Journal of Diabetes and Its Complications 31 (2017) 721–725

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

# Data collection on retinopathy as a public health tool: The Hubble telescope equivalent of looking back in time

Maria I. Constantino [a,b,*], Lynda Molyneaux [a,b], Ted Wu [a], Stephen M. Twigg [a,b], Jencia Wong [a,b], Dennis K. Yue [a,b]

[a] Diabetes Centre, Royal Prince Alfred Hospital, Sydney, NSW, Australia
[b] Sydney Medical School, University of Sydney, Sydney, NSW, Australia

ARTICLE INFO

*Article history:*
Received 27 October 2016
Received in revised form 14 December 2016
Accepted 17 December 2016
Available online 21 January 2017

*Keywords:*
Retinopathy
HbA1c
Type 2 diabetes
Public health
Complications

ABSTRACT

*Objective:* To test whether the rate of diabetic retinopathy development in a population calculated from the prevalence of retinopathy and duration of diabetes can be used to assess their prior glycemic control.
*Research Design and Methods:* 9281 patients with type 2 diabetes (T2DM) were grouped by duration of diabetes and plotted against the % of retinopathy in each band. The slope was used to calculate retinopathy development/year (RD/y). We correlated the RD/y with updated HbA1c within groups of different ethnicity, age of diabetes onset, year of the eye examination, socio-economic status and fluency in English.
*Results:* Differences in ethnicity, age of diabetes onset and year of the eye examination affect RD/y to a degree predictable from their respective updated HbA1c. No such relationship with updated HbA1c was evident when a factor has no apparent effect on RD/y.
*Conclusions:* This relationship between prevalence of retinopathy and duration of diabetes can be used to assess future retinopathy burden. Perhaps more intriguing, the camera can be reversed to allow an estimate of prior glycemic control of a population from its retinopathy prevalence. Health care organizations can use this method to project future needs and to assess adequacy of prior glycemic control.


## 1. Introduction

Diabetic retinopathy (DR) is an important complication of diabetes which causes considerable morbidity and also associated with significant increase in mortality of those affected. At an individual level, the presence of retinopathy is best predicted, although far from perfectly, by the duration of diabetes and the overall glycemic exposure of the individual in the previous years (Klein, Klein, Moss, & Cruickshanks, 1994; Nathan, Singer, Godine, Harrington, & Perlmuter, 1986; Wong, Molyneaux, Constantino, Twigg, & Yue, 2008; Nordwall et al., 2015). By contrast to the relatively poor predictability at an individual level, investigators have previously demonstrated a strong linear relationship between duration of diabetes and prevalence of retinopathy at a population level, e.g., in a Wisconsin and a Western Australian population (Harris, Klein, Welborn, & Knuiman, 1992). The slope of such relationship between prevalence of retinopathy and duration of diabetes is a measure of the rate of retinopathy development per unit time for that population. We used patient information stored in our electronic database to test the hypothesis that the rate of retinopathy development calculated in this manner can be used to estimate the prior glycemic control of the population.

Our electronic database collected information including retinopathy status, duration of diabetes and glycemic control of our patients over more than two decades (McGill, Molyneaux, Yue, & Turtle, 1993). We used these data to construct the linear relationship between duration of diabetes and prevalence of retinopathy. As duration of diabetes is already accounted for in the *x*-axis, the slope of the linear regression should correlate well with the prior glycemic control of the individual group being examined. The implication being that, if this assumption is proven, cross-sectional data of retinopathy prevalence at various duration of diabetes in a defined population can be used to retrospectively assess the adequacy of glycemic control of that population in the preceding years. Health Maintenance Organizations and some community screening programs could have information on the status of retinopathy and duration of diabetes of their participants but not serial measurements of HbA1c (Scanlon, Aldington, & Stratton, 2014). Their data could be analyzed by our method to serve as an indirect measurement of the average glycemic control of their patients in the preceding 1–2 decades. By examining data of patients with defined criteria (e.g., according to their ethnicity or age of diabetes onset), the prior glycemic control of specifically defined groups of diabetic patients can be compared. Our

Conflicts of interest: The authors have no relevant conflicts of interest to declare.

* Corresponding author at: The Diabetes Centre, Royal Prince Alfred Hospital, Level 6, West Wing, Missenden Road, Camperdown, Sydney, NSW 2050, Australia. Tel.: +1 61 2 9515 5888; fax: +1 61 2 9515 5820.
*E-mail addresses:* maria.constantino@sydney.edu.au (M.I. Constantino), lyndamolyneaux@bigpond.com (L. Molyneaux), ted.wu@sswahs.nsw.gov.au (T. Wu), stephen.twigg@sydney.edu.au (S.M. Twigg), jencia.wong@sswahs.nsw.gov.au (J. Wong), dennis.yue@sydney.edu.au (D.K. Yue).

http://dx.doi.org/10.1016/j.jdiacomp.2016.12.016
1056-8727/

method which only requires cross-sectional and retrospective data could be a simple but useful public health tool.

