First diabetic retinopathy prevalence study in Portugal: RETINODIAB Study—Evaluation of the screening programme for Lisbon and Tagus Valley region

Marco Dutra Medeiros,1,2,3 Edgar Mesquita,4 Ana Luísa Papoila,5,6,7 Victor Genro,1 João Filipe Raposo1,8

ABSTRACT

Background/aims In Portugal, so far, there is no study or even accurate data on the prevalence of diabetic retinopathy (DR), based on a large representative sample and on a long-term follow-up. The objective of our study was to determine the prevalence of DR based on a national screening community-based programme.

Methods A 5-year retrospective analysis of the RETINODIAB screening programme results was implemented in Lisbon and Tagus Valley area between July 2009 and October 2014. We estimated the prevalence of retinopathy for all patients with type 2 diabetes and studied the association between known risk factors and retinopathy emergence at their first screening.

Results Throughout this period, from a total of 103 102 DR readable screening examinations, 52 739 corresponded to patients who attended RETINODIAB screening at entry. Globally, DR was detected in 8584 patients (16.3%). Of these, 5484 patients (10.4%) had mild non-proliferative (NP) DR, 1457 patients (2.8%) had moderate NPDR and 672 (1.3%) had severe NPDR. Finally, 971 patients (1.8%) had proliferative DR requiring urgent referral to an ophthalmologist. The presence of any DR, non-referable DR or referable DR was strongly associated with increasing duration of diabetes and earlier age at diagnosis.

Conclusions The prevalence rate of DR in our study (16.3%) was slightly lower than other published international data. The RETINODIAB network proved to be an effective screening programme as it improved DR screening in Lisbon and Tagus Valley surrounding area.

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of legal blindness in the working-aged population of industrialised societies.1–3 In 2013, 382 million people had diabetes; this number is expected to rise to 592 million by 2035, according to the International Diabetes Federation (IDF).4,5

It is well established that the effectiveness of the laser treatment depends on the accuracy and timely treatment of DR among patients with diabetes mellitus, particularly those with a high risk of DR.6 Indeed, DR represents an excellent paradigm for screening as laid out in the principles for screening of human disease described by Wilson and Jungner in 1968.7,8

In order to decrease by about 30% the new cases of blindness caused by diabetes, the declaration of St. Vincent (1989) called for the implementation of national strategies for screening for DR in a systematic manner.9 WHO and the Directorate-General of Health (DGS) co-organised (1997) the Fourth Meeting in Lisbon for the Implementation of the St. Vincent Declaration on Diabetes Care and Research in Europe, which was attended by delegates from 60 countries.10 This conference reinforced once again the need for greater engagement from all signatory countries for the St. Vincent Declaration in order to address diabetes complications, particularly DR. This international challenge was strengthened at the Liverpool meeting in 2005.11 Despite all, it is only in the last decade that significant progress has been made in implementing screening programmes to detect and monitor DR.

Portugal currently has a population of 10.6 million, predominantly Caucasian, whose majority (around 8.5 million) is located on the western coast (~80%).12 According to the National Observatory for Diabetes, nearly one million Portuguese have diabetes, the equivalent to 13% of the population between 20 and 79 years.13 Of these, about 400 000 people are undiagnosed. It is imperative that these people are identified through early diagnosis in order to significantly reduce the incidence of serious complications.

The Portuguese Diabetes Association (APDP) is the world’s oldest diabetes association and a senior member of the IDF. From the moment it was founded, early in the 20th century, APDP has been driven by a single overarching objective: to improve the quality of life of people with diabetes. Involved nationally in diabetes advocacy and the provision of education, as well as the delivery of care, APDP has become a key player in the healthcare arena in Portugal.

Following a pilot regional DR screening programme which was launched in 2008, the Diabetic Retinopathy Screening Service for Lisbon and Tagus Valley—RETINODIAB—was commissioned and driven by APDP. This screening programme is supported by the Regional Health Administration of Lisbon and Tagus Valley (ARSLVT) and follows the norms of the DGS, which is a public body of the Ministry of Health. The major aim of the programme was to identify all undiagnosed sight-threatening DR in order to ensure timely onward referral to Lisbon area hospital eye services.

