

Diabetic Retinopathy Screening: Progress or Lack of Progress

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Keywords Screening • Diabetic retinopathy • Visual Impairment • Blindness • Diabetes control and complications trial • United Kingdom prospective diabetes study • Early treatment diabetic retinopathy study • St. Vincent Declaration

DEFINITIONS OF SCREENING FOR DIABETIC RETINOPATHY

The definition of screening that was adapted by the WHO [1] in 1968 was “the presumptive identification of unrecognized disease or defect by the application of tests, examinations or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment.”

Applying the principles for screening for human disease that were derived from the public health papers produced by the WHO [1] in 1968 to sight-threatening diabetic retinopathy raises the following questions [2]:

1. Is there evidence that sight-threatening diabetic retinopathy is an important public health problem?
2. Is there evidence that the incidence of sight-threatening diabetic retinopathy is going to remain the same or become an even greater public health problem?
3. Is there evidence that sight-threatening diabetic retinopathy has a recognizable latent or early symptomatic stage?
4. Is there evidence that treatment for sight-threatening diabetic retinopathy is effective and agreed universally?

5. Is a suitable and reliable screening test available, acceptable to both health-care professionals and (more importantly) to the public?
6. Are the costs of screening and effective treatment of sight-threatening diabetic retinopathy balanced economically in relation to total expenditure on health care – including the consequences of leaving the disease untreated?

Is There Evidence That Sight-Threatening Diabetic Retinopathy Is an Important Public Health Problem?

Studies Reporting the Prevalence of Diabetic Retinopathy

Reports from North America have shown that diabetic retinopathy continues to be prevalent in the USA:

1. In 2008–2009, Klein [3] reported the 25-year progression of retinopathy and of macular edema [4] in persons with type 1 diabetes from the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR study). The 25-year cumulative rate of progression of DR was 83%, progression to proliferative DR (PDR) was 42%, and improvement of DR was 18%. The 25-year cumulative incidence was 29% for macular edema and 17% for clinically significant macular edema.
2. In 1995, Klein [5] reported the incidence of macular edema over a 10-year period. This was 20.1% in the younger-onset group, 25.4% in the older-onset group taking insulin, and 13.9% in the older-onset group not taking insulin.
3. In 2004, Kempen [6] reported that, among an estimated 10.2 million US adults 40 years and older known to have DM, the estimated crude prevalence rates for retinopathy and vision-threatening retinopathy were 40.3 and 8.2%, respectively.

Worldwide reports have shown that sight-threatening diabetic retinopathy is prevalent in both type 1 and type 2 diabetes in the UK [7], India [8], Germany [9], Ethiopia [10], Australia [11], Denmark [12], Singapore [13], and China [14].

Reports on Blindness and Visual Impairment

In 1994, Moss [15] reported on the 10-year incidence of blindness in the WESDR study. 1.8, 4.0, and 4.8% in the younger-onset, older-onset taking insulin, and older-onset not taking insulin groups, respectively. Respective 10-year rates of visual impairment were 9.4, 37.2, and 23.9%.

In 1995, Evans [16] reported on the causes of blindness and partial sight in England and Wales from an analysis of all BD8 forms for the year April 1990 to March 1991. Among people of working age (ages 16–64), diabetes was the most important cause (13.8%) with 11.9% due to diabetic retinopathy. This study was repeated 10 years later and reported by Bunce [17] in 2006, and diabetic retinopathy was still the commonest cause of visual loss in the working age group.

In 2001, Cunningham [18] reported that 45 million people worldwide fulfill the World Health Organization's criterion for blindness and the cause of one-quarter of all blindness, which affects people in both developed and developing nations, includes diabetic retinopathy and macular degeneration. In 2002, Kocur [19] reported that in people of working age in Europe, diabetic retinopathy is the most frequently reported causes of serious visual loss.

Zhang [20] reported results from the national health and nutrition examination survey in the USA. People with diabetes were more likely to have uncorrectable VI than those without diabetes.

Is There Evidence That the Incidence of Sight-Threatening Diabetic Retinopathy Is Going to Remain the Same or Become an Even Greater Public Health Problem?

Numerous studies have shown that there is a rising incidence of diabetes and its complications in all age groups, both in the UK and worldwide.

In 1997, Amos [21] estimated that 124 million people worldwide have diabetes, 97% NIDDM, and that by 2010, the total number with diabetes is projected to reach 221 million.

In 2000, Sorensen [22] reported that the World Health Organization has recognized that there is a “global epidemic of obesity,” and the prevalence of type 2 diabetes is rising in parallel.

