

Epidemiology of diabetic retinopathy
- Contrast between the expected prevalence and the frequency of reported cases in the
French population -

C DELCOURT^a, P MASSIN^b, M ROSILIO^c

^a Inserm, U897, Bordeaux, F-33076 France ; Univ Bordeaux 2, Bordeaux, F-33076 France

^b Department of Ophthalmology, Lariboisiere Hospital, Assistance Publique - Hopitaux de Paris, 2 rue Ambroise Pare, 75475 Paris cedex, France.

^c Medical Unit, Endocrinology & Diabetes, Lilly France, 13 rue Pages 92158 Suresnes cedex, France.

Running title : Diabetic retinopathy in France

Corresponding author:

Cecile Delcourt

INSERM U897, ISPED – Université Victor Segalen Bordeaux 2.

146 rue Léo Saignat, 33076 Bordeaux Cedex

e-mail: cecile.delcourt@isped.u-bordeaux2.fr

phone: + 33 5 57 57 15 96

Summary

Aim: Visual impairment and loss of vision due to retinopathy are amongst the most feared complications in diabetic patients. As the number of diabetic patients is predicted to increase, a corresponding increase in the number of patients affected with diabetic retinopathy (DR) is also expected.

Methods: This review aimed at providing an update of the published literature pertaining to the epidemiology of DR.

Results: Over the last 20 years, eight population-based studies have been conducted in Western countries, using photographic evidence of DR. Results have consistently suggested that the prevalence of DR is close to 28.7% while Proliferative DR and Macular Oedema account for 9 % and 17 % of all diagnosed cases, respectively. Various longitudinal studies indicate a yearly incidence of DR of 2-6%.

In France, the epidemiology of DR has been mostly investigated in observational studies. The recorded prevalence of DR - based on physicians' declarations - is estimated at 10% suggesting that DR is under-diagnosed in the French diabetic population. This discrepancy between the expected and known prevalence of DR may be explained by the number of patients with unknown retinal status.

DR screening with non mydriatic fundus photography is effective in identifying early and advanced DR. Screening programs conducted over the last 5 years in different regions of France indicate that 10 to 20% of diabetic patients with previous unknown retinal status have retinopathy.

Conclusion: Further implementation of screening programs will be a key target for improving DR diagnosis and prevent visual loss in the French diabetic population.

Key words:

Diabetic retinopathy, epidemiology, prevalence, incidence, screening.

French title

Données épidémiologiques de la rétinopathie diabétique – Différence entre la prévalence attendue et la fréquence des cas déclarés en France

French abstract

Objectif : La rétinopathie est l'une des complications du diabète les plus redoutées, en raison du risque d'altération de la vision et de cécité. Dans les années à venir, la proportion de cas de rétinopathie diabétique (RD) devrait augmenter par suite d'un accroissement de la population diabétique.

Méthodes : L'objectif de cette revue a été de mettre à jour les données épidémiologiques sur la RD.

Résultats : La recherche bibliographique a retrouvé huit études d'exploration de la prévalence de la RD menées dans des pays occidentaux au cours des 20 dernières années; il s'agissait d'études de population et le diagnostic de RD était établi à partir de photographies rétiniennes. Les résultats superposables montrent une prévalence de la RD d'environ 28.7%; la RD proliférante et l'oedème maculaire rendent compte de 9% et 17% des cas de RD diagnostiqués. Différentes études de suivi indiquent que l'incidence annuelle de la RD est d'environ 2-6%.

En France, les données épidémiologiques reposent surtout sur les résultats d'études observationnelles. La prévalence de la RD déclarée par les médecins est estimée à 10%. La différence entre la prévalence attendue et la prévalence déclarée de la RD laisse supposer que pour un grand nombre de sujets diabétiques, l'examen de la rétine n'a pas été effectué et le statut rétinien n'est pas connu.

Le dépistage de la RD par photographies du fond d'oeil permet d'identifier la RD à un stade précoce ou avancé. Plusieurs campagnes de dépistage ont été menées en France depuis 5 ans. Une RD a été retrouvée chez 10 à 20% des patients dépistés n'ayant pas bénéficié d'une exploration rétinienne préalable.

Conclusion : Il paraît à présent nécessaire d'étendre les programmes de dépistage de la RD à l'ensemble du territoire afin d'améliorer le dépistage annuel, de traiter précocement les cas de DR et de prévenir la perte de vision chez le diabétique français.

French key words:

Rétinopathie diabétique, épidémiologie, prévalence, incidence, dépistage.

Introduction

Diabetes mellitus is a condition that affects 180 million people worldwide [1]. The total number of people with diabetes is expected to rise to an estimated 300 million by year 2025, resulting from the population growth, ageing, obesity and sedentary lifestyle [1]. In France, the estimated number of individuals affected with diabetes is 2.5 million in 2007 (10% with type 1 and 90% with type 2) [2]. The overall prevalence of the disease was 3.95%, confirming its constant progression over time [2].

