EFFICIENCY OF CURRENT DIABETIC RETINOPATHY SCREENING RECOMMENDATIONS IN A PEDIATRIC POPULATION

by

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ABSTRACT

Diabetic retinopathy (DR) is a microvascular complication that typically occurs with greater frequency as disease duration increases. Both the American Diabetes Association and the International Society for Pediatric and Adolescent Diabetes make recommendations that patients be screened for retinopathy starting at age 10 and after a disease duration of greater than 2 years. Because it is important to catch DR early to prevent vision loss to the patient, sensitive screening techniques such as digital fundus photography are in important tool in this effort. The public health cost of DR complications can be effectively reduced by instituting smarter screening recommendations, not screening those who are at very low risk, and preventing vision loss by early identification and treatment of DR.

In this study, patients attending a large pediatric diabetes clinic that met the screening recommendations were offered DR screening using digital fundus photography. A total of 440 patients both met screening criteria and had retinopathy screening data. Of the 440, 203 were screened in-clinic by an opthalmologist, and 236 had already been screened by an outside practitioner. 5.4% of those screened in-clinic were positive for DR, while 0.42%of those screened elsewhere were found to be DR+. Those with retinopathy had significantly longer disease duration, were older at the time of screening, had higher HbA1c, and higher triglycerides. All of the cases had measures exceeding the screening guidelines, with a minimum age at screening of 13.4 years, and a minimum diabetes duration of 6.5 years.

It is unknown if the difference in prevalence between the two screening locations is due to a true difference in prevalence, or a systematic underreporting of DR in the outside-screened group, or a combination of these factors. The screening method of the 236 screened outside was not reported, and cases may have been missed in this cohort. Further study will need to be done to better quantify who would benefit most from screening, but building a risk model will require a much larger, comprehensive study. While it appears that the current screening guidelines may be revised without decreasing sensitivity, when screening is done it must be done using the most accurate methods in order to be most effective in catching DR in early stages when treatment is still effective.

This study emphasizes the public health benefit to screening for diabetic retinopathy as a routine element of diabetes management. In fact, the patients who took advantage of screening offered by the clinic showed over 10 times the prevalence of those who had already received screening by an outside practice, and most of these patients would have not otherwise completed screening, even though they were within the guidelines. The benefit to state-of-the-art digital fundus photography DR screening in this at-risk cohort is clear.

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1.0 INTRODUCTION

1.1 DIABETES MELLITUS

1.1.1 Disease Characterization

Diabetes Mellitus is a group of disorders that involve glucose intolerance and is often associated with severe complications [1]. Specifically, patients with poorly-controlled diabetes are at a higher risk for heart disease, stroke, as well as blindness and kidney failure related to microvascular complications.

Type 1 diabetes is characterized by the body's destruction of insulin-producing beta cells by the immune system, and is most often diagnosed in adolescence. Type 2 diabetes is characterized by insulin resistance and is generally diagnosed in adulthood [2]. Recently, diabetes types have been characterized that include both autoimmune destruction of beta cells and insulin resistance [3]. In either case, risk of complications increases if glucose is not properly controlled.

In 2014, the CDC estimated that in the United States 29.1 million, or 9.3 percent of the population had diabetes mellitus, 27.8 percent of who were undiagnosed [1]. Diabetes specifically in youth is more difficult to characterize, with an estimated prevalence of 0.18 percent in 2006, with greater than 80 percent of these cases being Type 1 diabetes [4], compared to approximately 5 percent in adults [1].

1.2 DIABETIC RETINOPATHY

Diabetic retinopathy (DR) is a microvascular complication that is related to nephropathy and neuropathy. Specifically, damage to the retina tissue causes retinal blood vessles to weaken and form microanurysms and possibly hemmorhage. Patients are often asymptomatic until the disease has progressed far enough along that treatment is no longer effective [5]. Left untreated, DR can become proliferative and lead to a loss of vision. Therefore, it is imperative to identify the presence of DR early in its progression so that treatment can remain effective.

