



A PRACTICAL MANUAL OF **Diabetic Retinopathy Management**

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Peter H. Scanlon

Prologue

Peter H. Scanlon

THE SCOPE OF THE PROBLEM OF THE EPIDEMIC OF DIABETES

In 1997, Amos¹ estimated that 124 million people worldwide have diabetes, 97% non-insulin-dependent diabetes mellitus (NIDDM), and that by 2010 the total number with diabetes is projected to reach 221 million. The regions with the greatest potential increases are Asia and Africa, where diabetes rates could rise to 2 or 3 times those experienced in 1997.

In 2000, Sorensen² 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.

The International Diabetes Federation have estimated the prevalence of diabetes in 2003 in the 20–79 age groups and projected this to an estimate in 2025. This is shown in Fig. 1.

North America

Reports from the USA and Canada have shown the following rises.

- 1 In 2000, Burrows³ reported that the number of native Americans and Alaska natives with diagnosed diabetes increased by 29% from 43,262 to 64,474 individuals between 1990 and 1997. By 1997, the prevalence was 5.4%, and the age-adjusted prevalence was 8.0%.
- 2 In 2000, Mokdad^{4,5} reported the results of the Behavioral Risk Factor Surveillance System in the USA 1990–98. The prevalence of diabetes rose from 4.9% in 1990 to 6.5% in 1998 and to 6.9% in 1999. The prevalence of diabetes was highly correlated with the prevalence of obesity ($r = 0.64$, $p < 0.001$).
- 3 In 2001, Boyle⁶ estimated that the number of Americans with diagnosed diabetes is projected to increase 165%, from 11 million in 2000 (prevalence of 4.0%) to 29 million in 2050 (prevalence of 7.2%).
- 4 In 2007, Lipscombe⁷ reported the prevalence of

diabetes in Ontario, Canada to have increased substantially during the past 10 years, and by 2005 to have already exceeded the global rate that was predicted for 2030. Using population-based data from the province of Ontario, Canada, age-adjusted and sex-adjusted diabetes prevalence increased from 5.2% of the population in 1995 to 6.9% in 2000 and to 8.8% of the population in 2005.