Diabetes has many manifestations in the eye, of which diabetic retinopathy (DR) and cataract are the most frequent causes of visual impairment. In Western countries, diabetic eye disease represents one of the leading causes of blindness, following macular degeneration, glaucoma and cataract [3]. DR is broadly divided into two clinical stages: non-proliferative (NPDR) and proliferative diabetic retinopathy (PDR). DR progressively affects the integrity of retinal microvessels, resulting in abnormal permeability, non-perfusion of capillaries and leading to microaneurysms. PDR is observed when the occlusion of retinal capillaries leads to retinal ischemia and promotes the development of neovascularisation on the surface of the retina. Macular oedema (MO) develops when abnormal permeability results in the collection of fluid around the macula. Laser photocoagulation therapy has proven to be effective in reducing DR progression and vitrectomy can prevent severe vision loss in subjects with advanced DR. Because DR is a detectable and treatable condition, local and international guidelines have recommended an annual fundus examination for diabetic patients [4-8].

The prevalence of DR is supposed to be strongly related to the prevalence of diabetes. As the prevalence of diabetes is expected to rise in the future, an associated increase in the number of patients affected with DR should also be expected. Several factors have been identified as risk factors in the development of DR, including the duration of diabetes, diabetes type, poor glycemic and blood pressure control [9-11].

For the past 25 years, the epidemiology of DR has been dominated by the Wisconsin Epidemiologic Study of Diabetic Retinopathy, WESDR [9]. Other longitudinal population studies – UKPDS, DCCT and EDTRS – also investigated the prevalence and incidence of diabetes complications [10-12]. However, data from the WESDR are now outdated and reflect diabetes management used in the past. The objective of this review was to provide an update of the published literature pertaining to the epidemiology of DR and to focus on any relevant data on DR diagnosis in France.

Literature search methods

The Medline database was interrogated from 1980 to 2008. The strategy of search used the following terms: “diabetic retinopathy”, “epidemiology”, “prevalence” and “incidence”, limited to “Human” and “English language”. Relevant articles were original reports of population-based studies restricted to selected Western countries (ie Europe, USA, Canada, Australia) and designed to specifically describe the prevalence and/or incidence of DR. The original Medline search generated 2460 citations, among which 58 were considered relevant.

As there are inconsistencies between epidemiological studies and differences in study methods may contribute to conflicting reports of prevalence and incidence [13], we restricted the search to studies using the reference method for DR diagnosis (e.g. multi-field stereoscopic fundus photography graded by an ophthalmologist using the ETDRS classification [14]). In addition, we did not retain the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) in the present review, though a number of related articles were retrieved. There were various reasons for not selecting this study. The WESDR study was initiated in the early 1980’s. Patients included were grouped according to their age at diagnosis and treatment received but not according to the type of diabetes, as currently presented. Significantly higher prevalence rates of DR were reported (up to 70% in patients treated with insulin) in contrast to more recent studies. It is likely that improvements in the management of diabetes (better glycemic and blood pressure control) over time have led to a progressive decline in retinopathy frequency.

Epidemiology of DR – Western countries

Prevalence of DR

A total of eight studies provided prevalence data for DR, including PDR and MO. Studies included the Beaver Dam Eye Study, Exeter Diabetic Retinopathy Screening Program (EDRS), Blue Mountains study, Visual Impairment Project (VIP), Arhus County Study, Casteldaccia Eye Study, Australian Diabetes Obesity and Lifestyle study (AusDiab) and Multiethnic Study of Atherosclerosis (MESA) [15-22] (**Table 1**). All were population-based studies conducted from 1988 to 2002 in the USA, Australia and Europe (United Kingdom, Denmark, Italy) using the reference examination for DR diagnosis. Patients included had

known type 1 or type 2 diabetes (a few patients had newly diagnosed diabetes in [15, 17]), they were 65 years old on average (from 63 to 72) and had long-standing disease with an average duration of 15 years (from 7 to 14.6).

Despite heterogeneity in patient selection criteria, country and selection period, the percentage of patients found with DR was relatively similar, ranging from 21.9 % to 36.8% (weighted mean, using the number of subjects included in each study as weights, 28.7 %). PDR accounted for about 9% of all cases of diagnosed DR (ranging from 1.6 % to 4.5 %, weighted mean, 2.6%). Macular oedema accounted for about 17% of all diagnosed DR prevalence (ranging from 2.7 % to 7.6 %, weighted mean 4.8 %). In summary, the prevalence rates of DR were consistent in these selected studies, suggesting that the prevalence of DR is close to 28.7% in the Western world, i.e. in countries promoting the same strategies to manage diabetes and to control glycaemia/ blood pressure levels in their populations [23].

In **Table 1**, data is presented on the Caucasian populations only, although the prevalence and risk factors of DR have been described among multiethnic populations in the US studies. In MESA [22], African-American and Hispanic populations had a significantly higher prevalence of any DR than White/Caucasian and Chinese populations. However, ethnicity was not an independent predictor of any retinopathy, suggesting that other risk factors (diabetes duration, glycemic levels) may explain the higher rates of retinopathy in African-Americans and Hispanics. Ethnic differences in DR diagnosis were also reported in the Veteran Affairs Diabetes Trial cohort (VADT) [24]. Severe retinopathy was more frequent in African Americans and Hispanics than in non-Hispanic whites/Caucasians in VADT but, contrary to MESA, the differences could not be explained by standard risk factors. To our knowledge, the prevalence of DR according to ethnicity has not been investigated in EU countries.