## 2. Methods

The findings of this study were derived from a total cohort of 9281 patients with T2DM who had information collected prospectively during clinical consultations over a period of approximately two to three decades. For this study, the following data from each patient were retrieved from our electronic database: retinopathy status, HbA1c, ethnicity, date of diabetes diagnosis, date of last consultation with documented retinopathy data, socio-economic status and fluency in English. Retinopathy was detected by direct fundoscopy or in recent years by retinal photography and graded by a modified Airlie House Classification System into categories of no retinopathy or minimal, mild and moderate, severe non-proliferative retinopathy and proliferative retinopathy. All grades of retinopathy were pooled as "Any retinopathy" for analysis and the two most severe grades were also grouped as "Vision Threatening Retinopathy" for a separate analysis. For patients who had multiple visits, the eye data of the last visit were studied. HbA1c was measured by high performance liquid chromatography and updated HbA1c calculated according to the UKPDS formula (Stratton et al., 2000). Although the last eye data of each patient was used for analysis of retinopathy status, the updated HbA1c was calculated from all their visits and on average each patient had 4 measurements of HbA1c during follow up. Ethnicity was determined by self-reporting. Socio-economic strata were determined by the Index of Relative Socio-economic Disadvantage (IRSD) generated by the Australian Bureau of Statistics. The IRSD is a score derived from a range of information about economic and social conditions of people within a postcode area. Fluency in English was determined by the need for an interpreter during consultation and this was jointly determined by the patients and health professionals.

The prevalence of retinopathy of the total cohort was plotted against the duration of diabetes divided into four bands of 5 years up to 20 years. The median durations of diabetes for the four bands were 1.5, 7.3, 11.9 and 16.8 years respectively. Our study on mortality showed that after 20 years the mortality of patients with retinopathy became disproportionately higher and would lead to an under-estimation of the retinopathy prevalence. The slope of the regression line was calculated to derive the rate of retinopathy development per year. For validation purpose, in addition to each patient's last available eye data used for this study, we also determined the extent that calculated retinopathy development rate varied when using the data from the first or a randomly selected visit.

In addition to the study of the total cohort, patient data according to the following criteria were extracted for additional analysis:

(i) Ethnicity: Seven ethnic groups were studied including Anglo Celtic ($n = 3384$), Indigenous Australian ($n = 319$), Pacific Islander ($n = 236$), Mediterranean ($n = 1924$), Arabic ($n = 444$), Chinese ($n = 1040$) and Indian ($n = 456$). These ethnicities accounted for 78% of the total patient cohort attending the Diabetes Centre.
(ii) Age of diabetes onset: <30 y. ($n = 259$); 30-49 y. ($n = 3376$); ≥50 y. ($n = 5645$)
(iii) Year of the eye examination: between 1988 and 1997 ($n = 2864$); between 1998 and 2003 ($n = 2872$); after 2003 ($n = 3544$)
(iv) Socio-economic strata: Least disadvantaged ($n = 3837$); mid-disadvantaged (2337); most disadvantaged ($n = 2882$)
(v) Fluency in English: required an interpreter ($n = 1751$); not required an interpreter ($n = 6635$)

The linear regression equation between prevalence of retinopathy and duration of diabetes for each of the above studied group was constructed in the same way used for the total cohort. The slope of the regression was similarly used to calculate the rate of retinopathy development per year and results correlated with their respective updated HbA1c levels.

The ability of HbA1c and duration of diabetes and other factors (age, gender, blood pressure, and smoking status) to predict the presence of retinopathy in individuals of the 9281 subjects in the total cohort was determined by logistic regression. The rates of retinopathy development of different groups within a selection criteria were compared using multiple regression. Interaction terms were calculated between the groups and duration of diabetes, to establish any significant differences in the slope. ANOVA was used to detect differences in updated HbA1c between various subgroups with Bonferroni post-hoc test to adjust for multiple groups.

The collection of data from patients and its storage in our electronic database is approved by the Hospital Database Committee and approved by the Human Ethics Committee of the Area Health Service.

## 3. Results

Diabetes duration and updated HbA1c were relatively poor predictors for the presence of retinopathy in individuals. These two factors only accounted for 13.8% of the variance for the presence of retinopathy in individuals in the total cohort of 9281 patients. Other factors examined including age of diagnosis, blood pressure, smoking status and gender did not add to the prediction of retinopathy in individuals. By contrast, as shown in Fig. 1A and B, the relationship between duration of diabetes and group prevalence of retinopathy was extremely strong for both any retinopathy ($r = 0.99$) and vision threatening retinopathy ($r = 0.98$). From the slope of the regression, the rate of any retinopathy development for the total cohort can be calculated to be 2.62% per year and for vision threatening retinopathy 0.66% per year. Validation studies showed that the CV for the rate of retinopathy development calculated using the last or first or randomly selected visits of the patients was 4.3%.

The rates of retinopathy development/year for each of the criteria used in selecting patients and the corresponding updated HbA1c are shown in Table 1. These data indicate that patients of different ethnicity have differing rates of retinopathy development/year, to a degree strongly correlated with their updated HbA1c (Fig. 2A). The same pattern of results can also be observed on patients selected according to the year of eye examination (Fig. 2B) or according to the age of diabetes diagnosis (Fig. 2C). By contrast, there was no difference in retinopathy development among the subgroups for patients selected according to socio-economic status or language fluency and also no correlation with their respective updated HbA1c.

## 4. Discussion

It is well accepted that glycemic control and duration of diabetes are the major determinants for the presence of DR, but their predictive power for individual patients is only modest (Nathan, 2014; Group TDCaCTR, 1995). In our cohort these two factors only account for 13.8% of the variance of retinopathy, underlying the importance of routine screening in clinical practice. A less appreciated but the fundamental basis of our study is that, in contrast to the situation for individuals, duration of diabetes, even by itself, is an extremely powerful factor in predicting the prevalence of retinopathy in a group of individuals (Leal, Hayes, Gray, Holman, & Clarke, 2013). The slope of this relationship is a cross-sectional measure of the rate of retinopathy development for that population. The linear correlation coefficients between these two parameters in our study were always very strong. This relationship underpins the analysis made in the current study. The information in Table 1 provides examples of this. Knowing the trajectory of retinopathy development in any population facilitates the prediction for future burden due to retinopathy. Additionally, this type of data is also useful in assessing many other questions of potential public health importance. For example, our data revealed