Accuracy of glaucoma referrals: need to report precision of estimates

EDITOR,—Referral accuracy is an important measure of primary care effectiveness. It is defined as the proportion of patients referred for a particular condition who are subsequently diagnosed as having that condition (that is, the true positive proportion). Statistically, it estimates the probability that a patient who is referred will have the disease (positive predictive value), as well as all other positive and negative estimates, the value calculated in any sample will be subject to error, the magnitude of which decreases as the sample size increases. In recent years there has been an increase in the number of publications on the accuracy of referrals by optometrists to ophthalmologists. This letter has been prompted by reading some of those concerned with referrals for suspected glaucoma,1,2 but the issue applies generally to estimates of referral accuracy for any disease condition and, indeed, to all measures of screening effectiveness that involve calculation of sample proportions, such as sensitivity, specificity, and so on.

The majority of reports of estimated referral accuracy give no indication of the precision (standard error) of the estimates. Although some reported estimates of accuracy are obtained from relatively large samples of referrals, routinely others are based on samples of 10 patients or less. For example, Dayan et al3 and Newman et al4 each report samples of referred patients (sample sizes 11 and 10 respectively) in which there were all positively diagnosed cases. Using these data to estimate referral accuracy in the population gives 99% confidence intervals of 0 to 38% and 0 to 40% respectively. This means that if one sample of 10 patients shows referral accuracy of zero, then the referral accuracy in 99% of samples drawn from the same population would not necessarily be zero but would be expected to lie between 0 and 40%. Newman et al5, in subdividing their data according to the mode of screening, obtain some accuracy estimates from even smaller samples. They report, for example, that two out of five patients referred on the basis of optic disc and visual field assessment gave a positive diagnosis of glaucoma; referral accuracy of 40%. For this sample the 99% confidence interval ranges from 8 to 83%. Awareness of the lack of precision in small sample estimates of referral accuracy is important for correct clinical interpretation. The comparative effectiveness of different referral strategies or modes of screening should not be judged on the basis of estimates from very small samples. Clinicians should keep in mind that the population values for referral accuracy may in some situations be much higher, or indeed lower, than those observed.

It is therefore recommended that authors should routinely report 95% or 99% confidence intervals (CI) for all measures of diagnostic accuracy. When these measures are simple proportions, as is referral accuracy, the general equation for the confidence interval is CI = p ± z × (s × standard error of proportion). In this equation z is the standard normal deviate; z = 1.96 for a two sided 95% CI, or z = 2.58 for a 99% CI. The common simple formula for the standard error s, of a proportion p is

\[ \text{SE} = \sqrt{\frac{p(1-p)}{n}} \]

where n is the sample size; and the confidence interval is then

\[ \text{CI} = p \pm z \times \text{SE} \]

However a problem with this formula, which is based on a binomial approximation to the normal distribution, is that it can in some circumstances produce confidence limits of less than 0 or greater than 1, when clearly the true population proportion must always lie between 0 and 1. This common approximation should therefore be avoided in favour of exact binomial confidence intervals which are available in many statistical software packages. Although this involves calculation of sample proportions, the latter fact might be the result of failures, which have not been published. Therefore, we would like to communicate our disappointing results. Recently, the intradermal application of OK 432 (Picibanil, Chugai Pharmaceuticals Co, Tokyo, Japan) has been used successfully in the treatment of lymphangiomas in various body sites. Usually, OK 432 is injected in one of the cystic spaces of the tumour, leading to an inflammatory reaction and finally to complete shrinking of the tumour within 4–8 weeks. Encouraged by our own good experiences in the treatment of childhood lymphangiomas of the neck or trunk, we decided to choose this approach in the case of a 22 year old young woman suffering from a histologically proved lymphangioma of the left conjunctiva and anterior orbit. The tumour initially presented in early childhood but did not show significant growth until end of the second decade. One surgical debulking procedure had not led to a satisfactory result. Therefore, we performed two injections of OK 432 within 4 weeks. Though we observed the expected inflammatory reaction and shrinking of the mass, this was not followed by an involution of the tumour. Three months after OK 432 treatment the process of the conjunctival part of the tumour had even increased. A second and now more successful surgical reduction of the mass was necessary. While we have no explanation for the failure of OK 432 in our case, we believe that, though very successful in other localisations, this treatment might be inappropriate in cases of orbital lymphangioma.