Incidence of DR

Only three population-based studies assessed DR longitudinally using the reference method for DR diagnosis (Melbourne VIP [25]; Blue Mountains Eye Study [26] ; AusDiab [27]) (**Table 2**). In all three studies, which were limited to a small number of patients, the cumulative incidence of any DR was 11% (95% CI: 3.8-18.1), 22.2% (95% CI: 14.1-32.2) and 13.9 % respectively, after 5 years of follow-up [25-27].

Data of larger screening cohorts suggest that the incidence of DR is high, as well as the incidence of severe vision-threatening DR. Primary care patients from the Liverpool Diabetic Eye Study were initially screened between 1991 and 1999 and those with no baseline

DR were prospectively studied (501 type 1 and 3743 type 2 patients) [28,29]. Over a period of 5 years, the cumulative incidence of any DR was 36.8% and 30.5% in type 1 and type 2 patients respectively, while sight threatening DR occurred in 3.9% in both patient groups. Gender was not related to the incidence of any DR but longer duration of disease was associated to a greater risk of DR in both types of diabetes.

Results from long-term follow-up studies suggest that the cumulative incidence of DR decreased over the past 35 years, at least in type 1 diabetes. In the Danish Steno cohort, patients diagnosed between 1965 and 1984 were studied for up to 20 years [30]. In the most recently diagnosed patients, ie those referred between 1979 and 1984, a decrease of incident DR and incident MO was demonstrated, suggesting that modern strategies to control glucose level and to lower blood pressure contributed in reducing the incidence of this diabetes complication.

DR incidence has also been evaluated in clinical trials. The event rates in clinical trial populations should theoretically be lower than those of observational cohorts, partly due to the inclusion of more compliant patients. However, in the randomized comparative DIRECT-Prevent 1 study, incident retinopathy occurred in 25% of type 1 diabetic patients treated with candesartan vs 31% in the placebo group over a median period of 4.7 years [31]. The authors suggested that DR incident rate from the placebo group probably reflects the optimal rate achieved with the current practice.

In summary, data from different longitudinal studies suggest that the yearly incidence of any DR is approximately 2-6%. The incidence rates are therefore only about 5 to 10 times lower than the prevalence rates, suggesting a high turn-over of patients with retinopathy, which is probably related to their short life expectancy, due to advanced age and long-standing diabetes.

Prevalence of DR – France

Our search could not find any population-based studies conducted in France using a reference method to diagnose DR. In the CODIAB study [32-34] the sample was mainly hospital-based, limited to a small number of patients with type 2 diabetes regularly attending hospital endocrinology consultations. DR was explored using a reference method for diagnosis (direct ophthalmoscopy, slit lamp examination, fluorescein angiography). The prevalence of any DR, proliferative DR and macular oedema was 33%, 3.3% and 5.6%

respectively. Advanced retinopathy (PDR, MO) increased with increased duration of diabetes and was strongly linked to other diabetes complications studied, namely peripheral neuropathy and nephropathy. Interestingly, DR prevalence was similar to prevalence rates reported in population-based studies of Western countries, although CODIAB patients were not necessarily representative of the diabetic population as they were potentially more severely affected than patients seen in private practice.

Prevalence of declared DR

Several observational studies evaluated the prevalence of known DR in France on the basis of physicians' declarations (**Table 3**). Retinopathy was declared in 12% of patients with type 2 diabetes in Grimaldi et al. [35], DR frequency being significantly increased with increasing patient age and longer disease duration. In the cohort of patients with long-standing diabetes (mean duration, 10-15 yrs) described by Le Floch et al. [36], DR was declared more frequently in patients with type 1 diabetes than patients with type 2 diabetes either treated or not treated with insulin (31.1%, 12.9% and 8.6%, respectively).

ECODIA was a cross-sectional survey conducted on a representative sample of general practitioners and diabetologists/endocrinologists who collected data of 4119 ambulatory patients with type 2 diabetes [37]. The mean duration of diabetes was 8.9 yrs and more than a third of patients had complications linked to diabetes. In this setting, the prevalence of declared DR was 10.6% (CI 95%: 9.5%-11.6%).

In the ENTRED survey, ophthalmologic and neuropathic complications of diabetes were assessed in a representative sample, using questionnaires and patient reimbursement data from social security services [38]. Data were analysed for 3648 subjects who had been reimbursed for an oral antidiabetic drug and/or insulin during the fourth trimester 2001 and their 1718 corresponding physicians. According to the patient's questionnaire, 14.5% of subjects had already had previous laser treatment and 42.6% had had a fundus examination during 2001. According to the physician questionnaire, 9.9% of patients had DR, 4.5% had already had laser treatment and 65.3% had previously had an ophthalmologic examination. In contrast, reimbursement files showed that only 43% of patients had consulted an ophthalmologist over the past year. Results suggested that the physicians' declarations were biased, ie under-estimated, as illustrated by a lower reporting of laser treatment as compared to patients' declarations and measures were possibly under-evaluated as a smaller proportion of patients than that declared had had a fundus examination during the past year.

