Background: Diabetic retinopathy is a leading cause of adult blindness and accounts for about 10% of cases of legal blindness in Israel. Only about half of the patients with diabetes in Israel have regular eye examinations.

Objectives: To evaluate, for the first time in southern Israel, a new service for diabetic retinopathy screening that uses a mobile non-mydriatic mobile fundus camera in primary care patients.

Methods: Diabetic members of the largest health fund in southern Israel and over 18 years old were invited for non-mydriatic fundus examination between January and October 2009. Screening was performed by a trained photographer using the Topcon TRC NW-6S non-mydriatic camera in nine primary care centers.

Results: A total of 4318 diabetic patients were screened, of whom 53% were classified as normal. The incidence of diabetic retinopathy was 15.8% (1.2% had proliferative retinopathy and 2.4% had suspected macular edema and were referred for laser treatment). Other possible sight-threatening conditions were detected in 9.3%. Fundus pictures were inadequate for assessment in 16% of cases.

Conclusions: Diabetic retinopathy screening with a mobile non-mydriatic fundus camera improved the quality of care for diabetic patients in southern Israel. This screening method identified patients requiring prompt referral to the ophthalmologist for further complete eye examination. Extending this screening program to other areas in the country should be considered.

Diabetic retinopathy is the leading cause of new cases of legal blindness among working-age Americans [1]. In Israel, DR accounts for 14.4% of cases of legal blindness (the second highest cause of legal blindness after age-related macular degeneration, 2003 data) [2,3]. The prevalence rate of DR in adults aged 40 years and older in the United States is 3.4% [1].

The duration of diabetes is a major risk factor associated with the development of DR. After 5 years, approximately 25% of type 1 patients have retinopathy, and after 15 years 80%. Retinopathy is asymptomatic until an advanced stage, and consequently screening for its presence is essential to identify eyes that would benefit from laser therapy [1].

Screening for diabetic eye disease is usually performed with either direct screening by ophthalmologists or photographic screening (standard fundus photography or digital imaging, with and without eye dilation) [4]. The recently introduced and improved non-mydriatic fundus digital examination offers good technical results and is now widely accepted as an excellent DR screening method [5-10]. The technology has vastly improved patient access to DR screening in the UK, Australia, South Africa and Canada. Digital retinal imaging has been adopted as the DR screening standard in the UK [10].

A considerable difference in the prevalence of diabetic blindness is seen when comparing diabetic populations that have been involved in systematic screening programs with those that have not [4]. Adults with diabetes mellitus and without DR should have annual dilated eye examinations to detect the onset of DR. If some degree of DR is present, patients should have more frequent follow-ups.

From a socioeconomic point of view DR screening programs are very cost-effective. Compared to the cost of the prevention programs, the cost to society is 7–20 times greater when prevention is ignored and the consequences include supporting the blind [4]. Most major medical organizations and the World Health Organization recommend screening for diabetic eye disease. In Israel, only 62.79% of the patients with diabetes (2007 data) have regular eye examinations [11]. Therefore, screening for retinopathy can reduce the incidence of blindness in Israel.

The aim of the present study was to evaluate a new service for DR screening that uses a mobile non-mydriatic mobile fundus camera in primary care patients. This is the first time such a service has been evaluated in southern Israel.
PATIENTS AND METHODS

The research followed the tenets of the Declaration of Helsinki and the local Ethics Committee approved the study. Diabetic members of the largest health fund in Israel (Clalit), living in the southern region and > 18 years old were invited to non-mydriatic fundus examination between January and October 2009 as part of a new service offered to diabetic Clalit members. The main source of patients was those who, according to Clalit’s database, had not been examined by an ophthalmologist during the previous 12 months; also invited were diabetic patients undergoing regular eye examinations at the care center the same day and desiring digital fundus photography.