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1 Bell RWD, O’Brien C. Accuracy of referral to a glaucoma clinic. Ophthalmol Physiol Opt 1997;17:7–11
2 Brittain GPH, Austin DJ, Kelly SP. A prospective survey to determine sources and diagnostic accuracy of referral. Health Trends 1988;20:1–4
5 Harrison RJ, Wild JM, Hobley AJ. Referral patterns to an ophthalmic outpatient clinic by general practitioners and ophthalmic opticians and the role of these professionals in screening for ocular disease. BMJ 1988;297:1162–7

Topical steroid use in the treatment of ocular alkali burns

EDITOR,—The article by Davis et al1 mentions the use of 10% vitamin C eye drops with a pH 5.5–6.5 and the authors specify potassium ascorbate. Preparing for a future emergency I made vitamin C eye drops in my office by putting ordinary Norwegian vitamin C tablets in 10 ml saline and found the pH to be 3! I then realised that my vitamin C tablets were ascorbic acid or acetate. The ophthalmologist need not prepare homemade vitamin C eye drops in the emergency room. The pharmacist should prepare the eye drops, using either potassium or sodium ascorbate.

ANDERS OETHER
Axtraps Gate 3, Box 776, N-6501Kristiansund, Norway

Reply

EDITOR,—Dr Oether makes two important points with regard to the treatment of ocular alkali burns. We would agree that it is crucial to optimise that topical potassium ascorbate drops are readily available for emergen- cency use. Equally, we would agree that phar- macists, in an appropriately controlled environment,4 should perform the manufacture of these drops.

ALISON DAVIS

Orbital lymphangioma

EDITOR,—Tunç et al published a thorough analysis of the course and management of orbital lymphangiomas. They state that besides careful and sometimes repeated surgery there is little convincing evidence of other promising treatment options: “...few patients have been treated with other modalities including ...scle- rosing agents but there are sparse data with those approaches.”5 The latter fact might be the result of failures, which have not been pub- lished. Therefore, we would like to communi- cate own disappointing results. Recently, the intradermal application of OK 432 (Picibanil, Chugai Pharmaceuticals Co, Tokyo, Japan) has been used successfully in the treatment of lymphangiomas in various body sites.6 Usually, OK 432 is injected in one of the cystic spaces of the tumour, leading to an inflammatory reaction and finally to complete shrinking of the tumour within 4–8 weeks. Encouraged by our own good experiences in the treatment of childhood lymphangiomas of the neck or trunk, we decided to choose this approach in the case of a 22 year old young woman suffering from a histologically proved lymphangioma of the left conjunctiva and anterior orbit. The tumour initially presented in early childhood but did not show significant growth until end of the second decade. One surgical debulking procedure had not led to a satisfactory result. Therefore, we performed two injections of OK 432 within 4 weeks. Though we observed the expected inflammatory reaction and shrinking of the mass, this was not followed by an involution of the tumour. Three months after OK 432 treatment the pro- lapse of the conjunctival part of the tumour had even increased. A second and now more successful surgical reduction of the mass was necessary. While we have no explanation for the failure of OK 432 in our case, we believe that, though very successful in other localisations, this treatment might be inappropriate in cases of orbital lymphangioma.

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MATTHIAS DITTRICH
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Correspondence to: Dr. Pitz
External eye infections
The latest issue of Community Eye Health (no 30) discusses external infections of the eye. Included are papers on conjunctivitis, corneal ulcer, and transmission and control of infection. For further information please contact Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL. (Tel: (+44) 171 608 6908/6910/6923; fax: (+44) 171 250 3207; email: eyeresources@ucl.ac.uk). Annual subscription £25. Free to workers in developing countries.

Residents’ Foreign Exchange Programme
Any resident interested in spending a period of up to six months in departments of ophthalmology in the Netherlands, Finland, Ireland, Germany, Denmark, France, Austria, or Portugal should apply to: Mr Robert Acheson, Secretary of the Foreign Exchange Committee, European Board of Ophthalmology, Institute of Ophthalmology, University College Dublin, 60 Eccles Street, Dublin 7, Ireland.