The extent of recorded diagnoses of DR was recently explored and compared in diabetic patients living in different European countries [39]. DR was declared in 11.4% of French patients (CI95% 8.8%-13.9%) vs 10.3%, 19.6% and 19.7% in patients from Spain, UK and Italy, respectively. Data suggested that the severity of DR was related to longer duration of diabetes and was associated with the frequency of other comorbidities, particularly nephropathy and coronary heart disease. Proliferative DR accounted for 20.8 % of declared DR in French patients, which could reflect that patients were most likely to be diagnosed with DR only at later stages of the diabetic disease, or only when DR is at an advanced stage. Non

The value of such observational studies is obviously limited as the patient DR status exclusively relies on the physician's declaration. But for all studies combined, the frequency of "known" or "recorded" DR in French diabetic patients was around 10% and largely below the estimated prevalence of DR resulting from epidemiological studies of 28.7% on average, suggesting that DR is under-diagnosed in patients with diabetes, or that the prevalence of DR is much lower in France than in other Western countries, for instance because of different strategies in the screening and treatment of diabetes.

Prevalence of DR in screening programs

In 1998, a statistical analysis of the French healthcare database (French National Health Insurance CNAMTS - *Caisse Nationale d'Assurance Maladie des Travailleurs Salaries*) indicated that fewer than 40% of diabetic patients living in Metropolitan France had undergone an eye examination over the past year [40]. One contributing factor to the low number of eye examinations was the increasing number of diabetic patients and decreasing number of ophthalmologists to perform funduscopy examination [41]. These observations led to the development of more convenient methods for diagnosing or monitoring DR with at least the same sensitivity and specificity as examination by an ophthalmologist. Fundus photographs with a non mydriatic camera have been progressively used [42] and in parallel, ambulatory techniques have been promoted in order to enhance patient access to care [43]. During the last 5 years, a number of different screening programs have been conducted in France, using these alternative methods [44-49].

In DODIA (*Dépistage Ophtalmologique du Diabète*) initiated in 2002 in the Northern Area of Paris, 882 patients from the primary care setting were screened using either dilated eye examination performed by an ophthalmologist or non mydriatic eye fundus photography performed by an orthoptist and analysed by an expert site. DR was detected in 10.4% of patients with eye examination and 17.3% with fundus photography [45].

Following this conclusive experience, several screening programs were implemented using non mydriatic photography. In Artois (PREVART network), 7% of 1322 ambulatory screened patients were diagnosed with DR (NPDR, 2.8%; PDR, 4.8%; MO 0.5%) between 2002 and 2003 [47]. Over the 2004-2005 period, 676 patients living in rural areas of Burgundy were screened using an itinerant non mydriatic camera [48]. Of them, 8.6% were found to have DR. Patients screened had a satisfactory control of their diabetes (mean HbA1c, 7.2%) but 6.8% had never consulted an ophthalmologist and 55% had had no eye examination over the past 2 years. Not surprisingly, prevalence rates were lower than in DODIA, probably due to a selection bias. As patients are free to participate in such screening campaigns, those who volunteer are usually highly motivated and treatment-compliant. In these individuals, the rate of diabetes complications is likely to be less marked.

Finally, the largest experience of DR screening is from OPHDIAT (*Ophthalmology Diabetes Telemedicine*) a telemedical network covering the Ile-de-France area [49]. Over a 28-month period, 13777 diabetic patients with unknown retinal status were screened for DR using non mydriatic cameras. Photographs were taken by technicians (16 screening sites located in hospitals, healthcare centres and prisons) and images were graded by trained ophthalmologists in a reading center. Diabetic retinopathy was detected in 23.4% of patients. Of the patients diagnosed with DR, 0.5% had PDR and 3.4% had MO. In addition, 5.6% of patients (n=777) had undiagnosed severe DR requiring urgent referral to an ophthalmologist for laser treatment.

In summary, the evaluation of screening programs with non mydriatic fundus photography supports the view that they are effective in the identification of both early and advanced DR [43]. More importantly, results from recent screening programs indicate (**Table 4**) that 10 to 20% of French diabetic patients with previous unknown retinal status have retinopathy.

In conclusion

On the basis of robust epidemiological studies conducted in the Western world over the last 20 years, we suggest that the expected prevalence of Diabetic Retinopathy is close to 28.7% in the diabetic population, while proliferative DR and macular oedema may be present in 2.6% and 4.8% of patients, respectively. Results from different longitudinal studies suggest that the yearly incidence of DR is approximately 5-6%. According to observational studies

based on physicians' declarations, the recorded prevalence of DR in the French diabetic population is approximately 10%. The discrepancy between the expected prevalence and the recorded prevalence may be explained by the large proportion of patients with unknown retinal status. Although clinical guidelines recommend examination of diabetic patients for ophthalmologic complication at the time of diagnosis and on repeated annual surveillance [5,6,8], evidence suggests that patients do not fully comply with screening and that the prevalence of DR in non compliant patients could be as high as 10 to 20 %.