In 2001, Boyle [23] estimated the number of Americans with diagnosed diabetes is projected to increase from prevalence of 4.0% in 2000 to a prevalence of 7.2% in 2050.

The International Diabetes Federation estimated the prevalence of diabetes in 2003 in 20–79 age groups and projected this to an estimate in 2025. They predicted rises in numbers of people with diabetes of 7.07–15.04 million in Africa, of 19.24–39.41 million in Eastern Mediterranean and Middle East Region, of 48.38–58.64 million in Europe, of 23.02–36.18 million in America, of 14.16–26.16 million in South and Central American Region, of 39.3–81.57 million in Southeast Asian Region, and of 43.02–75.76 million in Western Pacific Region.

Is There Evidence That Sight-Threatening Diabetic Retinopathy Has a Recognizable Latent or Early Symptomatic Stage?

Numerous reports from the Wisconsin Epidemiological Study [24, 25] have shown that sight-threatening diabetic retinopathy in both type 1 and type 2 diabetes has a recognizable latent or early symptomatic stage. In patients with type 1 diabetes, Klein [3] reported that the 25-year cumulative rate of progression of DR was 83%, progression to PDR was 42%, and improvement of DR was 18%.

The Early Treatment Diabetic Retinopathy [26] documented all the photographic lesions of diabetic retinopathy and the risks of progression of DR relating to those lesions.

The United Kingdom Prospective Diabetes Study [27] documented the incidence and progression of diabetic retinopathy over 6 years from diagnosis of type 2 (non-insulin-dependent) diabetes.

Is There Evidence That Treatment for Sight-Threatening Diabetic Retinopathy Is Effective and Agreed Universally?

The Evidence That Diabetic Retinopathy Can Be Prevented or the Rate of Deterioration Reduced by Improved Control of Blood Glucose, Blood Pressure and Lipid Levels, and by Giving Up Smoking

Evidence for the link between poor glucose control and greater progression of diabetic retinopathy (DR) was provided by numerous early studies [28, 29]. The study that

confirmed that intensive blood glucose control reduces the risk of new-onset DR and slows the progression of existing DR for patients with IDDM was the Diabetes Control and Complications Trial (DCCT) [30].

Similarly, for type 2 diabetes, the United Kingdom Prospective Diabetes Study (UKPDS) [31] demonstrated that intensive blood glucose control reduces the risk of new-onset DR and slows the progression of existing DR for patients with type 2 diabetes.

Control of systemic hypertension has been shown [32, 33] to reduce the risk of new-onset DR and slow the progression of existing DR.

There is evidence [34, 35] that elevated serum lipids are associated with macular exudates and moderate visual loss, and partial regression of hard exudates may be possible by reducing elevated lipid levels.

There is some evidence that smoking may be a risk factor in progression of diabetic retinopathy in type 1 diabetes as described by Muhlhauser [36] and Karamanos [37]. However, in type 2 diabetes, the evidence is controversial [27].

The Evidence that Laser Treatment Is Effective

Evidence for the efficacy of laser treatment for diabetic eye disease has been shown from the Diabetic Retinopathy Study [38] and the Early Treatment Diabetic Retinopathy Study [39]. In 1976, the organizers of the Diabetic Retinopathy Study [40] modified the trial protocol and recommend treatment for control eyes with “high-risk characteristics.” In 1981, they reported [41] that photocoagulation, as used in the study, reduced the 2-year risk of severe visual loss by 50% or more.

In 1985, a report [42] from the Early Treatment Diabetic Retinopathy Study showed that focal photocoagulation of “clinically significant” diabetic macular edema (CSMO) substantially reduced the risk of visual loss.

Further studies that have shown evidence for the longer-term efficacy of laser treatment for diabetic eye disease have been reported by Blankenship [43] and Chew [44].

The Evidence That Vitrectomy for More Advanced Disease Is Effective

Smiddy [45], he noted that, according to the Early Treatment Diabetic Retinopathy Study, at least 5% of eyes receiving optimal medical treatment will still have progressive retinopathy that requires laser treatment and pars plana vitrectomy. He also noted that, although vitrectomy improves the prognosis for a favorable visual outcome, preventive measures, such as improved control of glucose levels and timely application of pan retinal photocoagulation, are equally important in the management.

There have been reports of improving visual results during the last 20 years following vitrectomy, the most recent being from Yorston [46].

Is a Suitable and Reliable Screening Test Available, Acceptable to Both Health-Care Professionals and (More Importantly) to the Public?

