduction and development of national screening programmes for diabetic retinopathy (DR). Technician based screening, which has been introduced since 2008, is now covering over 1.9 million UK people at risk and employing over 1,000 technicians across 96 programmes. Sweden and Scotland have introduced 2 and 3 year screening for patients with no DR based on UoL work on extended screen intervals. The UoL led the revision of the St. Vincent Declaration, the principal policy statement of the WHO on the management of diabetes, and has continued to develop pan European policy and influence national policies in several European countries (including Italy, Germany, Spain).

2. Underpinning research

The Liverpool Diabetic Eye Study is a collaboration at the UoL between Eye and Vision Science (Harding, Broadbent) and Obesity and Endocrinology (Vora) dating back to 1992.

Diabetic retinopathy (DR) is the commonest cause of blindness in the developed world in working age people. The WHO estimates that the prevalence of diabetes mellitus will rise from a current estimate of 170 million to 366 million worldwide by 2030. At any one time 40% will have DR. Treatment for DR is only effective in the early stages before visual impairment occurs.

Between 1993 and 1995 a model of screening for DR was studied in UoL comprising technician based, ambulatory, community based, 3 field retinal photography conducted through dilated pupils and graded using a standardised classification developed for the programme. Sensitivity and specificity for the detection of sight threatening DR (STDR) were shown to be superior to the then standard of direct ophthalmoscopy [1]. Between 1996 and 1999 the prevalence of DR categorised by these developed grades was estimated [2].

Between 1999 and 2004 work expanded to address key evidence gaps in order to develop the argument for establishment of a national DR screening programme. A cost effectiveness study was performed with colleagues from Liverpool John Moores University (James M, Turner DA) which demonstrated good cost effectiveness of the Liverpool model when compared to opportunistic screening [3]. Incidence and prevalence estimates were repeated and rates of progression used to estimate the appropriate time interval between screening episodes depending on levels of risk (duration of diabetes, retinopathy, glycaemic control) [4-6]. Results were obtained from 20,570 screening events in people with type 2 diabetes. For a 95% probability of remaining free of STDR, mean screening intervals by baseline status were: no retinopathy 5.4 years (95% CI 4.7–6.3), background 1.0 years (0.7–1.3), and mild pre-proliferative 0.3 years (0.2–0.5). Similar results were obtained for type 1 diabetes. We recommended that a 3 year screening interval could be safely adopted for patients with no retinopathy.

Since 2008 the UoL DR screening research team led by Harding has expanded to include academics with research expertise in primary care (Gabbay), biostatistics (van der Hoek), sociology (Byrne) and computer science (Fisher), referenced in Section 3, and has continued to influence the national and international research agenda.

Between 1999 and 2003 SP Harding and JP Vora were Honorary Senior Lecturers and DM Broadbent, Honorary Clinical Lecturer. As of 2010 SP Harding is Chair in Clinical Ophthalmology and Head, Department of Eye and Vision Science (DEVS), Institute of Ageing and Chronic Disease. JP Vora is Honorary Professor of Diabetes and Endocrinology and DM Broadbent is Honorary Senior Lecturer, DEVS. All of the research was conducted in the UoL.

3. References to the research

1. **Harding SP**, **Broadbent DM**, Neoh C, White MC, **Vora J**. Sensitivity and specificity of photography and direct ophthalmoscopy in screening for sight threatening eye disease - The

Liverpool Diabetic Eye Study. Br Med J 1995;311:1131-1135. Citations: 158 Impact factor: 17.215 This publication has continued to be regularly cited (average 7.28 per year in last 18 years)
2. **Broadbent DM**, Scott JA, **Vora JP**, **Harding SP**. Prevalence of diabetic eye disease in an inner city population: the Liverpool Diabetic Eye Study. Eye 1999;13:160-165. Citations: 37 Impact factor: 1.818
3. James M, Turner DA, **Broadbent DM**, **Vora J**, **Harding SP**. Cost-effectiveness analysis of screening for sight threatening diabetic eye disease. Br Med J 2000;320:1627-31 DOI: 10.1136/bmj. 320.7250.1627. Citations: 82 Impact factor: 17.215
4. Younis N, **Broadbent DM**, **Harding SP**, **Vora JP**. Prevalence of Diabetic Eye Disease in Patients Entering a Systematic Primary Care Based Eye Screening Programme. Diabetic Med 2002, 19: 1014-21. DOI: 10.1046/j.1464-5491.2002.00854.x. Citations: 27 Impact factor: 3.241
5. Younis N, **Broadbent DM**, **Vora JP**, **Harding SP**. Incidence of sight threatening retinopathy in type 2 diabetes in a systematic screening programme. Lancet 2003;361:195-200. Citations: 111 Impact factor: 39.060 This publication has been cited consistently since publication in 2003 and utilised by national and international research groups in design of clinical studies and setting of guidance.
6. Younis N, **Broadbent DM**, **Harding SP**, **Vora JP**. Incidence of sight-threatening retinopathy in Type 1 diabetes in a systematic screening programme. Diabetic Medicine 2003 20: 758-65. DOI: 10.1046/j.1464-5491.2003.01035.x Citations: 43 Impact factor: 3.421