Alternative methods of DR screening using non mydriatic fundus photography have been validated, showing the same sensitivity and specificity for DR diagnosis as ophthalmoscopy. In addition, DR screening programs using ambulatory screening and/or combined telemedical network have been successfully conducted on a local community basis, to facilitate access to regular annual evaluations of patients with diabetes. Implementing DR screening programs that cover the entire French territory will be without a doubt, a key target for improving DR diagnosis and shortening treatment delays in patients with referable retinopathy.

Conflicts of interest

Dr Delcourt has been a consultant for Chauvin-Bausch&Lomb, Alcon, Novartis, Pfizer and Lilly and received funds from Théa Laboratories.

Dr Massin has been a consultant for Lilly, Takeda, Novartis, Pfizer and Solvay.

Dr Rosilio is an employee of Eli Lilly and Company.

The authors thank Dr C Soubrouillard - Eltium for her assistance in the preparation of the manuscript.

References

1. World Health Organization. The World Health Report 2002. <http://www.who.int>.
2. Kusnik-Joinville O, Weill A, Ricordeau P, Allemand H. Diabète traité en France en 2007 : un taux de prévalence proche de 4 % et des disparités régionales croissantes. *Bulletin Epidémiologique Hebdomadaire* 2008 ; n°43 : 409-413.
3. Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, Mariotti SP. Global data on visual impairment in the year 2002, *Bull World Health Organ* 2004;82:844-851.
4. National Institute for Clinical Excellence, NICE. Type 2 diabetes. National clinical guidelines for management in primary and secondary care (update). 2008. <http://www.nice.org.uk>
5. Haute Autorité de Santé, HAS. Diabète de type 2. Guide affection de longue durée. Juillet 2007; 23 p.
6. Agence Française de Sécurité Sanitaire des Produits de Santé, AFSSAPS. Type 2 treatment. French Recommendations for good practice. AFSSAPS-HAS.2006. *Diabetes Metab* 2006 ; 32 : 643-648.
7. American Diabetic Association. Executive summary: Standards of medical care in 2008. *Diabetes Care* 2008;31(suppl 1):S5-S11.
8. Massin P, Angioi-Duprez K, Bacin F, Cathelineau B, Chainé G, Coscas G et al. Dépistage, surveillance et traitement de la rétinopathie diabétique. Recommandations de l'ALFEDIAM. Comité d'experts ci-dessus et validé par les membres des conseils d'administration et scientifique de l'ALFEDIAM., *Diabetes Metab* 1996;22:203-209.
9. Klein R, Klein BE, Moss SE, Davis MD and DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of diabetic retinopathy when age at diagnosis is 30 or more years, *Arch Ophthalmol* 1984;102:527-532.
10. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, Matthews DR. UKPDS 50: risk factors for incidence and progression of retinopathy in Type II diabetes over 6 years from diagnosis. *Diabetologia* 2001;44:156-163.
11. Diabetes Control and Complications Trial. Progression of retinopathy with intensive versus conventional treatment in the Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group. *Ophthalmology* 1995;102:647-661.

12. Davis MD, Fisher MR, Gangnon RE, Barton F, Aiello LM, Chew EY et al. Risk factors for high-risk proliferative diabetic retinopathy and severe visual loss: Early Treatment Diabetic Retinopathy Study Report #18. *Invest Ophthalmol Vis Sci* 1998;39:233-252.
13. Williams R, Airey M, Baxter H, Foerrestter J, Kennedy-Martin T and Girach A. Epidemiology of diabetic retinopathy and macular oedema: a systematic review. *Eye* 2004;18:963-983.
14. Gillow JT, Gray JA. The National Screening Committee review of diabetic retinopathy screening. *Eye* 2001; 15:1-2.
15. Klein R, Klein BE, Moss SE and Linton KL. The Beaver Dam Eye Study. Retinopathy in adults with newly discovered and previously diagnosed diabetes mellitus, *Ophthalmology* 1992;99:58-62.
16. Ling R, Ramsewak V, Taylor D, Jacob J. Longitudinal study of a cohort of people with diabetes screened by the Exeter Diabetic Retinopathy Screening Programme. *Eye* 2002;16:140-145.
17. Mitchell P, Smith W, Wang JJ, Attebo K. Prevalence of diabetic retinopathy in an older community. The Blue Mountains Eye Study. *Ophthalmology* 1998;105:406-411.
18. McKay R, McCarty CA, Taylor HR. Diabetic retinopathy in Victoria, Australia: the Visual Impairment Project. *Br J Ophthalmol* 2000; 84: 865-870.
19. Hove MN, Kristensen JK, Lauritzen T, Bek T. The prevalence of retinopathy in an unselected population of type 2 diabetes patients from Arhus County, Denmark. *Acta Ophthalmol Scand* 2004;82:443-448.
20. Giuffre G, Lodato G, Dardanoni G. Prevalence and risk factors of diabetic retinopathy in adult and elderly subjects: the Casteldaccia Eye Study. *Graefe's Arch Clin Exp Ophthalmol* 2004;242:535-540.
21. Tapp RJ, Shaw JE, Harper CA, deCourten MP, Balkau B, McCarty DJ et al. The prevalence of and factors associated with diabetic retinopathy in the Australian population. *Diabetes Care* 2003;26:1731-1737.
22. Wong TY, Klein R, Islam FM, Cotch MF, Folsom AR, Klein BE et al. Diabetic retinopathy in a multi-ethnic cohort in the United States. *Am J Ophthalmol* 2006;141:446-455.
23. Mohamed Q, Gillies MC, Wong TY. Management of diabetic retinopathy: a systematic review. *JAMA* 2007; 298:902-916.