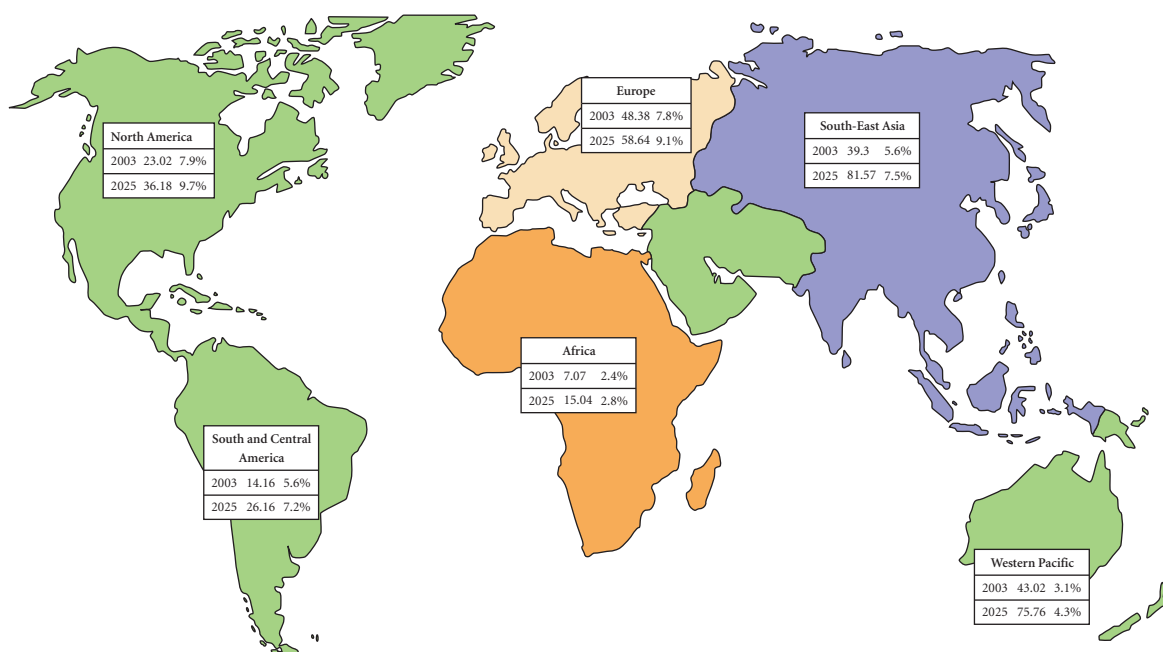
The UK

Reports from the UK have shown the following rises.

- 1 In 2000, Ehtisham⁸ reported type 2 diabetes emerging in UK children.
- 2 In 2001, Farouhi⁹ constructed an epidemiological model by applying age-, sex-, and ethnic-specific prevalence rates to resident populations of England at national, regional and PCT level. The estimated prevalence of total diabetes for all people in England was 4.41% in 2001 equating to 2.168 million people. Type 2 92.3% and type 1 7.7% (166,000 people).
- 3 In 2002, Feltbower¹⁰ reported an increasing incidence of type 1 diabetes in south Asians in Bradford.
- 4 In 2006, the latest data¹¹ in England for people diagnosed with diabetes have shown a national prevalence of diabetes of 3.35%.
- 5 In 2007, Evans¹² reported that a diabetes clinical information system in Tayside, Scotland, showed a doubling in incidence and prevalence of type 2 diabetes between 1993 and 2004, with statistically significant increasing trends of 6.3 and 6.7% per year respectively.

Worldwide reports

- 1 In 2000, Sidibe¹³ reported that the rise in complications of diabetes mellitus in Africa has gone hand in hand with the growing disease prevalence.
- 2 In 2001, Zimmet¹⁴ reviewed the global and societal implications of the diabetes epidemic.



Region	Year	Number with diabetes (millions)	% of population with diabetes
Africa	2003	7.07	2.4%
	2025	15.04	2.8%
Eastern Mediterranean and Middle East region	2003	19.24	7%
	2025	39.41	8%
Europe	2003	48.38	7.8%
	2025	58.64	9.1%
North America	2003	23.02	7.9%
	2025	36.18	9.7%
South and Central American region	2003	14.16	5.6%
	2025	26.16	7.2%
South-East Asian region	2003	39.3	5.6%
	2025	81.57	7.5%
Western Pacific region	2003	43.02	3.1%
	2025	75.76	4.3%

Fig. 1 World map and table showing the International Diabetes Federation prevalence estimates of diabetes in 2003 and 2025 in 20–79 age group.

3 In 2001, Aspray¹⁵ reported that the prevalence of diabetes in sub-Saharan Africa varied from 1% of the rural population to 5.3% of the urban population.

4 In 2004, Wild¹⁶ reported the prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030.

The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030.

The prevalence of diabetes is higher in men than in women, but there are more women with diabetes than men. The urban population in developing countries is projected to double between 2000 and 2030. The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people over 65 years of age.

