Institution: University College London

Unit of Assessment: 1 - Clinical Medicine

Title of case study: Improving vision of patients with angle-closure glaucoma

1. Summary of the impact

Glaucoma is one of the major causes of blindness world-wide and is characterised by visual loss arising from death of retinal ganglion cells. One important form, angle-closure glaucoma, is particularly prevalent in Asia. Based on experience of large-scale epidemiological surveys, UCL researchers devised a classification for angle-closure glaucoma that has become the international standard for this condition. The research been used as the basis for the development of the current framework for the management of angle-closure glaucoma, informing the development of both new and revised guidelines used around the world.

2. Underpinning research (indicative maximum 500 words)

Glaucoma is a progressive blinding condition and one of the most important causes of blindness in the world. Characterised by loss of retinal ganglion cells (which send visual information to the brain), it causes patients to progressively lose areas of visual field. Of the different forms of glaucoma, the most prevalent in Western societies is known as open-angle glaucoma and this has been extensively studied. However, prior to 1995 there were few published data to guide clinical decision-making on angle-closure glaucoma, which makes up only 10% of glaucoma cases in Western societies, and occurs when there is obstruction to drainage of fluid from the front chamber of the eye. Since then, research conducted by Paul Foster at the UCL Institute of Ophthalmology has improved understanding of the epidemiology of glaucoma, has established popular screening techniques for early detection and management of the condition, and has measured the safety and efficacy of preventative treatment for angle-closure glaucoma by laser surgery. This has included extensive population-based research, much of which has been used to identify novel environmental and lifestyle associations with glaucoma.

The first step in finding a solution to a clinical problem is often to define it. A series of epidemiological studies led to the first high-quality reports of glaucoma prevalence and risk factors in Mongolia and Singapore **[1-3]**. Foster also pioneered similar work in China, where he was the first to identify large numbers of angle-close glaucoma sufferers. These studies not only contributed to awareness of the magnitude of the problem of angle-closure glaucoma in Asian populations, but also led to a deeper understanding of its natural history. Ascertaining the mechanism of angle closure (pupillary block, plateau, lens-related, retro-lenticular) is essential for management, and these findings had important implications for clinicians' ability to assess prognosis and describe the need for treatment at different stages of natural history of the disease.

This was followed by a pivotal, highly cited (>700) publication in 2002 **[4]**. Although the research was initially framed to facilitate clinical studies, it also provided the basis for how clinicians consider and manage the condition. The classification system set out in this publication defined three stages of the condition:

(a) primary angle-closure suspect (PACS); patients where there are anatomical risk factors at the front of the eye that could cause obstruction, but **no** evidence of obstruction
(b) primary angle closure (PAC); patients with anatomical risk factors and evidence of obstruction but **no** evidence of glaucoma
(c) primary angle closure glaucoma (PACG); patients with PAC **and** evidence of glaucoma

The acceptance and significance of this classification system in the research domain is indicated by its adoption in about 50% of epidemiological studies since its definition **[5]**. It has also provided the basis for subsequent major clinical trials generating additional 'downstream' impact. For example, UCL researchers determined that laser peripheral iridotomy (the standard first-line intervention for acute and chronic angle closure) reversed the anatomical abnormality that leads to

PACG in around 75% of Chinese patients. It also identified four independent anatomical factors on anterior segment imaging which predicted the probability of a successful outcome of laser iridotomy **[6]**.

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

[1] Foster PJ, Baasanhu J, Alsbirk PH, Munkhbayar D, Uranchimeg D, Johnson GJ. Glaucoma in Mongolia. A population-based survey in Hövsgöl province, northern Mongolia. Arch Ophthalmol. 1996 Oct;114(10):1235-41. http://dx.doi.org/10.1001/archopht.1996.01100140435011

[2] Seah SK, Foster PJ, Chew PT, Jap A, Oen F, Fam HB, Lim AS. Incidence of acute primary angle-closure glaucoma in Singapore. An island-wide survey. Arch Ophthalmol. 1997 Nov;115(11):1436-40. Copy available

[3] Foster PJ, Oen FT, Machin D, Ng TP, Devereux JG, Johnson GJ, Khaw PT, Seah SK. The prevalence of glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the Tanjong Pagar district. Arch Ophthalmol. 2000 Aug;118(8):1105-11. http://dx.doi.org/10.1001/archopht.118.8.1105

[4] Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002 Feb;86(2):238-42. http://dx.doi.org/10.1136/bjo.86.2.238

[5] He M, Foster PJ, Ge J, Huang W, Zheng Y, Friedman DS, Lee PS, Khaw PT. Prevalence and clinical characteristics of glaucoma in adult Chinese: a population-based study in Liwan District, Guangzhou. Invest Ophthalmol Vis Sci. 2006 Jul;47(7):2782-8. Copy available

[6] He M, Friedman DS, Ge J, Huang W, Jin C, Lee PS, Khaw PT, Foster PJ. Laser peripheral iridotomy in primary angle-closure suspects: biometric and gonioscopic outcomes: the Liwan Eye Study. Ophthalmology. 2007 Mar;114(3):494-500. http://dx.doi.org/10.1016/j.ophtha.2006.06.053

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

The underpinning research has improved clinical management of patients with or at risk of developing angle-closure glaucoma. These benefits have arisen primarily through the impacts of the research on global understanding of and guidelines for glaucoma management and, subsequently, on clinical practice in this area.