Interpretation of the research and setting of the agenda in screening for DR was covered in the following policy setting articles and editorials:

7. Owens DR, Gibbins RL, Kohner E, Grimshaw GM, Greenwood R, **Harding SP**. Screening for diabetic retinopathy. Editorial. Diab Med 2000;17:493-494. DOI: 10.1046/j.1464-5491.2000.00333.x
8. **Harding SP**, Greenwood RM, Aldington A, Gibson JM, Owens DR, Taylor R, Kohner E, Scanlon P, Leese GR. Grading and disease management in national screening for diabetic retinopathy in England and Wales. Diabet Med 2003; 20:965-971 DOI: 10.1111/j.1464-5491.2003.01077.x This publication sets out the national screening committee grading classification that has been adopted worldwide.
9. **Harding SP**, Talbot JF, Garvican L. The impact of national diabetic retinopathy screening on ophthalmology: the need for urgent planning. Eye 2005;19:1009-1011.

The quality and importance of this work has been recognised by the award of a NIHR Programme Development Grant (end of grant report available) and a full Programme Grant for Applied Research, with the UoL the leading partner in a programme of research to measure safety and acceptability of extended screen intervals in England based on individualised risk.

- 2010-2011. **NIHR Programme Development Grant**. Acceptability and effectiveness of risk based intervals in screening for diabetic retinopathy – towards a personalised approach, £99k, **Harding SP**, **Gabbay M**, Grey P, James M, Stratton I, **Broadbent DM**, Fisher A, **Vora JP**, Roberts J, **Byrne P**, **Garcia-Finana M**. (RP-DG-0709-10138).
- 2013-2018. **NIHR Programme Development Grant**. Introducing personalised risk based intervals in screening for diabetic retinopathy: development, implementation and assessment of safety, cost-effectiveness and patient experience, **Harding SP**, **Broadbent DM**, **Gabbay M**, Grey P, James M, Stratton I, Fisher AC, **Vora JP**, Roberts J, **Byrne P, Garcia-Finana M, Breen R, Williamson P**. (RP-DG-1210-12016). £1,961,766

4. Details of the impact

The UoL research has directly led to national screening programmes for DR in the UK and overseas which are being increasingly implemented since 2008. The National Screening Committee (Chair J Muir Gray [20]) commissioned reviews and an economic analysis between 1999 and 2001 which references the UoL work and supported the introduction of screening [10-12].The UoL team was heavily involved in the design of the national screening programme which launched in 2006.

After initial pilot work the English programme started roll-out in 2006 gradually expanding over subsequent years to cover the target population nearing full capacity after 2008. Most recent figures from the English Diabetic Eye Screening Programme (DESP) give estimates for 2012-13 that 1.9 million people with diabetes have been screened [17].

Significant impact for these people includes the detection of 100,800 (7.6%) cases of sight threatening maculopathy and 22,800 (1.2%) of sight threatening retinopathy with referral for management in the hospital eye service. Also in 2012-13 an estimated 14,000 (0.74%) people were referred for urgent laser therapy for proliferative retinopathy and between 21,250 and 42,500 for treatment of clinically significant macular oedema. This would not have occurred if the DESP had not been established; as a result these patients received timely and appropriate treatment. The Clinical Director of the Diabetic Eye Screening Programme (England) confirms that, *"The introduction of screening has had a significant impact reducing the risk of visual loss for large numbers of people"* and *"The Liverpool evidence contributed significantly to the case for the establishment of a National Risk Reduction Programme."* [17]

Scotland's DR Screening Programme launched in 2007 and gradually expanded post 2008 to a current annual rate of 240,388; approx. 7,000 of these are referred for assessment/treatment [13,14]. The Director of Scottish Grading Programme said "*At all stages, from the initial SIGN guidelines, the Health Technology Board for Scotland's Health Technology Assessment, to the Scottish Government's Diabetic Retinopathy Screening Services in Scotland implementation report, evidence from the University of Liverpool has played a pivotal role in shaping Scotland's Retinal Screening Programme." and "The Liverpool Diabetic Eye Study, using mobile fundus cameras, played a pivotal role in making the case for retinal screening in Scotland and throughout the United Kingdom*."[18]

The English DESP has provided training and employment for retinal screeners who have been employed specifically to support the DESP. 1,600 technicians have completed the National Level 3 Retinal Screener qualification (DM Broadbent developed course and certificate); 831 were actively studying [17].