These findings indicate that the ‘diabetes epidemic’ will

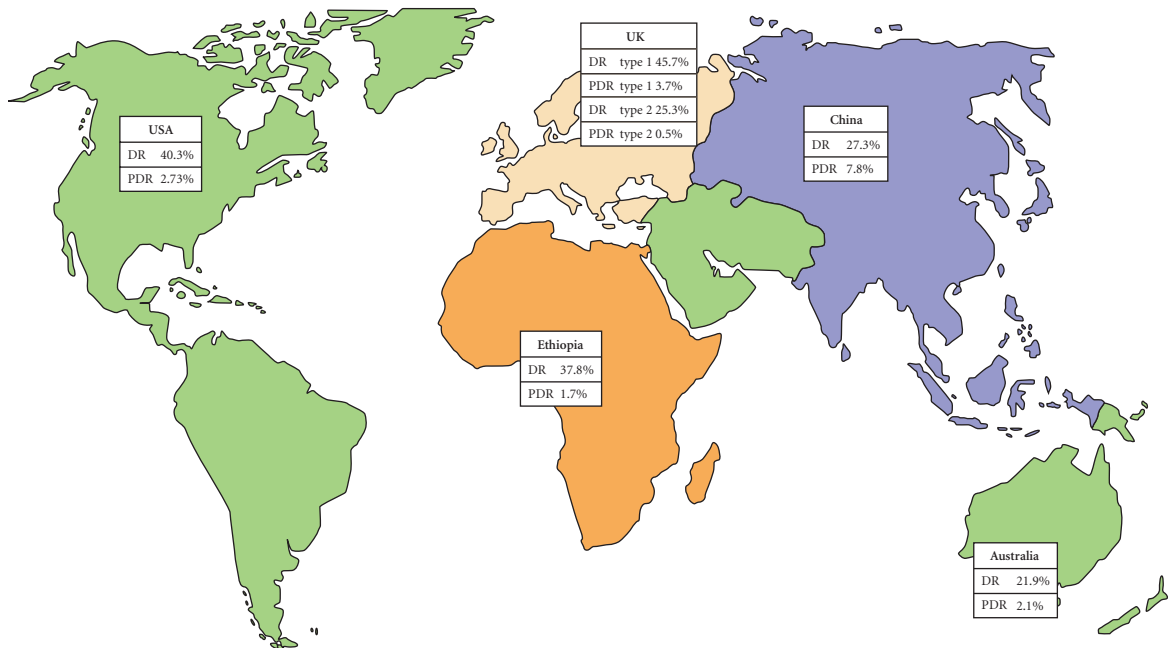
continue even if levels of obesity remain constant. Given the increasing prevalence of obesity, it is likely that these figures provide an underestimate of future diabetes prevalence.

In 2006 Cugati¹⁷ reported data from the Blue Mountains Eye Study (BMES) in Australia that examined 3654 residents (82.4% response) aged over 49 years in BMES I (1992–1994). Survivors (n = 2335) and newly eligible residents (n = 1174) were examined in BMES II (1997–

2000). Diabetes was defined by history or fasting plasma glucose ≥ 7.0 mmol/L. The overall diabetes prevalence increased from 7.8 to 9.9% ($p = 0.002$).

THE PREVALENCE OF SIGHT-THREATENING DIABETIC RETINOPATHY WORLDWIDE

See Fig. 2.



<i>USA</i>		<i>Ethiopia</i>	
Prevalence of DR	40.3%	Prevalence of DR	37.8%
Prevalence of proliferative DR	2.73%	Prevalence of proliferative DR	1.7%
<i>UK</i>		<i>China</i>	
Prevalence of DR in type 1	45.7%	Prevalence of DR	27.3%
Prevalence of proliferative DR in type 1	3.7%	Prevalence of proliferative DR	7.8%
Prevalence of DR in type 2	25.3%		
Prevalence of proliferative DR in type 2	0.5%		
<i>India</i>		<i>Oman</i>	
Prevalence of DR	13.4%	Prevalence of DR	14.4%
Prevalence of proliferative DR	1.9%	Prevalence of proliferative DR	2.7%
		<i>Australia</i>	
		Prevalence of DR	21.9%
		Prevalence of proliferative DR	2.1%

Variations in screening methodology may explain some of these differences.

Fig. 2 World map and table showing the reported prevalence of diabetic retinopathy (DR) and proliferative DR.

The USA

Reports have shown that diabetic retinopathy (DR) continues to be prevalent in the USA.