1.2.1 Disease Stages

The progression of DR can be classified into one of four stages, depending on swelling, blockage of retinal blood vessels, and presence of proliferation:

- Non-proliferative retinopathy: characterized by tiny microaneurysms that may leak fluid. The non-proliferative stage is further sub-staged into mild, moderate, and severe non-proliferative retinopathy
- Proliferative diabetic retinopathy: new blood vessels are growing into the retina, leaking and obscuring vision

1.2.2 Risk Factors

In children and adolescents, retinopathy most commonly occurs after puberty onset and after at least 5 years of diabetes duration[6]. Duration of disease is a known major risk factor, as is poor glycemic control and high blood pressure.

In adults, retinopathy is 4 times more common in Type 1 patients than Type 2 patients [7]. This is understandable, because Type 1 patients are more likely to have been diagnosed at a young age, and therefore to have experienced a longer disease duration. This relationship may not translate well to a pediatric population, however, because of the much lower prevalence of Type 2 diabetes in this group.

1.2.3 Screening Guidelines

In their most recent 2016 screening guidelines, the American Diabetes Association recommends that screening be performed "at age ≥ 10 or after puberty has started, whichever is earlier, once the youth has had diabetes for 3-5 years"[8].

2.0 METHODS

2.1 SAMPLING FRAME

Electronic medical records from Children's Hospital of Pittsburgh (CHP) Diabetes Center were reviewed of patients who had been diagnosed with diabetes mellitus and had attended the clinic in the period between February 1 and November 23, 2015. Inclusion was limited to those patients who met the current screening guidelines for DR: age ≥ 10, diabetes duration ≥ 2. Of these patients, a classification was made as to DR screening location:

1. Screened in-clinic by CHP opthalmology
2. Screened at an outside facility or in private practice
3. No record of screening during inclusion period

Patients that were screened by CHP had an assessment of diabetic retinopathy presence made using digital fundus photography and by two different highly trained screeners. The assessment of Reviewer 1 was agreed upon beforehand to be the measure used in the analysis. The screening methods of those screened at an outside facility were unreported or unknown, although it is likely that the majority were screened using opthalomoscopy.

For this analysis, only patients in groups 1 or 2 (received screening) were considered. Those in group 3 were either not offered screening due to logistical issues, or declined screening due to other concerns. The characteristics of this cohort will be considered in future analyses.

2.2 DATA COLLECTED

A total of 68 measures were extracted from the records. Eighteen variables were used for this analysis, including screening result, screening location, sex, race, diabetes type, age at screening, age at DM diagnosis, DM duration, insulin dose, BMI, systolic and diastolic blood pressures, Hemoglobin A1c, triglycerides, and total, LDL and HDL cholesterols. For some measures, multiple time points were available.

Urine and antibody measures were available for some patients, but were not uniformly reported, and omitted from this analysis.

2.3 DESCRIPTIVE STATISTICS

The prevalence of DR in this population will be estimated, along with a 95% confidence interval.

The distributions for each of the variables were characterized by both screening status and screening location, and appropriate descriptive statistics were calculated. For measures that were non-normal, a Wilcoxon Rank-Sum test was performed, otherwise a two-sample t-test was performed.

2.4 REPRODUCIBILITY OF SCREENING MEASURE

The discordance of the two screening measures will be calculated using the κ-statistic, and its reproducibility will be assessed.

3.0 RESULTS

Four hundred and forty patients met the inclusion criteria for the analysis, 12 of who were positive for diabetic retinopathy. Sex of the eligible patients, categorized by DR status, is presented in Table 1. Sex was found to be a statistically significant predictor of DR screening result, with a two-sided Fisher's Exact p-value of 0.0018.

Diabetes type of the eligible patients is presented in Table 2. With a two-sided Fisher's Exact p-value of 0.1163, diabetes type was found to be statistically unrelated with DR screening result.

Screening results by insulin delivery method are presented in Table 3. With a two-sided Fisher's Exact p-value of 1.000, insulin delivery method was found to be not significantly related with DR screening result.

Races of the eligible patients is presented in Table 4. Race was found to be statistically unrelated with DR status, with a Fisher's Exact two-sided p-value of 0.4774.