Since 2005, UoL research has been used by policy makers from Europe and around the world to set screening models and implement DR services including screening. Dissemination has been through published research and the initiative, "Screening for Diabetic Retinopathy in Europe" (www.drscreening.eu) with international conferences in 2008 [15] and 2011 [16] including WHO, European Commission and International Diabetes Foundation engagement. The Liverpool team (Harding, Broadbent) established this initiative in 2005 producing The Liverpool Declaration which set targets on screening for DR in Europe and shared experience of implementation of evidence based service changes. Nationally identified policy makers from over 20 countries in Europe have joined the initiative. This has proven to be highly influential as the second and subsequent meetings have shown that countries have adopted the screening approaches. National representatives have requested continuation of the initiative.

An example of this is from Sweden where Liverpool's pivotal work extended screen intervals to three years in 2010 for people with no DR reducing the cost of screening and the burden of attendance for an estimated 356,000 people. A past Director of the Swedish Diabetic Retinopathy Screening Programme said, *"In 2009, thanks to the Liverpool work, we found it both safe and cost effective to revise our national guidelines and since then extension of retinal examination intervals from two to three years in type 2 diabetic subjects without retinopathy are recommended since 2010. The recommendation was based on previous estimates of the low risk for progression from no to sight-threatening retinopathy in this particular group in Liverpool (Younis et al. Lancet 2003)."* [19]. For England, this output has triggered debate on the safety of introducing extended screen intervals across the much larger and diverse target population of 3 million people leading to the aforementioned two NIHR grants.

Other examples of the effect of the "Screening for Diabetic Retinopathy in Europe" initiative reported in 2011 [11] include10% decrease in the incidence of blindness due to DR in the Czech Republic; a significant improvement in vision loss in Iceland; Denmark, The Netherlands and Spain introduced national screening programmes; Poland and Romania have patchy screening which is slowly widening; Greece and Portugal have introduced local screening programmes; Italy saw a big improvement in the quality of DR diagnosis and treatment; Albania has used the initiative to

improve access to lasers. In 2012 Eire introduced a national screening programme [21].

UoL work [3-6,8] has been widely referred to in the 2012 RCOphth Guidelines on Diabetic Retinopathy in statements on disease definitions,[8] epidemiology [4,5,6] and screening [8]. Accessed at http://www.rcophth.ac.uk/page.asp?section=451&sectionTitle=Clinical+Guidelines.

This case study demonstrates major impacts on health and welfare, public policy and services, practitioners and services and international development. The beneficiaries have been the diabetic patients in the UK and elsewhere who have seen a reduction in the rates of visual impairment and laser therapy since the introduction of screening. Without the Liverpool work on cost-effectiveness and methodology the introduction of systematic screening would not have been possible or would have been delayed, nor would the St. Vincent declaration have been revised and implemented internationally. Outcomes for patients and the public health have improved, a new clinical intervention and technology has been developed and adopted with improved disease prevention and detection, and new guidelines have been developed. The NHS has adopted new technology and new jobs have been created. The cost effectiveness and access to a public service have been improved and international agencies and policy have been influenced.

5. Sources to corroborate the impact

Each source listed below provides evidence for the corresponding numbered claim made in section 4 (details of the impact).

10. Garvican, L., et al. Preservation of sight in diabetes: developing a national risk reduction programme." Diabet Med 2000;17:627-634
11. Gillow JT and Gray JA. The National Screening Committee review of diabetic retinopathy screening. Eye 2001;15:1-2
12. James MA, Little R. Diabetic retinopathy. Report to the National Screening Committee. Centre for Health Planning. Keele University. April 2001
13. Facey K, et al. Health Technology Assessment Report 1. Organisation of services for diabetic retinopathy screening. http://www.ndrs.scot.nhs.uk/Links/Docs/hta1.pdf
14. Diabetic Retinopathy Screening Services in Scotland: Recommendations for Implementation http://www.ndrs.scot.nhs.uk/Links/Docs/Recommendations%20for%20Implementing%20DRS.pdf

International Conferences

15. Amsterdam 2008 http://www.drscreening2005.org.uk/amsterdam_2008.html
16. Gdansk 2011 http://www.drscreening2005.org.uk/gdansk_2011.html including links to national guidelines on screening for diabetic retinopathy have been linked to the initiative and are available for Czech Republic, Finland, Hungary, Italy, Norway, Scotland, Spain, and Sweden.

Clinical Health Service Leaders who can corroborate the impact of this case study:

17. Letter: National Diabetic Eye Screening Programme (England)
18. Letter: Scottish Diabetic Retinopathy Screening Programme
19. Letter: Department of Ophthalmology, Skåne University Hospital
20. Contact: National Screening Committee.
21. Contact: Diabetic Retinopathy Screening Programme, Ireland.