- 1 In 1992, Klein¹⁸ reported results from the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR study). This was a population-based study in southern Wisconsin of 996 insulin-taking younger-onset diabetic persons (given diagnoses of diabetes under 30 years) and 1370 patients given diagnoses of diabetes at age 30 years or older who were examined using standard protocols to determine the prevalence and severity of DR and associated risk variables. Proliferative diabetic retinopathy (PDR) was found to be a prevalent complication: 23% in the younger-onset group, 10% in the older-onset group that were taking insulin, and 3% in the group not taking insulin.
- 2 In 1995 Klein¹⁹ reported the incidence of macular oedema 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 2001, West²⁰ studied Hispanic patients with diabetes over 40 years in Arizona. The prevalences were any DR 48%, and moderate to severe non-proliferative DR (NPDR) and PDR 32%.
- 4 In 2003, Brown²¹ reported that, despite improvement in levels of glycaemia and blood pressure, PDR remains prevalent.
- 5 In 2004, Kempen²² reported that, among an estimated 10.2 million US adults 40 years and older known to have diabetes, the estimated crude prevalence rates for retinopathy and vision-threatening retinopathy were 40.3% and 8.2%, respectively.
- 6 In 2006 Wong²³ reported on a multiethnic population of 778 individuals from ages 45 to 85 years with diabetes; the prevalence of any retinopathy was 33.2% and of macular oedema 9.0%.

In WESDR,²⁴ one-third of the eyes that developed vision-threatening DR had proliferative DR and two-thirds had clinically significant macular oedema. Hence, taking the estimated crude prevalence rates for vision-threatening retinopathy of 8.2% from the paper by Kempen,²² the estimated crude prevalence rates for PDR would be 2.73%.

The UK

Reports from the UK have shown that sight-threatening DR is prevalent in the UK.

- 1 In 1998, Kohner²⁵ reported baseline retinopathy levels in 2964 patients with diabetes enrolled in the United Kingdom Prospective Diabetes Study (UKPDS). Retinopathy, defined as microaneurysms or worse lesions in at least one eye, was present in 39% of men and 35% of women. Marked retinopathy with cotton wool spots or intraretinal microvascular abnormalities was present in 8% of men and 4% of women.
- 2 In 2002, Younis^{26,27} reported baseline results from population screening in Liverpool of 831 people with type 1 diabetes and 7231 people with type 2 diabetes. The results showed a baseline for the type 1 diabetes group of any DR 45.7%, PDR 3.7% and STED 16.4%, and for the type 2 group of any DR 25.3%, PDR 0.5% and sight threatening eye disease (STED) 6.0%.

Worldwide reports

Worldwide reports have shown that sight-threatening DR is prevalent worldwide.

- 1 In 1997, Kernell²⁸ reported the youngest child in the literature (11.8 years) at that time with preproliferative DR to be from Sweden.
- 2 In 1999, Donaghue²⁹ described the youngest child reported in the literature to have background DR at that time (1999) to be 7.9 years (duration 5.6 years, HbA1c 8.9%) and from Australia.
- 3 In 2000, McKay³⁰ reported results of 4744 people over 40 years from nine randomly selected Melbourne clusters and four randomly selected rural Victorian clusters in Australia. The prevalence of any DR among people with self-reported diabetes was 29.1% and untreated vision-threatening retinopathy was 2.8%.
- 4 In 2000, Ramachandran³¹ studied 617 patients with type 1 diabetes in India reporting a prevalence of any DR of 13.4% and proliferative DR of 1.9%.
- 5 In 2001, Hesse³² reported on 2801 people with diabetes employed by Volkswagen in Germany. Of 263 patients aged over 40 years, 18.8% had mild or moderate NPDR, 3.3% severe NPDR and 2.2% PDR. Of 2228 patients aged over 40 years, 11.9% mild or moderate NPDR, 2.6% severe NPDR and 0.9% PDR.
- 6 In 2001, Seyoum³³ studied 302 patients with diabetes in Ethiopia, reporting a prevalence of 37.8% any DR and 1.7% PDR.
- 7 In 2002, Liu³⁴ found a prevalence of any DR 27.3%, and PDR 7.8% among 773 newly diagnosed patients in Beijing, China.