Table 1: DR Screening Results by Sex

	DR Status				
Sex	+	-	Total	Prevalence	95% CI
Male	8	110	118	6.76%	(2.97%, 12.92%)
Female	3	82	85	3.53%	(0.73%, 9.97%)
Total	11	192	203	2.72%	(1.42%, 4.72%)

Table 2: DR Screening Results by Diabetes Type

	DR Status				
Diabetes Type	+	-	Total	Prevalence	95% CI
1	9	181	190	4.74%	(2.19%, 8.80%)
2	2	11	13	15.38%	(1.92%, 45.45%)
Total	11	192	203	2.72%	(1.42%, 4.72%)

CI is 95% Exact Binomial Confidence Interval

Table 3: DR Screening Results by Insulin Delivery Method

	DR Status				
Delivery Method	+	-	Total	Prevalence	95% CI
Multiple Daily Injections	8	127	135	5.93%	(2.59%, 11.34%)
Continuous Delivery	3	59	62	4.84%	(1.01%, 13.50%)
No Insulin	0	5	5	0.00%	

CI is 95% Exact Binomial Confidence Interval

Table 4: DR Screening Results by Race

	DR Status				
Race	+	-	Total	Prevalence	95% CI
White	9	156	165	5.45%	(2.52%,10.10%)
Black	2	31	33	6.06%	(0.74%,20.23%)
Other / Mixed Race	0	5	4	0.0%	
Total	11	192	203	5.42%	(2.74%, 9.49%)

CI is 95% Exact Binomial Confidence Interval

Table 5: Retinopathy Screening Results by Location

	DR Status				
Screening Location	+	-	Total	Prevalence	95% CI
In-Clinic	192	11	203	5.42%	(1.42%, 4.72%)
Outside	236	1	237	0.42%	(0.01%, 2.33%)
Total	428	12	440	2.73%	(1.42%, 4.72%)

CI is 95% Exact Binomial Confidence Interval

3.1 RETINOPATHY PREVALENCE

The prevalence of diabetic retinopathy in the total population studied was estimated at 2.73%, with a 95% exact binomial confidence interval of (1.21%, 4.25%).

3.2 SCREENING LOCATION

Distribution of screening location for eligible patients is shown in Table 5. 237 (53.9%) out of 440 patients chose to be screened outside of the clinic. Retinopathy was not evenly distributed by screening location, with all but one case occurring in the in-clinic screened population (Fisher's Exact $p = 0.0018$). Patients screened at CHP had an estimated DR prevalence of 5.42%, while patients screened outside CHP had an estimated prevalence of 0.42%.

3.3 OVERALL CHARACTERISTICS

A summary of the overall variable characteristics is provided in Table 6.

Table 6: Overall Characteristics

Variable	**Q1**	**Median**	**Q3**	**Mean**	**Std. Dev.**
Age at Screening (years)	13.14	15.34	17.46	15.40	3.02
Age at Diagnosis (years)	5.72	8.41	10.97	8.31	3.85
DM Duration (years)	4.07	6.43	9.39	7.09	3.73
Insulin Dose (units/kg/day)	0.76	0.92	1.09	0.92	0.30
BMI (kg/m^2)	20.04	22.78	25.75	23.68	5.52
BMI percentile	55.42	79.64	89.91	70.80	24.34
Systolic Blood Pressure Percentile	40.21	61.18	76.65	58.34	22.98
Diastolic Blood Pressure Percentile	60.79	72.65	81.87	69.80	16.85
HbA1c (%)	7.4	8.0	9.1	8.47	1.74
Triglycerides (mg/dl)	60	88	139	119.99	128.34
Total Cholesterol (mg/dl)	143	164	189	167.16	34.75
HDL Cholesterol (mg/dl)	46	56	66	57.05	14.82
LDL Cholesterol (mg/dl)	76	92	109	94.34	28.10

3.4 CHARACTERISTICS BY DIABETIC RETINOPATHY SCREENING RESULT

A summary of the variable characteristics by screening result is provided in Table 7. Median age at screening was significantly higher in the retinopathy group, with a Wilcoxon Rank-sum two-sided p-value of 0.003. Diabetes duration was significantly longer in the retinopathy group, with a Wilcoxon Rank-sum two sided p-value of 0.002. HbA1c and Triglycerides were both significantly higher in the DR group at the $\alpha = 0.05$ level.