Herein, the authors describe the first Portuguese study regarding the prevalence of DR, as well as focus on the screening programme for DR (2009–2014) implemented in the area of Lisbon and Tagus Valley.
METHODS
The RETINODIAB network
RETINODIAB (Study Group for Diabetic Retinopathy Screening) is a m-health screening system carried out by APDP, which focuses on clinical aspects of DR screening. Its primary aim is to promote the advancement of knowledge on all aspects of DR through an active cooperation between ophthalmologists and other specialists such as endocrinologists, internists and neurologists. Additionally, APDP has fostered the development of important scientific studies in epidemiology and diabetology in Portugal.14 15

Lisbon and Tagus Valley area
Lisbon and Tagus Valley is one of the five Regions of Portugal (Nomenclature of Territorial Units for Statistics (NUTS) II divisions). It corresponds to 13% of the Portuguese territory, it has a population of 3.7 million (34.7% of the total population) and it represents 44% of the national Gross domestic product (GDP). There are 15 primary care groups (ACES) in this area (figure 1) organised according to the five existing NUTS III (subregions: Greater Lisbon, Setúbal Peninsula, Middle Tagus and Lezíria West Coast).

Figure 1  Regional Health Administration of Lisbon and Tagus Valley geographic area.

were classified as having proliferative retinopathy. Both eyes were assessed for DR and the worse grade from the two eyes was used in the analysis. Retinal images were considered not gradable if retinas of both eyes could not be visualised properly—that is, retinal vessels were not visible within 1 disc diameter of the fovea and fine vessels were not visible across the surface of the optic disc. Where only one eye was gradable, the presence or absence of DR relied on this eye. The reader-automatically generated report displays diagnosis of DR level, diagnosis of non-diabetic ocular disorders and recommendations for follow-up (figure 2).

APDPSoft software
The APDPSoft is a software developed since 1999, which accompanies the evolution of the services provided by the APDP. Currently, this software supports and monitors several valences, especially in terms of clinical data file, markings management, laboratory parameters, invoicing the health subsystem, integration of numerous diagnosis equipments as well as an effective liaison with the electronic services of the Ministry of Health. It makes the storage of clinical data, fundus photographs and statistics. All stored images were downloaded by certified ophthalmologists at the RETINODIAB Reading Centre comprising three readers.

Statistical methods
The features of the study participants were described using means (SD) for continuous variables and percentages for categorical variables. The age at diagnosis was categorised into four groups (40–49 years, 50–59 years, 60–69 years and >70 years) for all analyses at first screening. The duration of diabetes was discretised into four categories (<5 years, 5–9 years, 10–15 years and >15 years). Adjusted ORs and corresponding 95% CIs were calculated. Furthermore, we defined referable diabetic retinopathy (RDR) to all patients graded as moderate non-proliferative (NP) DR, severe NPDR or proliferative retinopathy DR (with or without maculopathy) or maculopathy with mild retinopathy. This category relates to those who would, according to the guidelines, need referral to the hospital eye service for further clinical evaluation. Univariable and multivariable logistic regression models were used to assess the association of the collected variables with retinopathy status, separately for each subset of diabetes (any DR; RDR; non-referable diabetic retinopathy (NRDR)). A level of significance of α=0.05 was considered. All data were analysed using the Statistical Package for the Social Sciences for Windows V22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, V22.0. Armonk, New York: IBM Corp.).

RESULTS
Our 5-year retrospective analysis included data for all patients with type 2 diabetes, diagnosed over the age of 40 years, and who attended APDP between July 2009 and October 2014. Throughout this period, from a total of 103 102 DR readable screening examinations, 52 739 corresponded to patients who attended RETINODIAB screening at entry. The baseline features of study participants are included in table 1. Patients’ mean age is 69.13 (SD=11.13) years. Women accounted for 49.6% (n=26 149) of all patients. The mean duration of diabetes was 8.5 years (SD=7.89).

Overall, not all screening examinations resulted in assessable images. In our present study, retinal photographs of at least one eye could not be graded in 2757 of the 55 496 total screening patient examinations performed at entry (4.96%). This subset of patients was not included in the final group used to calculate several prevalence rates (total number of DR diagnoses performed).

The prevalence of the different categories of DR is shown in table 2, regarding to the total number of assessable images. Globally, DR was detected in 8584 patients (16.3%). Of these, 5484 patients (10.4%) had mild NPDR, 1457 patients (2.8%) had moderate NPDR and 672 (1.3%) had severe NPDR. Finally, 971 patients (1.8%) had proliferative DR requiring urgent referral to an ophthalmologist. A total of 732 patients (1.4%) had maculopathy.