There is an increasing acceptance that, in population-based screening programs, digital photography offers the best method of screening for sight-threatening diabetic retinopathy. Digital photography has been shown to provide higher sensitivities and specificities across large numbers of operators than examination techniques such as direct ophthalmoscopy [47, 48], or slit lamp biomicroscopy [49, 50]. Digital photography also

has the advantage that a percentage of images can be reexamined for quality assurance purposes.

The acceptance of digital photography for population-based screening does not imply that this replaces the comprehensive eye examination as pointed out by Chew [51].

In screening studies, far more controversial than the use of digital photography has been the use of mydriasis or nonmydriasis and the number of fields photographed.

There have been strong proponents [52] of nonmydriatic photography for many years. However, it has been recognized in more recent years that ungradable image rates for nonmydriatic digital photography in a predominantly white Caucasian population [53, 54] are of the order of 19–26%. Scotland has developed a national screening program based on one-field nonmydriatic photography following a report [55] from the Health Technology Board for Scotland. Other proponents of nonmydriatic digital photography have attempted to capture three-fields [56], five-fields [57], and remarkably Shiba [58] excluded the over 70 years age group and attempted 9× overlapping nonmydriatic 45° fields.

Mydriatic digital photography studies [49, 53] have shown that consistently good results can be achieved, with sensitivities of >80% and high levels of specificity. In these studies, specificity does vary depending on whether ungradable images are regarded as test positive, but levels of >85% are consistently achieved. England has developed a national screening program [7] based on two-field mydriatic photography.

In 2004, Williams produced a report [59] for the American Academy of Ophthalmology summarizing the use of single-field fundus photography for diabetic retinopathy screening.

In 2007–2008, reports of diabetic retinopathy screening were published from France [60], Spain [61], the Canary Islands [62], Western Cape [63], the USA [64], and England [7].

The debate over whether mydriasis should be used for screening and the number of fields used has continued around the world with two of the recent studies coming to very different conclusions [60, 61].

Are the Costs of Screening and Effective Treatment of Sight-Threatening Diabetic Retinopathy Balanced Economically in Relation to Total Expenditure on Health Care – Including the Consequences of Leaving the Disease Untreated?

In 1982, Savolainen [65] reported on the cost-effectiveness of photocoagulation for sight-threatening diabetic retinopathy in the UK. There have been reports of computer simulation models of diabetic retinopathy screening by Javitt [66, 67], Dasbach [68], Caro [69], and Fendrick [70], based on the health systems in the USA and Sweden, that concluded that screening for sight-threatening diabetic retinopathy was cost-effective.

James et al [71]. reported results for an organized screening program in the UK using 35-mm retinal photography and demonstrated this to be more cost-effective than the previous system of opportunistic screening.

Meads [72] reviewed published studies of the costs of blindness and compared Fould's 1983 estimate [73] inflated to £7,433 in 2002 costs, Dasbach's 1991 estimate [68] inflated to £5,391 in 2002 costs, and Wright's 2000 estimate [74] inflated to £7,452 (4,070–£11,250) in 2002 costs. He concluded that much of the uncertainty in any

sensitivity analysis of the cost of blindness in older people is associated with the cost of residential care and that the excess admission to care homes caused by poor vision is impossible to quantify at the present time.

Only four studies have been published that assess the costs of screening using digital photography. The first was from a telemedicine program in Norway [75] where, at higher workloads, telemedicine was cheaper. The second compared an optometry model with a digital photographic model in the UK [76]. However, in this study, there were poor compliance rates in the newly introduced screening program in both models. A cost-effectiveness analysis [77] of use of a telemedicine screening program in a prison population in Texas concluded that teleophthalmology holds great promise to reduce the cost of inmate care and reduce blindness caused by diabetic retinopathy in type 2 diabetic patients. Tung [78] concluded that screening for DR in Chinese with type 2 diabetes is both medically and economically worthwhile and recommended annual screening.

PROGRESS OF LACK OF PROGRESS IN SCREENING FOR DIABETIC RETINOPATHY IN DIFFERENT PARTS OF THE WORLD

In 1990, the St. Vincent Declaration [79] recognized diabetes and diabetic retinopathy to be a major and growing European health problem, a problem at all ages and in all countries. The first of the five-year targets that were unanimously agreed by government health departments and patient's organizations from all European countries was to reduce new blindness due to diabetes by one-third or more. In 2005 in Liverpool UK, a conference took place to review progress in the prevention of visual impairment due to diabetic retinopathy since the publication of the St. Vincent Declaration. Delegates attended as representatives from 29 European countries, and there were invited experts from Europe and the US. It was clear from this meeting that the health-care systems in Europe were at very different stages of development, and the funding of those health-care systems varied considerably. For example, if the population did not have access to adequate treatment facilities, there was little point in concentrating on screening for diabetic retinopathy until adequate treatment facilities were established.