24. Emanuele N, Sacks J, Klein R, Reda D, Anderson R, Duckworth W et al. Ethnicity, race and baseline retinopathy correlates in the veterans affairs diabetes trial. *Diabetes Care* 2005; 28:1954-1958.
25. McCarty DJ, Fu CL, Harper CA, Taylor HR, McCarty CA. Five-year incidence of diabetic retinopathy in the Melbourne Visual Impairment Project. *Clin Exp Ophthalmology* 2003;3:397-402.
26. Cikamatana L, Mitchell P, Rochtchina E, Foran S, Wang JJ. Five-year incidence and progression of diabetic retinopathy in a defined older population: the Blue Mountains Eye Study. *Eye* 2007;21:465-471.
27. Tapp RJ, Tikellis G, Wong TY, Harper CA, Zimmet PZ, Shaw JE. Longitudinal association of glucose metabolism with retinopathy: results from the Australian Diabetes Obesity and Lifestyle (AusDiab) Study. *Diabetes Care* 2008; 31: 1349-54.
28. 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; 20:758-765.
29. Younis N, Broadbent DM, Vora JP, Harding SP: Liverpool Diabetic Eye Study. Incidence of sight-threatening retinopathy in patients with type 2 diabetes in the Liverpool Diabetic Eye Study: a cohort study. *The Lancet* 2003; 361:195–200.
30. Hovind P, Tarnow L, Rossing K, Rossing P, Eising S, Larsen N et al. Decreasing incidence of severe diabetic microangiopathy in type 1 diabetes. *Diabetes Care* 2003; 26:1258-1264.
31. Chaturvedi N, Porta M, Klein R, Orchard T, Fuller J, Parving HH et al. Effect of candesartan on prevention (DIRECT-Prevent 1) and progression (DIRECT-Protect 1) of retinopathy in type 1 diabetes: randomised, placebo-controlled trials. *The Lancet* 2008; 372: 1394-1402.
32. Delcourt C, Vauzelle-Kervroedan F, Cathelineau G and Papoz L. Low prevalence of long-term complications in non-insulin-dependent diabetes mellitus in France: a multicenter study. CODIAB-INSERM-ZENECA Pharma Study Group. *J Diabetes Complications* 1998;12:88-95.
33. Delcourt C, Villatte-Cathelineau B, Vauzelle-Kervroedan F, Papoz L and the CODIAB-INSERM-Zeneca Pharma study group. Clinical correlates of advanced retinopathy in type II diabetic patients: implications for screening. *J Clin Epidemiol* 1996;49:679-685.

34. Delcourt C, Villatte-Cathelineau B, Vauzelle-Kervroedan F, Cathelineau G, Papoz L and the CODIAB-INSERM-Zeneca Pharma study group. Visual impairment in type 2 diabetic patients. *Acta Ophthalm Scand* 1995;73:293-298.
35. Grimaldi A, Grangé V, Allanic H, Passa P, Rodier M, Cornet P et al. Epidemiological analysis of patients with type 2 diabetes in France. *J Diabetes Complications* 2000;14:242-249.
36. LeFloch JP, Thervet F, Desriac I, Boyer JF, Simon D. Management of diabetic patients by general practitioners in France 1997: an epidemiological study. *Diabetes & Metab* 2000;26:43-49.
37. Detournay B, Cros S, Charbonnel B, Grimaldi A, Liard F, Cogneau J et al. Managing type 2 diabetes in France: the ECODIA survey. *Diabetes Metab* 2000;26:363-369.
38. Fagot-Campagna A, Fosse S, Weill A, Simon D, Varroud-Vial M. Rétinopathie et neuropathie périphérique liées au diabète en France métropolitaine: dépistage, prévalence et prise en charge médicale, étude Entred 2001. *BHE* 2005;12-13:48-50.
39. Rubino A, Rousculp MD, Davis K, Wang J, Girach A. Diagnosed diabetic retinopathy in France, Italy, Spain and the United Kingdom. *Primary Care Diabetes* 2007;1:75-80.
40. Weill A, Ricordeau P, Vallier N, Bourrel R, Allemand H. Les modalités de suivi des diabétiques non insulino traités en France métropolitaine durant l'année 1998. *Diabetes Metab* 2000;26:39-48.
41. De Pourville G. Démographie en ophtalmologie 2000-2020. Caisse Nationale de l'Assurance Maladie des Travailleurs Salariés. Rapport 24; septembre 2003.
42. Societe Française d'Ophtalmologie, SFO. Recommandations médicales pour le dépistage de la rétinopathie par photographies du fond d'œil. 2006; 27 p.
43. Direction Générale de la Santé, DGS. La prévention des complications du diabète. Rencontre presse. 6 juillet 2005. 32 p.
44. Aptel F, Gensburger M, Rouberol F, Denis PH, Thivolet C [Abstract]. Dépistage de la rétinopathie diabétique par rétinocamera non-mydriatique. *Diabetes Metab* 2006;32:1S49.
45. Massin P, Aubert JP, Eschwege E, Erginay A, Bourovitch JC, BenMehidi A et al. Evaluation of a screening program for diabetic retinopathy in a primary care setting DODIA (Depistage Ophtalmologique du DIAbete) study. *Diabetes Metab* 2005;31:153-162.
46. Lesven S, Roudaut N, Sonnet E, Bettembourg O, Kerlan V [Abstract]. Retinophotographe:fiabilité des images et interprétation. *Diabetes Metab* 2006;32 :1S48.