Joachim Kuhlmann Fellowship for Ophthalmologists 2000
The Joachim Kuhlmann AIDS Foundation, Essen, Germany, is sponsoring two fellowships per year for ophthalmologists at a well known institute, who want to train in CMV retinitis and other HIV related ophthalmological diseases. The fellowships are valued at $US5000 each. Deadlines for applications are 31 January and 31 July. Detaiged applications, including CV and publication list, should be sent to the Joachim Kuhlmann AIDS Foundation, Bismarckstrasse 55, 45128 Essen, Germany (tel: 0201 87910-37; fax: 0201 87910-99; email: jk-stiftung@t-online.de).

16th Congress of the International Society for Geographical and Epidemiological Ophthalmology (ISGEO)
The 16th Congress of the ISGEO will be held at the Institut D’Ophthalmologie Tropicale De L’Afrique (IOTA) in Bamako, Mali on 21–22 February 2000. Further details: Dr Paul Courtright, ISGEO Secretary, BC Centre for Epidemiologic & International Ophthalmology, University of British Columbia, 601 Hospital Drive, Vancouver, BC V6Z 1Y6, Canada (email: pcourtright@spaulshosp.bc.ca; website: www.interchange.ubc.ca/bceio/isgeo/).

Leonhard Klein Foundation
The Leonhard Klein Foundation in the Donors’ Association for the Promotion of Sciences and Humanities in Germany is to bestow the Leonhard Klein Award 2000 of DM 30 000 for innovative work in the development and application of microsurgical instruments and microsurgical operating techniques. Deadline for applications is 31 March 2000. Further details: Stiftverbund fur die Deutsche Wissenschaft e V, Herrn Peter Beck, Postfach 16 44 60, D-45224 Essen, Germany.

American Institute of Ultrasound in Medicine
The American Institute of Ultrasound in Medicine will hold the 44th annual convention in San Francisco, California on 2–5 April 2000. Further details: AIUM Professional Development Department, 14750 Sweitzer Lane, Suite 100, Laurel, MD 20707-5906 (tel: 800-638-5353; fax: 301-498-4100; email: conv_edu@aium.org; website: www.aium.org).

XXII Tuebingen Detachment Course
The XXII Tuebingen Detachment Course, retinal and vitreous surgery, will be held in the congress centre Incheba, Bratislava, Slovak Republic 6–7 April 2000 preceding the congress on retinal detachment of the Slovak Ophthalmological Society 8–9 April 2000. Further details: Professor Peter Strmen 81369 Bratislava, Miczakiewicoza 13 (tel/fax: 00421-7-52964641; email: strmen@faneba.sk).

Vth Mediterranean Ophthalmological Society
The combined meeting of the Vth Mediterranean Ophthalmological Society and the Vth Michaelson Symposium on Ocular Circulation and Neovascularisation will be held in Jerusalem on 21–26 May 2000. Further details: Secretariat, c/o Unitours Israel Ltd, PO Box 3190, 61031 Tel Aviv, Israel (tel: +972-3-5209999; fax: +972-3-5239099; email: meetings@unitours.co.il). The Vth Michaelson medal and award will be delivered on 24 May 2000 in Jerusalem. The medal and award ($15 000 monetary prize) are sponsored by the Israel Academy of Sciences and Humanities and by the Hadassah Hebrew University Hospital and Medical School of Jerusalem, Israel. Nominations are sought from the ophthalmic community at large. Suggestions and reasons for choice and CV highlights should be sent to Professor David Ben-Ezra, Secretary for the International Nominating Committee, Pediatric Ophthalmology Unit, Hadassah Hebrew University Hospital, PO Box 12000, Jerusalem 91120, Israel.

DB-2000, International Forum on Diabetic Retinopathy
The International Forum on Diabetic Retinopathy will take place on 7–9 September 2000 at the Palazzo Reale, Naples, Italy. Further details: Francesco Bandello, Congress Secretary, MGR Congressi, Via Servio Tullio, 4, 20123 Milano, Italy (tel: 39 02 430071; fax: 39 02 48008471; email: dr2000@mgr.it).

12th Afro-Asian Congress of Ophthalmology
The 12th Afro-Asian Congress of Ophthalmology (Official Congress for the Afro-Asian Council of Ophthalmology) will be held on 11–15 November 2000 in Guangzhou (Canton), China. The theme is “Advances of ophthalmology and the 21st century”. Further details: Professor Lezheng Wu, Zhongshan Eye Center, SUMS, New Building, Room 919, 54 Xianlie Nan Road, Guangzhou 510060, PR China (tel: +86-20-8760 2402; fax: +86-20-8777 3370; email: lwuwc@gzsums.edu.cn).