Hence, the conference recommended the following steps in the development of systematic screening programs for sight-threatening DR:

Step 1

Access to effective treatment

- Minimum number of lasers per 100,000 population
- Equal access for all patient groups
- Maximum time to treatment from diagnosis, 3 months

Step 2

Establish opportunistic screening

- Dilated funduscopy at time of attendance for routine care
- Annual review
- National guidelines on referral to an ophthalmologist

Step 3

Establish systematic screening

- Establish and maintain disease registers
- Systematic call and recall for all people with diabetes
- Annual screening
- Test used has sensitivity of $\geq 80\%$ and specificity of $\geq 90\%$
- Coverage $\geq 80\%$

Step 4

Establish systematic screening with full quality assurance and full coverage

- Digital photographic screening
- All personnel involved in screening will be certified as competent
- 100% coverage
- Quality assurance at all stages
- Central/regional data collection for monitoring and measurement of effectiveness

The European countries that were most advanced in development of national screening programs were those that had nationalized health systems that facilitated the development of public health screening programs. Iceland, England, Scotland, Wales, and Northern Ireland had all developed national screening programs, whereas Denmark, Finland, and Sweden had regional programs, all with good coverage. At that time, these countries had an estimated overall prevalence of diabetes in Europe approximating 4%.

The wealthier European countries that had private health-care systems (e.g., Eire, France, Germany, Greece, Israel, Italy, Luxembourg, the Netherlands, Portugal, Spain) had developed local screening programs, many of which are based upon the initiatives of individual persons. However, there was a lack of uniformity between different centers on screening methodology and classification of diabetic retinopathy. More recently, there have been attempts within some of these countries to standardize [80] their screening systems and to develop a framework [81] for the development of a national screening program.

With respect to Eastern Europe (Czech Republic, Turkey, Hungary, Romania, and Serbia and Montenegro), the Czech Republic introduced diabetic retinopathy screening and treatment guidelines published in 2002; Hungary, Romania, and Turkey have local or regional screening programs. Turkey reported that 7.2% of their population was known to have diabetes. Serbia and Montenegro reported that they did not have a formalized screening program, but had taken steps to introduce protocols. In parts of Serbia, there was a lack of available lasers.

Posters were also presented from the following countries—Albania, Bulgaria, Georgia, Kazakhstan, Lithuania, Uzbekistan, and St. Petersburg. Bulgaria has 17 lasers, but there are insufficient in the other countries: Uzbekistan appears to have none and Kazakhstan only one or two. Lasers are available for the “general” population in Lithuania, with one in Albania, one in St. Petersburg, and some in Bulgaria. Other lasers are in private offices.

In Australia, there are local screening programs that have developed to serve individual populations such as the aboriginal [82] population and rural Victoria [83].

Similarly, localized screening programs have developed in the Western Cape [63], India [8], Japan [58], and China [14].

A recent study [84] by Boucher from Canada attempted to increase uptake of diabetic retinopathy screening by locating mobile screening imaging units within pharmacies. This produced further communication within the same journal to which Boucher replied [85], “Despite efforts to educate both patients and physicians about the importance of routine diabetic screening and despite the publication of Canadian screening guidelines, a large percentage of the diabetic population continues to receive inadequate retinopathy screening. This has led to the search for strategies to better detect vision-threatening retinopathy and reduce the incidence of complications and blindness from diabetic retinopathy.”

In America, health-care delivery is chiefly driven by market forces, and the key to any new preventive health program is reimbursement. Provision of medical care is based on private insurance for those who can pay for it and a patchwork of Federal programs for the indigent and the elderly. It is estimated that there are more than 43 million Americans who have no health-care insurance whatsoever.

The Center for Medicare and Medicaid Services (CMS) sets reimbursement standards for Federal programs and also influences private insurers’ reimbursement policies. Currently, CMS does not offer reimbursement for image-based diabetic retinopathy screening, and only a few private insurers do so.

Hence, screening programs in America have usually been developed by enthusiasts such as the Vine Hill program [64] where digital retinal imaging is undertaken in an inner-city primary care clinic, in the Joslin Diabetes Center [56], or in a Veterans Affairs Medical Center [86].