47. Lemaire C, Bonnel P, Fasquel V, Gillot C, Douillard C, Fruchart D et al [Abstract]. Dépistage itinérant de la rétinopathie diabétique au moyen d'un rétinographe non mydriatique: une première expérience française. *Diabetes Metab* 2004;30 (suppl 1):1S64.
48. Soulié-Strougar M, Charles A, Métral P, Quercia P, Souchier M, Chirpaz L et al. Dépistage de la rétinopathie diabétique en Bourgogne par un rétinographe non mydriatique itinérant. *J Fr Ophtalmol* 2007;30:121-126.
49. Massin P, Chabouis A, Erginay A, Viens-Bitker C, Lecleire-Collet A, Meas T et al. OPHDIAT: A telemedical network screening system for diabetic retinopathy in the Ile-de-France. *Diabetes Metab* 2008; 34:227-234.

Tables

Table 1 – Prevalence of diabetic retinopathy in Western countries (population based studies, reference method for DR diagnosis)

Table 2 – Incidence of diabetic retinopathy in Western countries

Table 3 - Prevalence of known diabetic retinopathy in France (physicians' declarations)

Table 4 - Prevalence of diabetic retinopathy in France (screening programs)

Table 1 – Prevalence of diabetic retinopathy in Western countries (population based studies, reference method for DR diagnosis)

Study (reference)	Setting Country, Period	No. of diabetic patients Diabetes type	Mean age (yrs) (min-max or ± SD)	Mean duration of diabetes (yrs) (min-max or ± SD)	Prevalence of DR		
					Any DR	PDR	MO
Beaver Dam Eye Study [15]	Population-based USA, 1988-1990	445 (435 with gradable photographs) Type 2 Known, 395; newly diagnosed, 50	NK (≥ 43 yrs)	NK	36.8%	1.8%	3.0
EDRS, Exeter Diabetic Retinopathy Screening Programme [16]	Population from Exeter United Kingdom, 1992	775 Type 1 & 2	72.1 (15-100)	13.0 (1-79)	24.2%	2.8%;	6.1%
Blue Mountains Study [17]	Older residents (age ≥ 49) from Sydney Australia, 1992-1994	256 (253 with gradable photographs) Type 1 & 2 Known, 214; newly diagnosed, 39	NK (≥ 49 yrs)	Newly diagnosed: 15.4% 1-9 yrs: 54.9% 10-19 yrs: 20.9% ≥ 20 yrs: 8.7%	32.4%	1.6%	4.3%
VIP, Visual Impairment Project [18]	Victorian residents (age ≥ 40) Australia, 1992-1996	234 Type 1 & 2	64.2* (45-91)	14.6* (0-44)	29.1%	4.2%;	5.6%
Arhus County [19]	Representative sample of diabetic patients from Arhus County Denmark, 2000	378 Type 2	65 ± 12	9 ± 8	31.5%	2.9%,	5.3%
Casteladaccia Eye study [20]	Population-based (age ≥ 40) Italy (Sicily)	132 Type 1 & 2	40-49:7.6% 50-59:18.2% 60-69:46.2% ≥70: 28.0%	* 1-9 yrs: 29.5% 10-19 yrs: 40.9 % ≥ 20 yrs: 29.5%	34.1%	4.5%	7.6%
AusDiab, Australian Diabetes, Obesity and Lifestyle study [21]	Population-based (age ≥ 25) Australia, 2002	333 with type 2 known diabetes	65± 11**	7 ** (0-15)	21.9%	2.1%	3.3%
MESA, Multi Ethnic Study of Atherosclerosis [22]	Subjects free of cardiovascular disease Prospective cohort USA, 2002-2006	153 *** Type 1 & 2	64.3 ± 9.5	8.5± 8	24.8%	2.6%	2.7%
Total					Weighted Mean****		

DR, diabetic retinopathy; PDR, proliferative diabetic retinopathy; MO, macular oedema; NK, not known (not indicated in the article) * patients diagnosed with DR only ** type 2 known diabetic patients diagnosed with DR only *** subset of Caucasian patients only. ****: weighted mean, using the numbers of subjects included in each study as weights.