Screening was performed by a trained photographer using the Topcon TRC NW6S non-mydriatic camera in nine primary care centers: Beer Sheva, Rahat, Dimona, Sderot, Ashkelon, Kiryat Gat, Netivot, Arad, and Ofakim.

At least two 45-degree non-dilated fundus photographs of each eye were taken, centered on the disc, the macula, the temporal superior area, and the temporal area of the macula. The images were initially saved on the local hard drive in tagged image file (tif) format and transmitted at the end of each day to the Clalit server.

Within the next 2 weeks, the retinal images were reviewed and classified by a single experienced ophthalmologist (J.L.) at the reading center using one integrated workstation and monitor based on standard accepted scales. Reports were written in the patient digital file system and sent to both the family doctor and the patient. Cases with DR were followed according to the American Academy of Ophthalmology guidelines. Cases with other ocular sight-threatening pathologies and cases in which the quality of the digital pictures was considered inadequate for interpretation were referred for ophthalmic examination.

Between January and April 2010 a less trained photographer performed the screening. Comparison of the percentage of fundus pictures inadequate for evaluation between both photographers was also done. Since all pictures were examined by the same reviewer we also calculated the intra-observer agreement. Three hundred random pictures were evaluated in a masked fashion 8 months apart, at least of the first examination. The overall proportion of agreement was of 97.7% with an “almost perfect” kappa coefficient of 0.92.

RESULTS

Diabetic members of Clalit Health Services from nine primary care centers in southern Israel were invited for non-mydriatic fundus examination. The overall proportion of non-attendance was 41.8% (range 26.6–52.1%). Altogether, 4318 diabetic patients were screened. Among them, 33% were classified as normal and invited for digital fundus photography within one year. During the 2 years preceding the study 184 patients (4.26%) had not undergone an ophthalmic examination.

The incidence of DR was 15.8%: 10.6% of patients (456 cases) had mild non-proliferative diabetic retinopathy [Figure 1], 1.6% (70 cases) had moderate non-proliferative diabetic retinopathy, 1.2% (54 cases) had proliferative diabetic retinopathy, and 2.4% (102 cases) had suspected macular edema [Figure 2]. Patients were referred for close follow-up, laser...
We found that the percentage of fundus pictures inadequate for assessment in 16% of cases. Fundus pictures were considered inadequate for assessment in 16% of cases. In both of the above, patients were referred for complete ophthalmic examination. Other non-diabetic retinopathy frequent diagnoses detected were myopic changes, large drusen, macular scar/atrophy, and choroidal nevus.

The percentage of fundus pictures inadequate for evaluation was similar between the more trained photographer (16%, from January to October 2009) and the less trained photographer (14.7%, from January to April 2010, 1453 patients).

At the end of 2009 the rate of diabetic patients from Clalit in southern Israel undergoing at least one annual ophthalmic examination increased from 58% (2008 data) to 64.1% (vs. the national average of 62.79%).

**DISCUSSION**

Diabetes affects 8% of the population in Israel and about 20% of the population older than 65 years of age [11]. DR accounts for 14.4% of cases of legal blindness in Israel [2,3]. To reliably identify patients who are at risk for visual loss, annual dilated retinal examination is recommended and is considered the standard of care. Unfortunately, using this traditional approach to detect DR, only approximately half of all diabetic patients in the United States receive the recommended annual screening for DR [12]. There is an annual increment of 0.2% in the prevalence of diabetes in Israel, part of the worldwide increase of diabetes (the so-called diabetes epidemic) [11]. Eye fundus examinations will be required more and more frequently as the incidence of diabetes increases. This will increase the cost of medical care. These findings suggest that yearly screening for retinopathy using new screening programs is likely to be developed to satisfy future needs.