REFERENCES

1. Wilson J, Jungner G. The principles and practice of screening for disease. Public Health Papers 34. Geneva: WHO; 1968.
2. Scanlon P. An evaluation of the effectiveness and cost-effectiveness of screening for diabetic retinopathy by digital imaging photography & technician ophthalmoscopy & the subsequent change in activity, workload and costs of new diabetic ophthalmology referrals. [M.D.]. London; 2005.
3. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: XXII the twenty-five-year progression of retinopathy in persons with type 1 diabetes. *Ophthalmology*. 2008;115(11):1859–68.
4. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy XXIII: the twenty-five-year incidence of macular edema in persons with type 1 diabetes. *Ophthalmology*. 2009;116(3):497–503.
5. Klein R, Klein BE, Moss SE, Cruickshanks KJ. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. XV. The long-term incidence of macular edema. *Ophthalmology*. 1995;102(1):7–16.
6. Kempner JH, O’Colmain BJ, Leske MC, Haffner SM, Klein R, Moss SE, et al. The prevalence of diabetic retinopathy among adults in the United States. *Arch Ophthalmol*. 2004;122(4):552–63.
7. Scanlon PH. The English national screening programme for sight-threatening diabetic retinopathy. *J Med Screen*. 2008;15(1):1–4.
8. Raman R, Rani PK, Reddi Rachepalle S, Gnanamoorthy P, Uthra S, Kumaramanickavel G, et al. Prevalence of diabetic retinopathy in India: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study report 2. *Ophthalmology*. 2009;116(2):311–8.

9. Hesse L, Grusser M, Hoffstadt K, Jorgens V, Hartmann P, Kroll P. Population-based study of diabetic retinopathy in Wolfsburg. *Ophthalmologe*. 2001;98(11):1065–8.
10. Seyoum B, Mengistu Z, Berhanu P, Abdulkadir J, Feleke Y, Worku Y, et al. Retinopathy in patients of Tikur Anbessa Hospital diabetic clinic. *Ethiop Med J*. 2001;39(2):123–31.
11. Tapp RJ, Shaw JE, Harper CA, de Courten MP, Balkau B, McCarty DJ, et al. The prevalence of and factors associated with diabetic retinopathy in the Australian population. *Diabetes Care*. 2003;26(6):1731–7.
12. Knudsen LL, Lervang HH, Lundbye-Christensen S, Gorst-Rasmussen A. The North Jutland County Diabetic Retinopathy Study: population characteristics. *Br J Ophthalmol*. 2006;90(11):1404–9.
13. Wong TY, Cheung N, Tay WT, Wang JJ, Aung T, Saw SM, et al. Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. *Ophthalmology*. 2008;115(11):1869–75.
14. Wang FH, Liang YB, Zhang F, Wang JJ, Wei WB, Tao QS, et al. Prevalence of diabetic retinopathy in rural China: the Handan Eye Study. *Ophthalmology*. 2009;116(3):461–7.
15. Moss SE, Klein R, Klein BE. Ten-year incidence of visual loss in a diabetic population. *Ophthalmology*. 1994;101(6):1061–70.
16. Evans J. Causes of blindness and partial sight in England and Wales 1990–1991. London: OPCS; 1995. p. 1–29.
17. Bunce C, Wormald R. Leading causes of certification for blindness and partial sight in England & Wales. *BMC Public Health*. 2006;6:58.
18. Cunningham Jr ET. World blindness—no end in sight. *Br J Ophthalmol*. 2001;85(3):253.
19. Kocur I, Resnikoff S. Visual impairment and blindness in Europe and their prevention. *Br J Ophthalmol*. 2002;86(7):716–22.
20. Zhang X, Gregg EW, Cheng YJ, Thompson TJ, Geiss LS, Duenas MR, et al. Diabetes mellitus and visual impairment: national health and nutrition examination survey, 1999–2004. *Arch Ophthalmol*. 2008;126(10):1421–7.
21. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med*. 1997;14 Suppl 5:S1–85.
22. Sorensen TI. The changing lifestyle in the world. Body weight and what else? *Diabetes Care*. 2000;23 Suppl 2:B1–4.
23. Boyle JP, Honeycutt AA, Narayan KM, Hoerger TJ, Geiss LS, Chen H, et al. Projection of diabetes burden through 2050: impact of changing demography and disease prevalence in the U.S. *Diabetes Care*. 2001;24(11):1936–40.
24. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. IX. Four-year incidence and progression of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol*. 1989;107(2):237–43.
25. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. X. Four-year incidence and progression of diabetic retinopathy when age at diagnosis is 30 years or more. *Arch Ophthalmol*. 1989;107(2):244–9.
26. Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. *Ophthalmology*. 1991;98(5 Suppl):823–33.
27. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, et al. UKPDS 50: risk factors for incidence and progression of retinopathy in Type II diabetes over 6 years from diagnosis. *Diabetologia*. 2001;44(2):156–63.
28. Brinchmann-Hansen O, Dahl-Jorgensen K, Sandvik L, Hanssen KF. Blood glucose concentrations and progression of diabetic retinopathy: the seven year results of the Oslo study. *BMJ*. 1992;304(6818):19–22.