Table 7: Subject Characteristics by DR Screening Result

	Retinopathy			No Retinopathy			
Variable	**Q1**	**Median**	**Q3**	**Q1**	**Median**	**Q3**	**p-value**
Age at Screening (years)	**16.03**	**17.84**	**20.79**	**12.88**	**15.07**	**17.30**	**0.003**
Age at Diagnosis (years)	6.14	7.13	12.05	6.16	9.01	11.42	0.687
DM Duration (years)	**7.90**	**9.01**	**12.10**	**3.45**	**5.57**	**8.98**	**0.002**
Insulin Dose (units/kg/day)	0.62	0.94	1.46	0.74	0.94	1.16	0.840
BMI (kg/m^2)	20.24	23.18	28.87	19.74	22.24	25.60	0.328
BMI percentile	28.43	56.60	83.23	52.56	78.16	89.75	0.131
Systolic Blood Pressure Percentile	31.47	63.80	80.65	41.52	59.95	74.18	0.977
Diastolic Blood Pressure Percentile	61.02	78.87	87.23	62.99	72.42	81.93	0.451
HbA1c (%)	**7.8**	**12.5**	**14.0**	**7.5**	**8.3**	**9.7**	**0.003**
Triglycerides (mg/dl)	**108**	**130**	**156**	**62**	**87**	**146**	**0.018**
Total Cholesterol (mg/dl)	174	196	220	144	165	192	0.073
HDL Cholesterol (mg/dl)	53	67	72	48	57	67	0.342
LDL Cholesterol (mg/dl)	88	108	129	78	94	115	0.114

P-values based on two-sample Wilcoxon rank-sum test for equality of medians.

3.5 CHARACTERISTICS BY SCREENING LOCATION

A summary of the variable characteristics by screening location is provided in Table 8. Age at DM diagnosis, DM duration, Hemoglobin A1c, Total cholesterol, and LDL cholesterol differed significantly by screening location.

Table 8: Characteristics by Screening Location

	CHP			Outside			
Variable	**Q1**	**Median**	**Q3**	**Q1**	**Median**	**Q3**	**p-value**
Age at Screening (years)	12.94	15.36	17.45	13.42	15.29	17.46	0.632
Age at Diagnosis (years)	**6.16**	**8.99**	**11.42**	**5.25**	**8.14**	**10.66**	**0.048**
DM Duration (years)	**3.52**	**5.72**	**9.03**	**4.39**	**6.76**	**9.57**	**0.030**
Insulin Dose (units/kg/day)	0.73	0.94	1.18	0.77	0.91	1.04	0.321
BMI (kg/m^2)	19.79	22.26	25.60	20.33	22.98	25.83	0.194
BMI percentile	51.91	77.19	89.95	59.01	80.12	90.61	0.276
Systolic Blood Pressure Percentile	40.21	60.06	75.31	39.74	61.42	79.11	0.733
Diastolic Blood Pressure Percentile	62.97	72.59	81.99	59.39	72.73	81.81	0.657
HbA1c (%)	**7.6**	**8.3**	**9.8**	**7.2**	**7.9**	**8.7**	**0.000**
Triglycerides (mg/dl)	64	89	146	58	87	131	0.326
Total Cholesterol (mg/dl)	**144**	**166**	**192**	**143**	**162**	**181**	**0.035**
HDL Cholesterol (mg/dl)	48	57	67	45	55	64	0.091
LDL Cholesterol (mg/dl)	**79**	**95**	**116**	**73**	**89**	**107**	**0.037**

P-values based on two-sample Wilcoxon rank-sum test for equality of medians.