The results of the multivariable logistic regression analysis are shown in table 3. Men had increased odds of all severities of DR compared with women. The odds of all grades of DR increased with the duration of diabetes. There was a 2.50-fold, 4.99-fold and 8.20-fold increased odds of any DR associated with a duration of diabetes.
of diabetes of 5–9, 10–15 and ≥15 years compared with <5 years (reference subgroup) and a 2.38-fold, 4.19-fold and 5.03-fold increased odds of NRDR in the same subgroups, respectively. For RDR subset of patients, the odds increased by a factor of 2.80 with a known duration of diabetes of 5–9 years and 6.37-fold for a known duration of diabetes of 10–15 years. Finally, for patients with a duration over 15 years the odds increased 12.43-fold compared with the reference subgroup.

Additionally, the ORs of any DR, NRDR and RDR groups were significantly lower with the increasing of age at diagnosis of diabetes. For instance, the odds of any DR increased to 1.12, to 1.48 and to 2.00 in the age ranges 60–69 years, 50–59 years and > under 50 years, respectively, compared with the reference group (> 70 years).

Regarding insulin treatment, all patients with diabetes under insulin therapy had a significant increased odds for all different DR subgroups.

**DISCUSSION**

Until now, there have been no studies addressing the prevalence of DR in Portuguese type 2 diabetic population, which include a large sample size and a long-term follow-up.

Diabetes has a high prevalence in Portugal. The PREVADIAB Study\(^4\) which was carried out by APDP found a diabetes prevalence of 11.7%, with a significant difference between men (14.2%) and women (9.5%). While 6.6% (approximately 508 000 people) had previously been diagnosed with diabetes, 5.1% (around 393 000 persons) were undiagnosed. On the other hand, the prevalence of ‘pre-diabetes’ (impaired fasting glucose, impaired glucose tolerance or both) in the population was 23.3%. In our study, we reported a prevalence of any DR, NRDR and RDR in patients with type 2 diabetes of 16.3%, 10.4% and 5.9%, respectively.

The teleophthalmology network constitutes an efficient means to overcome the lack of ophthalmologists.\(^1\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\) In accordance with the aforementioned, Portugal may have about one million people with diabetes, of whom 700 000 diagnosed and on medical treatment and who should be consulted annually according to the criteria stated above. According to the Portuguese Ophthalmology Society (SPO), each of the 930 Portuguese ophthalmologists (2012 data) would have to observe about 753/each year, an infeasible number in terms of logistics specialty requirements. Moreover, screening centres or mobile units using non-mydriatic cameras should be allocated in areas with a high rate of poverty and a low number of ophthalmologists, like the West Region of Portugal, which is covered by RETINODIAB programme. Additionally, the centralisation of the network around a central reading headquarters provides a quality control and uniformity between graders.

The epidemiological studies addressing DR prevalence in type 2 diabetes have varied worldwide, at least partly due to different ethnic populations and different sample sizes.\(^10\)\(^1\)\(^2\)\(^3\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\)\(^12\) Nevertheless, the comparison of the DR prevalence rates between published studies is difficult due to the lack of uniformity regarding the different grading protocols employed. In France, Massin et al \(^1\) carried out several epidemiological studies addressing DR screening in Paris and the surrounding area.\(^2\) They documented a prevalence of any DR around 24%. Several UK screening programmes evaluated the prevalence of DR for type 2 diabetes. The Scottish programme ascertained the DR prevalence in 47 090 newly diagnosed patients with type 2 diabetes and reported at 19.3% for any DR and 1.9% for RDR.\(^2\)\(^1\)\(^2\)\(^3\) Furthermore, Thomas et al\(^2\)\(^4\) undertook a cross-sectional analysis of 86 390 patients with type 2 diabetes in Wales. They documented a prevalence of any DR and sight-threatening DR of 30.3% and 2.9%, respectively. Similarly, the presence of DR, non-sight-threatening and sight-threatening, was strongly associated with either variables: increasing duration of diabetes and earlier age at diagnosis. In Iceland, the prevalence of DR was higher in type 2 diabetes, estimated at 41.0%.\(^2\)\(^5\) The prevalence rate of DR in our study (16.3%) was slightly lower than other published data. Indeed, all patients previously diagnosed with DR had been already previously forwarded, and only patients whose retinal status was unknown were included in this study.