29. Danne T, Weber B, Hartmann R, Enders I, Burger W, Hovener G. Long-term glycemic control has a nonlinear association to the frequency of background retinopathy in adolescents with diabetes. Follow-up of the Berlin Retinopathy Study. *Diabetes Care*. 1994;17(12):1390–6.
30. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329(14):977–86.
31. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998;352(9131):837–53.
32. Chase HP, Garg SK, Jackson WE, Thomas MA, Harris S, Marshall G, et al. Blood pressure and retinopathy in type I diabetes. *Ophthalmology*. 1990;97(2):155–9.
33. Matthews DR, Stratton IM, Aldington SJ, Holman RR, Kohner EM. Risks of progression of retinopathy and vision loss related to tight blood pressure control in type 2 diabetes mellitus: UKPDS 69. *Arch Ophthalmol*. 2004;122(11):1631–40.
34. Chew EY, Klein ML, Ferris FL, Remaley NA, Murphy RP, Chantry K, et al. Association of elevated serum lipid levels with retinal hard exudate in diabetic retinopathy. Early Treatment Diabetic Retinopathy Study (ETDRS) report 22. *Arch Ophthalmol*. 1996;114(9):1079–84.
35. Cusick M, Chew EY, Chan CC, Kruth HS, Murphy RP, Ferris 3rd FL. Histopathology and regression of retinal hard exudates in diabetic retinopathy after reduction of elevated serum lipid levels. *Ophthalmology*. 2003;110(11):2126–33.
36. Muhlhauser I, Bender R, Bott U, Jorgens V, Grusser M, Wagener W, et al. Cigarette smoking and progression of retinopathy and nephropathy in type 1 diabetes. *Diabet Med*. 1996;13(6):536–43.
37. Karamanos B, Porta M, Songini M, Metelko Z, Kerenyi Z, Tamas G, et al. Different risk factors of microangiopathy in patients with type I diabetes mellitus of short versus long duration. The EURODIAB IDDM complications study. *Diabetologia*. 2000;43(3):348–55.
38. The Diabetic Retinopathy Study Research Group. Indications for photocoagulation treatment of diabetic retinopathy: Diabetic Retinopathy Study Report no. 14. *Int Ophthalmol Clin*. 1987;27(4):239–53.
39. Treatment techniques and clinical guidelines for photocoagulation of diabetic macular edema. Early treatment Diabetic Retinopathy Study Report Number 2. Early treatment Diabetic Retinopathy Study Research Group. *Ophthalmol*. 1987;94(7):761–74.
40. Spalter HF. Photocoagulation of circinate maculopathy in diabetic retinopathy. *Am J Ophthalmol*. 1971;1(1 Part 2):242–50.
41. The Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy. Clinical application of Diabetic Retinopathy Study (DRS) findings, DRS Report Number 8. *Ophthalmology*. 1981;88(7):583–600.
42. Early Treatment Diabetic Retinopathy Study research group. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. *Arch Ophthalmol*. 1985;103(12):1796–806.
43. Blankenship GW. Fifteen-year argon laser and xenon photocoagulation results of Bascom Palmer eye institute's patients participating in the diabetic retinopathy study. *Ophthalmology*. 1991;98(2):125–8.
44. Chew EY, Ferris 3rd FL, Csaky KG, Murphy RP, Agron E, Thompson DJ, et al. The long-term effects of laser photocoagulation treatment in patients with diabetic retinopathy: the early treatment diabetic retinopathy follow-up study. *Ophthalmology*. 2003;110(9):1683–9.
45. Smiddy WE, Flynn Jr HW. Vitrectomy in the management of diabetic retinopathy. *Surv Ophthalmol*. 1999;43(6):491–507.