- 8 In 2003, in the Australian Diabetes, Obesity and Lifestyle study (AusDiab) of 11,247 adults over 25 years in 42 randomly selected areas of Australia, Tapp³⁵ showed a prevalence of any DR of 21.9% in those with known type 2 diabetes and 6.2% in those newly diagnosed. The prevalence of PDR was 2.1% in those with known diabetes.
- 9 In 2003, Khandekar³⁶ found that amongst 2249 patients with diabetes in Oman, 14.39% were found to have any DR and the prevalence of, PDR was 2.66%.
- 10 In 2006, Knudsen³⁷ reported the point prevalence of proliferative retinopathy in the county of North Jutland, Denmark to be 0.8% and 0.3% for type 1 and type 2 diabetes. Equivalent prevalence rates of clinically significant macular oedema were 7.9% and 12.8%, respectively.
- 11 A published systematic review by Williams³⁸ in 2004 on the epidemiology of DR and macular oedema concluded that studies of sufficient size to stratify for age and duration of eye disease show an increase in DR in older age groups with long-standing disease.

ADVANCES IN THE MANAGEMENT OF DIABETES

Advances in management of diabetes have had a substantial impact on DR. These are discussed in detail in Chapter 2.

The demonstration by the Diabetes Control and Complications Trial³⁹ that retinopathy in type 1 diabetes could be reduced by intensive treatment of blood glucose has led to much better control and retinopathy progression has been reduced.

Studies^{40,41} in the early 1990s showed the link between hypertension in type 1 diabetes and a higher occurrence of retinopathy and progression of pre-existing retinopathy.

A similar demonstration in the United Kingdom Prospective Diabetes Study⁴² (UKPDS) that in type 2 diabetes the development of retinopathy (incidence) was strongly associated with baseline glycaemia and glycaemic exposure and that progression was associated with hyperglycaemia (as evidenced by a higher HbA1c) has led to better control in type 2 diabetes and in reduction in retinopathy progression. The UKPDS⁴³ also demonstrated that high blood pressure is detrimental to every aspect of DR in type 2 diabetes and that a tight blood pressure control policy reduces the risk of clinical complications from diabetic eye disease (see Fig. 3).

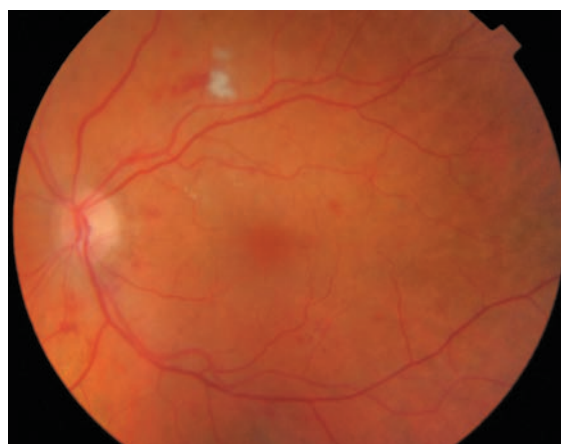


Fig. 3 Uncontrolled hypertension in a person with diabetes. Left macular colour photograph showing flame haemorrhages and cotton wool spots.

ADVANCES IN THE MANAGEMENT OF DIABETIC RETINOPATHY

Since Spalter⁴⁴ described the photocoagulation of circinate maculopathy in DR, clear evidence for the efficacy of laser treatment for diabetic eye disease has been shown from the Diabetic Retinopathy Study^{45–49} and the Early Treatment Diabetic Retinopathy Study^{50–58}. In 1981 they reported⁴⁷ that photocoagulation, as used in the study, reduced the 2-year risk of severe visual loss by 50% or more (see Fig. 4).

In 1985, a report⁵⁰ from the Early Treatment Diabetic Retinopathy Study showed that focal photocoagulation of ‘clinically significant’ diabetic macular oedema (CSMO) substantially reduced the risk of visual loss.

Smiddy⁵⁹ wrote an excellent review in 1999 when 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 favourable visual outcome, preventive measures, such as improved control of glucose levels and timely application of panretinal photocoagulation, are equally important in the management. Vitrectomy clearly does have a place in the management of diabetic eye disease (Fig. 5). Evidence of improving visual results during the last 20 years following vitrectomy has been shown in studies reported by Blankenship,⁶⁰ Thompson,^{61–64} Sigurdsson,⁶⁵ Flynn,⁶⁶ Nakazawa⁶⁷, Karel,⁶⁸ Harbour,⁶⁹