Table 2 – Incidence of diabetic retinopathy in Western countries

Study (reference)	Setting Country, Period	No. of patients Diabetes type	Incidence of DR
Visual Impairment Project [25]	Population-based Australia 1992-1994 (follow-up data conducted 5 years later)	121 Type 1 & 2	Cumulative incidence (5-year): Any DR: 11% (95% CI: 3.8-18.1) Proliferative DR: 2.9% (95% CI: 0-6.4) Macular Oedema: 8% (95% CI: 2.7-13.3%)
Blue Mountains Study [26]	Population-based (older residents) Australia 1992-1994	150 Type 1 & 2	Cumulative incidence (5-year): Any DR: 22.2% (95% CI: 14.1-32.2)
AusDiab, Australian Diabetes, Obesity and Lifestyle study [27]	Population-based (age ≥ 25) Australia, 2002	144 with known diabetes 168 with newly diagnosed diabetes	Cumulative incidence (5-year): Any DR: 13.9 % PDR : 0.7 % Any DR: 3.0 % PDR : 0.0 %
Steno Diabetes Center [30]	Clinic-based cohort Denmark Patients managed until year 2000	600 Type 1 (4 groups of patients, based on the year of diabetes onset)	Cumulative incidence of DR (patients followed ≥ 20 years): Group A, B, C (onset of diabetes between 1965 and 1979): 31.2 % (95% CI: 22.2-39.8), 30.3 % (95% CI: 22.2-38.4), 19.3 % (95% CI: 11.2-27.4), respectively. Group D (patients referred between 1979 and 1984): 12.5 % (95% CI: 5.2-19.8)
Liverpool Diabetic Eye Study [28]	Screening population in primary care Scotland 1991-1999	501 Type 1	Cumulative incidence (5-year): Any DR: 36.8% (95% CI: 29.6-44.1) Sight-threatening DR: 3.9% (95% CI: 1.4-5.4) Sight-threatening maculopathy: 3.2% (95% CI: 1.0-5.4)
[29]		3743 Type 2	Cumulative incidence (5-year): Any DR: 30.5% (95% CI: 28.2-32.8) Sight-threatening DR: 3.9% (95% CI: 2.8-5.0) Sight-threatening maculopathy: 3.2% (95% CI: 2.2-4.2)

DIRECT-Prevent 1 [31]	Randomized, placebo-controlled trial with candesartan International, multicenter 2001-2008	1421 (placebo, 710) Type 1 Normotensive patients, Treated with insulin	Cumulative incidence (4.7 years) in the placebo group: 31%
---------------------------------	---	---	---

CI, Confidence Interval; DR: diabetic retinopathy

Table 3 - Prevalence of known diabetic retinopathy in France (physicians' declarations)

Reference	Setting Study period	Diabetes type Number of patients	Prevalence of known DR (physicians' declarations)
Grimaldi et al. [35]	1203 GPs 1996-1997	5548 Type 2 Patients planned to be treated with acarbose	12%
LeFloch et al. [36]	3084 GPs 1996-1997	7391 Type 1, 8.9%; Type 2 + insulin, 18.7%, Type 2 no insulin: 72.4%	31.1% (type 1) 12.9% (type 2, receiving insulin) 8.6% (type 2, not receiving insulin) 62.9%, 51.5% and 49.4% respectively consulted an ophthalmologist within the past year
ECODIA [37]	Representative sample: 311 GPs, 51 diabetologists/endocrinologists 1998-1999	4119 Type 2	10,6 % (95% CI, 9.5-11.6)
Entred [38]	Representative sample: Patients reimbursed for OADs or insulin 1718 physicians 2001	3648 Type 1 & 2	9,9 % 43% consulted an ophthalmologist during the past year (based on reimbursement data)
Rubino et al. [39]	France, Italy, Spain, UK: total 162 physicians (France, 49 GPs) 2005	Recorded diagnosis of DR: Total: 752 patients* (type 2, 72%) France : 130 patients (type 2, 59.2%)	France: 11,4 % (95% CI, 8.8-13.9%)

CI, Confidence Interval; GPs, general practitioners; OAD, oral antidiabetic drug,* patients with recorded diagnosis of DR

Table 4 – Prevalence of diabetic retinopathy in France (screening programs)

Reference	Characteristics, Study period	No. of patients Diabetes type	Prevalence of DR
DODIA [45]	Non mydriatic photography <i>versus</i> dilated eye examination Patients from primary care North of Paris 2002	882 Type 1 & 2	17.3% (non mydriatic camera) <i>vs</i> 10.4% (dilated eye exam)
Lesven et al. [46]	Non mydriatic photography Inpatients, Brest's Hospital	767	10%
PREVART [47]	Ambulatory screening Non mydriatic photography Artois 2002-2003	1322 Type 2	7%
Soulié-Strougar et al. [48]	Ambulatory screening Non mydriatic photography Burgundy 2004-2005	676 Type 1 & 2	8.6% (n=58, including 2 patients with known, inactivated DR)
OPHDIAT [49]	Non mydriatic photography 16 screening centres, Ile de France Sept 2004 – Dec 2006	13777 Type 1 & 2	23.4% 5.6% with severe DR requiring urgent referral

DR, diabetic retinopathy