46. Yorston D, Wickham L, Benson S, Bunce C, Sheard R, Charteris D. Predictive clinical features and outcomes of vitrectomy for proliferative diabetic retinopathy. *Br J Ophthalmol*. 2008;92(3):365–8.
47. Moss SE, Klein R, Kessler SD, Richie KA. Comparison between ophthalmoscopy and fundus photography in determining severity of diabetic retinopathy. *Ophthalmology*. 1985;92(1):62–7.
48. 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. *BMJ*. 1995;311(7013):1131–5.
49. Olson JA, Strachan FM, Hipwell JH, Goatman KA, McHardy KC, Forrester JV, et al. A comparative evaluation of digital imaging, retinal photography and optometrist examination in screening for diabetic retinopathy. *Diabet Med*. 2003;20(7):528–34.
50. Warburton TJ, Hale PJ, Dewhurst JA. Evaluation of a local optometric diabetic retinopathy screening service. *Diabet Med*. 2004;21(6):632–5.
51. Chew EY. Screening options for diabetic retinopathy. *Curr Opin Ophthalmol*. 2006;17(6):519–22.
52. Leese GP, Ahmed S, Newton RW, Jung RT, Ellingford A, Baines P, et al. Use of mobile screening unit for diabetic retinopathy in rural and urban areas. *BMJ*. 1993;306(6871):187–9.
53. Scanlon PH, Malhotra R, Thomas G, Foy C, Kirkpatrick JN, Lewis-Barned N, et al. The effectiveness of screening for diabetic retinopathy by digital imaging photography and technician ophthalmoscopy. *Diabet Med*. 2003;20(6):467–74.
54. Murgatroyd H, Ellingford A, Cox A, Binnie M, Ellis JD, MacEwen CJ, et al. Effect of mydriasis and different field strategies on digital image screening of diabetic eye disease. *Br J Ophthalmol*. 2004;88(7):920–4.
55. Facey K, Cummins E, Macpherson K, Morris A, Reay L, Slattery J. Organisation of Services for Diabetic Retinopathy Screening. Glasgow: Health Technology Board for Scotland; 2002. p. 1–224.
56. Bursell SE, Cavallerano JD, Cavallerano AA, Clermont AC, Birkmire-Peters D, Aiello LP, et al. Stereo nonmydriatic digital-video color retinal imaging compared with early treatment diabetic retinopathy study seven standard field 35-mm stereo color photos for determining level of diabetic retinopathy. *Ophthalmology*. 2001;108(3):572–85.
57. Massin P, Erginay A, Ben Mehidi A, Vicaud E, Quentel G, Victor Z, et al. Evaluation of a new non-mydiatic digital camera for detection of diabetic retinopathy. *Diabet Med*. 2003;20(8):635–41.
58. Shiba T, Yamamoto T, Seki U, Utsugi N, Fujita K, Sato Y, et al. Screening and follow-up of diabetic retinopathy using a new mosaic 9-field fundus photography system. *Diabetes Res Clin Pract*. 2002;55(1):49–59.
59. Williams GA, Scott IU, Haller JA, Maguire AM, Marcus D, McDonald HR. Single-field fundus photography for diabetic retinopathy screening: a report by the american academy of ophthalmology. *Ophthalmology*. 2004;111(5):1055–62.
60. Aptel F, Denis P, Rouberol F, Thivolet C. Screening of diabetic retinopathy: Effect of field number and mydriasis on sensitivity and specificity of digital fundus photography. *Diabetes Metab*. 2008;34(3):290–3.
61. Baeza M, Orozco-Beltran D, Gil-Guillen VF, Pedrera V, Ribera MC, Pertusa S, et al. Screening for sight threatening diabetic retinopathy using non-mydiatic retinal camera in a primary care setting: to dilate or not to dilate? *Int J Clin Pract*. 2009;63(3):433–8.
62. Lopez-Bastida J, Cabrera-Lopez F, Serrano-Aguilar P. Sensitivity and specificity of digital retinal imaging for screening diabetic retinopathy. *Diabet Med*. 2007;24(4):403–7.