Regarding logistic regression analysis, the duration of diabetes was a significant risk factor for the presence of any DR, NRDR and referable diabetic retinopathy (RDR) in subjects with type 2 diabetes. Multivariable adjusted ORs were much higher in all DR subgroups, in the longer time frame (over 15 years), compared with other shorter periods of time. The strong association with disease duration demonstrates the importance of early detection and enrolling to a screening programme. Moreover, a later age

### Table 1  Baseline features of study participants at time of first screening event

<table>
<thead>
<tr>
<th>Features</th>
<th>Type 2 diabetic patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients screened</td>
<td>55 496</td>
</tr>
<tr>
<td>Total number of diagnoses done*</td>
<td>52 739</td>
</tr>
<tr>
<td>Patients screened with unassessable images</td>
<td>2757</td>
</tr>
<tr>
<td>Gender n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 590 (50.4)</td>
</tr>
<tr>
<td>Female</td>
<td>26 149 (49.6)</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>69.13 (11.13)</td>
</tr>
<tr>
<td>Mean age at diagnosis, years</td>
<td>60.63 (12.15)</td>
</tr>
<tr>
<td>Mean duration of diabetes, years</td>
<td>8.5 (7.89)</td>
</tr>
<tr>
<td>Treatment of diabetes</td>
<td></td>
</tr>
<tr>
<td>Oral hypoglycemic agents/diet only</td>
<td>50 581 (95.9)</td>
</tr>
<tr>
<td>Insulin</td>
<td>2157 (4.1)</td>
</tr>
</tbody>
</table>

*Total number of examinations with gradable photographs (used to calculate prevalences).

### Table 2  The prevalence of diabetic retinopathy (DR) at first screening for all patients successfully screened

<table>
<thead>
<tr>
<th>DR status</th>
<th>Patients</th>
<th>Per cent</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>52 739</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>No DR</td>
<td>44 155</td>
<td>83.7</td>
<td></td>
</tr>
<tr>
<td>Any DR</td>
<td>8584</td>
<td>16.3%</td>
<td>(16 to 16.5)</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>5484</td>
<td>10.4%</td>
<td>(10.1 to 10.7)</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>1457</td>
<td>2.8%</td>
<td>(2.6 to 2.9)</td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>672</td>
<td>1.3%</td>
<td>(1.2 to 1.4)</td>
</tr>
<tr>
<td>PDR</td>
<td>971</td>
<td>1.8%</td>
<td>(1.7 to 2.0)</td>
</tr>
<tr>
<td>Maculopathy</td>
<td>732</td>
<td>1.4%</td>
<td>(1.3 to 1.5)</td>
</tr>
<tr>
<td>Non-referable DR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild NPDR without maculopathy</td>
<td>5258</td>
<td>9.99%</td>
<td>(9.9 to 10.1)</td>
</tr>
<tr>
<td>Referable DR</td>
<td>3326</td>
<td>6.31%</td>
<td>(6.2 to 6.4)</td>
</tr>
<tr>
<td>Mild NPDR with maculopathy</td>
<td>226</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate NPDR with maculopathy</td>
<td>1220</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe NPDR with maculopathy</td>
<td>237</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDR without maculopathy</td>
<td>516</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDR with maculopathy</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDR without maculopathy</td>
<td>858</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDR with maculopathy</td>
<td>113</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.
of diagnosis has a protective effect regarding all grades of DR. Indeed, all patients who were diagnosed over the age of 70 years have twofold lower risk of developing any DR compared with all patients with diabetes diagnosed under 50 years old. This is in accordance with several studies that advise a variable schedule distribution of screening intervals according the individual patients’ risk. In fact, increasing the length of the screening intervals for lower risk cases would involve less screening episodes, with resulting benefits in terms of health costs.24,25

The main purpose of RETINODIAB implementation was to improve DR screening in Lisbon and Tagus Valley surrounding area in order to efficiently perform, within an acceptable time frame, all eye examinations according to the guidelines of the DGS.25

This study provides the first estimate of the prevalence of DR for subjects over the age of 40 years and not receiving ophthalmological assistance in Portugal. In line, to the best of our knowledge, this study represents the second largest reported international community-based DR screening network. We will continue to follow these patients to better define all clinical and epidemiological data regarding this diabetic population.

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Contributors All authors have contributed to the planning, conduct and reporting of the work described in the article.

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Competing interests None.

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