Glaucoma causes irreversible loss of vision. It ranks second only to cataract as a cause of blindness worldwide, and angle-closure glaucoma accounts for half of all glaucoma blindness. The number of people with glaucoma has been projected to increase by 33% between 2010 and 2020, from 16 million globally in 2010 to an estimated 21 million by 2020 **[a]**. Prevalence of glaucoma increases exponentially with age, making it a significant global public health problem. In England, NHS data show that 7% of all outpatient activity occurs within hospital eye services, and glaucoma accounts for around 25% of all eye outpatient activity.

The research outlined above has made a major contribution to widespread recognition of the scale and significance of angle-closure glaucoma as a global problem, particularly in Asia but also in Europe, where an estimated 1.6 million are currently affected **[b]**. The classification system designed initially for epidemiological studies ([1] above) has now become the international standard classification system for natural history staging of angle-closure glaucoma. In 2006 it was adopted by the World Glaucoma Association as its international classification system, which has resulted in a global impact on understanding and influence on guidelines through the period 2008-13 **[c]**.

Key clinical guidelines in Asia Pacific, Europe and the US have been influenced by the research

described above. Foster was a member of the Working Party that produced the first ever Asia Pacific Glaucoma Guidelines. These draw on his work particularly in their opening section on epidemiology. These guidelines were first published in 2004, and have remained in use throughout the period 2008-13 **[d]**. Foster also advised on production of the 3rd edition of the European Glaucoma Society's Terminology and guidelines for glaucoma, which were published in 2008 **[e]**. These guidelines likewise frequently draw on and directly cite the research outlined above. They are widely distributed to and used by clinicians across Europe. The American Academy of Ophthalmology (AAO) Preferred Practice Patterns (PPP), also make use of the underpinning research described above. The PPP for Primary Angle Closure (published in 2010) makes similarly extensive use of Foster's research, citing [1], [2], [3], and [5] **[f]**. Again, these references appear particularly frequently in the section dealing with epidemiology. PPP documents are published by the AAO as "a service to its members and the public", allowing them to "identify characteristics and components of quality eye care".

The development of these guidelines drawing on the research has had a significant effect on clinical practice and, in turn, has had positive impacts on patient experience, wellbeing and clinical outcomes. More specifically, the new guidelines have catalysed a more proactive approach to the management of angle-closure glaucoma in the UK, especially as a result of increased awareness of its early stages. This direct impact of the research-based change in guidelines on the management of angle-closure glaucoma is evident from Hospital Episodes Statistics (HES) data revealing trends in laser surgery for angle-closure glaucoma between 1998 to 2010. These data show a stable rate of laser iridotomies of 2-3,000 per annum between 1998 and 2003 in the UK. Between 2003 and 2010, however, laser iridotomy rates in the UK have risen almost 3-fold, from 3,093 to 8,669 per year **[g]**. This increase in treatment rates, which reflects findings and recommendations made in the underpinning research (particularly [6]) corresponds with a 45% fall in the rate of acute attacks of angle-closure glaucoma in the UK. Emergency angle-closure glaucoma treatments between 1998 and 2002 averaged 1,242/annum. Between 2007 and 2010, this had fallen to 703/annum.

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

[a] Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020.Br J Ophthalmol. 2006 Mar;90(3):262-7. http://dx.doi.org/10.1136/bjo.2005.081224

[b] Day AC, Baio G, Gazzard G, Bunce C, Azuara-Blanco A, Munoz B, Friedman DS, Foster PJ. The prevalence of primary angle closure glaucoma in European derived populations: a systematic review. Br J Ophthalmol. 2012 Sep;96(9):1162-7. http://dx.doi.org/10.1136/bjophthalmol-2011-301189

[c] Weinreb R, Friedman DS. Angle closure and angle closure glaucoma. Amsterdam: Kugler Publications 2006. http://www.worldglaucoma.org/pages/Consensus/3/3rdconsensus.php

[d] South East Asia Glaucoma Interest Group. Asia Pacific Glaucoma Guidelines. Sydney: SEAGIG; 2004. Available from the SEAGIG website: http://www.apglaucomasociety.org/content/view/21/116/ For references to Foster's work, including [1], [2] and [3], see esp. pp. 6-7. See p. ii for his membership of the working party.

[e] European Glaucoma Society. Terminology and guidelines for glaucoma (third edition). Savona, Italy; 2008. http://www.eugs.org/eng/EGS_guidelines.asp. Contains numerous references to work by Foster, including [4] (see p. 112, *n*. 116) and [6] (p. 164, *n*, 141). See also p. 7 for Foster's inclusion among the guidelines' contributors and reviewers.

[f] American Academy of Ophthalmology Glaucoma Panel. Preferred Practice Pattern® Guidelines. Primary Angle Closure. San Francisco, CA: American Academy of Ophthalmology; 2010. Available at: http://one.aao.org/preferred-practice-pattern/primary-angle-closure-ppp--october-2010. For references to [1] see pp. 6 (*n*.6) and 24 (*n*.8); to [2], p. 23 (*n*. 4); to [3], pp. 6

(*n*.8) and 24 (*n*, 20); and [5] pp. 5 (*n*. 5) and 24 (*n*. 17).

[g] Day AC, Foster PJ. Increases in rates of both laser peripheral iridotomy and phacoemulsification have accompanied a fall in acute angle closure rates in the UK. Br J Ophthalmol. 2011 Sep;95(9):1339-40. http://dx.doi.org/10.1136/bjophthalmol-2011-300255.