63. Mash B, Powell D, du Plessis F, van Vuuren U, Michalowska M, Levitt N. Screening for diabetic retinopathy in primary care with a mobile fundal camera—evaluation of a South African pilot project. *S Afr Med J*. 2007;97(12):1284–8.
64. Taylor CR, Merin LM, Salunga AM, Hepworth JT, Crutcher TD, O'Day DM, et al. Improving diabetic retinopathy screening ratios using telemedicine-based digital retinal imaging technology: the Vine Hill study. *Diabetes Care*. 2007;30(3):574–8.
65. Savolainen EA, Lee QP. Diabetic retinopathy - need and demand for photocoagulation and its cost-effectiveness: evaluation based on services in the United Kingdom. *Diabetologia*. 1982;23(2):138–40.
66. Javitt JC, Aiello LP, Chiang Y, Ferris 3rd FL, Canner JK, Greenfield S. Preventive eye care in people with diabetes is cost-saving to the federal government. Implications for health-care reform. *Diabetes Care*. 1994;17(8):909–17.
67. Javitt JC, Aiello LP. Cost-effectiveness of detecting and treating diabetic retinopathy. *Ann Intern Med*. 1996;124(1 Pt 2):164–9.
68. Dasbach EJ, Fryback DG, Newcomb PA, Klein R, Klein BE. Cost-effectiveness of strategies for detecting diabetic retinopathy. *Med Care*. 1991;29(1):20–39.
69. Caro JJ, Ward AJ, O'Brien JA. Lifetime costs of complications resulting from type 2 diabetes in the U.S. *Diabetes Care*. 2002;25(3):476–81.
70. Fendrick AM, Javitt JC, Chiang YP. Cost-effectiveness of the screening and treatment of diabetic retinopathy. What are the costs of underutilization? *Int J Technol Assess Health Care*. 1992;8(4):694–707.
71. James M, Turner DA, Broadbent DM, Vora J, Harding SP. Cost effectiveness analysis of screening for sight threatening diabetic eye disease. *BMJ*. 2000;320(7250):1627–31.
72. Meads C, Hyde C. What is the cost of blindness? *Br J Ophthalmol*. 2003;87(10):1201–4.
73. Foulds WS, MacCuish A, Barrie T. Diabetic retinopathy in the West of Scotland: its detection and prevalence, and the cost-effectiveness of a proposed screening programme. *Health Bull*. 1983;41(6):318–26.
74. Wright SE, Keeffe JE, Thies LS. Direct costs of blindness in Australia. *Clin Experiment Ophthalmol*. 2000;28(3):140–2.
75. Bjorvig S, Johansen MA, Fossen K. An economic analysis of screening for diabetic retinopathy. *J Telemed Telecare*. 2002;8(1):32–5.
76. Tu KL, Palimar P, Sen S, Mathew P, Khaleeli A. Comparison of optometry vs digital photography screening for diabetic retinopathy in a single district. *Eye*. 2004;18(1):3–8.
77. Aoki N, Dunn K, Fukui T, Beck JR, Schull WJ, Li HK. Cost effectiveness analysis of telemedicine to evaluate diabetic retinopathy in a prison population. *Am J Ophthalmol*. 2005;139(2):399.
78. Tung TH, Shih HC, Chen SJ, Chou P, Liu CM, Liu JH. Economic evaluation of screening for diabetic retinopathy among Chinese type 2 diabetics: a community-based study in Kinmen, Taiwan. *J Epidemiol*. 2008;18(5):225–33.
79. Diabetes care and research in Europe: the Saint Vincent declaration. *Diabet Med*. 1990;7(4):360.
80. Massin P, Chabouis A, Erginay A, Viens-Bitker C, Lecleire-Collet A, Meas T, et al. OPH-DIAT: a telemedical network screening system for diabetic retinopathy in the Ile-de-France. *Diabetes Metab*. 2008;34(3):227–34.
81. HSE. Framework for the development of a diabetic retinopathy screening programme for Ireland. Dublin, 2008:1–96.
82. Jaross N, Ryan P, Newland H. Incidence and progression of diabetic retinopathy in an Aboriginal Australian population: results from the Katherine Region Diabetic Retinopathy Study (KRDRS). Report no. 2. *Clin Experiment Ophthalmol*. 2005;33(1):26–33.

83. Harper CA, Livingston PM, Wood C, Jin C, Lee SJ, Keeffe JE, et al. Screening for diabetic retinopathy using a non-mydratic retinal camera in rural victoria. *Aust N Z J Ophthalmol*. 1998;26(2):117–21.
84. Boucher MC, Desroches G, Garcia-Salinas R, Kherani A, Maberley D, Olivier S, et al. Teleophthalmology screening for diabetic retinopathy through mobile imaging units within Canada. *Can J Ophthalmol*. 2008;43(6):658–68.
85. Boucher MC, Desroches G, Garcia-Salinas R, Kherani A, Maberley D, Olivier S, et al. Diabetic retinopathy screening. *Can J Ophthalmol*. 2009;44(1):100–1.
86. Cavallerano AA, Cavallerano JD, Katalinic P, Blake B, Rynne M, Conlin PR, et al. A telemedicine programme for diabetic retinopathy in a Veterans Affairs Medical Center—the Joslin Vision Network Eye Health Care Model. *Am J Ophthalmol*. 2005;139(4):597–604.

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