The introduction and improvement of non-mydriatic digital fundus examination has shown better sensitivity than direct ophthalmoscopy in screening for DR [13,14], although there is still some controversy about the importance of mydriasis and the number of photographic fields needed for adequate evaluation. Mydriasis has been reported to reduce the technical failure rate, although neither mydriasis nor more photographic fields appears to increase the sensitivity or specificity of detecting diabetic retinopathy [15], which is the ultimate objective in every DR screening program. The training of the photographer does not affect the image quality [16]. We found that the percentage of fundus pictures inadequate for evaluation was similar between the more trained photographer (16%) and the less trained photographer (14.7%).

In our study, the DR screening procedure with eye fundus digital non-mydriatic photographs primarily enabled the identification of a number of sight-threatening cases of DR that needed referral to the ophthalmologist. The proportion of inadequate images (16%) requiring additional eye fundus examination was found acceptable and comparable to other non-mydriatic screening methods. Secondly, DR screening with the non-mydriatic camera identified a majority of patients (53%) who were free of DR and did not need further eye examination. As a result, a number of ophthalmologic consultations could be spared and more medical time could be spent by the ophthalmologist for the affected DR cases and urgent conditions.

To the best of our knowledge there is only one report of DR screening using a non-mydriatic fundus camera in Israel [17]. Hauser et al. reported results on 3579 diabetic patients from Maccabi Health Services in the central and Jerusalem Districts examined between April 2008 and July 2009. These patients had not been examined by an ophthalmologist during the previous 12 months. DR was found in 6% of patients (after removing for analysis 34% of cases in which the quality of the images was inadequate for analysis). The number of normal cases was 51%, similar to the 53% rate in our study.

The main limitation of our study is the lack of comparison with a “standard” dilated retina examination to evaluate the sensitivity and specificity of the fundus camera (reported to be very good worldwide) in the Israeli setting, and the lack of correlation with epidemiological and laboratory data, such as duration of diabetes and treatment, chronic disease, glycosylated hemoglobin, creatinuria and body mass index, as reported in the literature. However, one must recognize that the nationally approved projects – mainly in the UK, South Africa and Canada – are not comparable with our pilot project. We are currently studying the data in some of the photographed cases to learn how to integrate all the electronic platforms (epidemiological, laboratory, and photographic data) and apply the learning in the near future.

**CONCLUSIONS**

DR screening with a mobile non-mydriatic fundus camera improved the quality of care for diabetic patients in southern Israel. The incidence of DR was 15.8% in the population examined. The use of digital retinal images was a suitable method for detecting and grading DR in primary care patients, and for filtering eye-threatening cases requiring complete eye analysis by an ophthalmologist. This study may suggest that this screening program be extended to other regions in Israel.

AAO = American Academy of Ophthalmology


**References**


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**Capsule**

**Hsp90 and environmental stress transform the adaptive value of natural genetic variation**

How can species remain unaltered for long periods yet also undergo rapid diversification? By linking genetic variation to phenotypic variation via environmental stress, the Hsp90 protein-folding reservoir might promote both stasis and change. However, the nature and adaptive value of Hsp90-contingent traits remain uncertain. In ecologically and genetically diverse yeasts, Jarosz and colleagues find such traits to be both common and frequently adaptive. Most are based on preexisting variation, with causative polymorphisms occurring in coding and regulatory sequences alike. A common temperature stress alters phenotypes similarly. Both selective inhibition of Hsp90 and temperature stress increase correlations between genotype and phenotype. This system broadly determines the adaptive value of standing genetic variation and, in so doing, has influenced the evolution of current genomes.

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**Capsule**

**Decoding a childhood cancer**

The identification of recurrent genetic changes in human tumors can provide important mechanistic insights into how tumors arise and, ideally, prompt new ideas for effective therapies. To date, this “cancer genomics” strategy has been applied only to adult cancers. Parsons et al. catalog the genetic alterations present in medulloblastoma, a brain tumor that mainly affects children. Interestingly, there were 5 to 10 times fewer genetic alterations in these tumors compared with solid tumors that typically affect adults. Among the most frequently mutated genes were those coding for enzymes that methylate histones, as well as genes affecting signaling pathways critical for normal brain development.

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