3.6 REPRODUCIBILITY OF SCREENING ASSESSMENT

One hundred fifty eight patients screened in-clinic had their retinal images re-analyzed by a second reviewer. The results are displayed in Table 9. 151 of the results were agreed upon by the reviewers, while 7 were discordant. Although the proportion of concordance is 0.955, Cohen's κ-statistic was calculated to be 0.5128, indicating fair-to-good agreement between the reviewers. Additionally, Reviewer 1 identified twice as many cases than Reviewer 2. Consequently, the prevalence rate for the population is twice as high when basing the estimate on Reviewer 1's assessment.

Table 9: Concordance of Reviewers

		Reviewer 1		
		+	-	Total
Reviewer 2	+	4	1	5
	-	6	147	153
	Total	10	148	158

4.0 DISCUSSION

The results found in this study replicate the risk factors for diabetic retinopathy found in previous studies for both adults and adolescents. Namely, age at screening, diabetes duration, higher HbA1c, higher blood pressure, and higher triglycerides and cholesterol were all found to be significantly related to the development of retinopathy.

The difference in prevalence of retinopathy between the screening location groups may either be due to a true decreased prevalence or an underreporting of the complication in the group screened outside CHP. The variability of the measure was clearly demonstrated by the re-reading of the images screened by CHP, and so the reliability of the screening reports from outside sources is possibly in question. Specifically, the outside screeners did not follow a standardized protocol and may not have used the most up-to-date screening measures, namely opthalmoscopy instead of digital fundus photography. However, the difference in sample characteristics may counteract the possible underreporting of retinopathy in this group.

4.1 IMPROVEMENTS OVER PREVIOUS STUDIES

The class of patients in this analysis that did receive screening at CHP underwent a standardized protocol using the most sensitive screening method available. The difference in prevalence between the two screening locations may indicate that this protocol is better in identifying those positive for retinopathy, but this is uncertain because the true prevalence of the complication is not known for the population.

4.2 LIMITATIONS

Because patients had the option to decline screening if they had been screened somewhere else, the sample analyzed here is not a truly random sample from the population. Patients screened elsewhere had significantly lower risk factors for DR in HbA1c and total cholesterol, but also had a significantly higher diabetes duration. There are likely other confounding factors that contributed to the determination of screening location. A propensity score analysis may be warranted to balance the effect of the choice of screening location.

Another limitation of this analysis is that the retinopathy outcome measure is binary and the information of the stage of disease of the patient has been collapsed. This information could be used to do an ordinal logistic regression analysis and may assist in the formulation of a risk model.

Finally, the class of patients that did not receive screening at all may have different risk characteristics than the other two groups. This poses a problem if those most at risk are not receiving the necessary screening.

4.3 FUTURE DIRECTIONS

A larger study should be implemented to better assess the variables that are associated with diabetic retinopathy in this population, with an ultimate goal in producing a risk model that can better inform the screening guidelines.

Future work should implement a very careful and thorough screening protocol where all subjects are screened in-house using digital fundus photography. Effort should be made to obtain participation from all eligible subjects and reduce the numbers of patients screened elsewhere or not at all. A possible next-step would be to re-screen all those screened elsewhere at CHP using the standardized protocol, in order to get an estimate of under reporting of retinopathy in that cohort.

APPENDIX

SAS CODE

```
LIBNAME chp '~/Projects/Thesis/data/';
OPTIONS nofmterr;

ODS PDF file='~/Projects/Thesis/output/retinopathy_FinalReport';

DATA ret2 not_eligible;
SET chp.eligible2;

* Calculate duration, age at onset and age at screening;
Duration = (ExamDate - DxDate)/365.25;
Age_at_dx = (DxDate - DOB)/365.25;
Age_at_screen = (ExamDate - DOB)/365.25;

* calculate if any drug;
IF (metformin OR levothyroxine OR statin OR antihypertensive OR other_meds)
THEN anyDrug = 1;
ELSE anyDrug = 0;

* Divide age groups into 5yr increments;
* recode missing;
```

```
total_insulin_dose = insulin_dose / weight__kg_;


IF (height__cm_=-999) THEN height__cm_=.;
IF (systolic_1=-999) THEN systolic_1=.;
IF (diastolic_1=-999) THEN diastolic_1=.;
IF (systolic_2=-999) THEN systolic_2=.;
IF (diastolic_2=-999) THEN diastolic_2=.;
IF (systolic_3=-999) THEN systolic_3=.;
IF (diastolic_3=-999) THEN diastolic_3=.;
IF (day_of_screening_hba1c__poc_=-999) THEN day_of_screening_hba1c__poc_=.;
IF (last_hba1c__poc_simultaneous_wit=-999)
THEN last_hba1c__poc_simultaneous_wit=.;
IF (Triglycerides=-999) THEN Triglycerides=.;
IF (total_Cholesterol=-999) THEN total_Cholesterol=.;
IF (c_peptide_at_diagnosis=-999) THEN c_peptide_at_diagnosis=.;
IF (Insulin_Dose=-999) THEN Insulin_Dose=.;
IF (BMI=-999) THEN BMI=.;
IF (BMI_percentile=-999) THEN BMI_percentile=.;
IF (HDL=-999) THEN HDL=.;
IF (LDL=-999) THEN LDL=.;


* Take mean of blood pressure readings;
mean_bps = MEAN(systolic_1, systolic_2, systolic_3);
mean_bpd = MEAN(diastolic_1, diastolic_2, diastolic_3);


** other housekeeping;
```

```
sex=gender;


FORMAT sex sexfmt. DiabetesType typefmt. retinExam screenfmt.;

* choose which retinExam measure to use;
retinExam = retinopathy_exam_Nischal;
*retinExam = retinExamS;



* subset;
IF (diabetesType IN (1,2)) and
age_at_screen >= 10 and
duration >= 2
and (retinExam IN (0,1))
THEN OUTPUT ret2;
ELSE OUTPUT not_eligible;

RUN;

PROC PRINT data=not_eligible;
TITLE 'Subjects not eligible';
TITLE2 'Age < 10, Duration < 2, Diabetes type not 1 or 2,
or Missing screening result';
VAR MRN DOB ExamDate retinExam diabetesType age_at_screen duration;
RUN;

* Save resulting dataset;
```

```
DATA chp.eligible2;
SET work.ret2;
RUN;

DATA ret_chponly;
SET chp.eligible2;
IF screening_location=1;
total_insulin_dose = insulin_dose / weight__kg_;
RUN;

DATA ret_all;
SET chp.eligible2;
total_insulin_dose = insulin_dose / weight__kg_;
RUN;

********************************** Retinopathy ********************************;

PROC TABULATE data=ret_all;
TITLE 'Screening Results';
TITLE2 'by Sex / Diabetes Type';
CLASS sex diabetesType retinExam;
TABLE (diabetesType*sex ALL='Total'), (retinExam ALL='Total')*N='';
RUN;

PROC TABULATE data=ret_all;
TITLE 'Screening Results';
TITLE2 'by Screening Location';
CLASS screening_location retinExam;
TABLE (screening_location ALL='Total'), (retinExam ALL='Total')*N='';
RUN;
```

```
PROC FREQ data=ret_all;
TABLES screening_location*retinExam / fisher;
RUN;



********************************** Gender ************************************;

TITLE 'Gender';

PROC FREQ data=ret_chponly;
TITLE2 'by Screening Result';
TABLES gender*retinExam / fisher;
RUN;

PROC FREQ data=ret_all;
TITLE2 'by Screening Location';
TABLES gender*screening_location / fisher;
RUN;



********************************** Race ************************************;

TITLE 'Race';

PROC FREQ data=ret_chponly;
TITLE2 'by Screening Result';
TABLES race*retinExam / fisher;
RUN;
```

```
PROC FREQ data=ret_all;
TITLE2 'by Screening Location';
TABLES race*screening_location / fisher;
RUN;



********************************* Diabetes Type ****************************;

TITLE 'Diabetes Type';

PROC FREQ data=ret_chponly;
TITLE2 'by Screening Result';
TABLES DiabetesType*retinExam / fisher;
RUN;

PROC FREQ data=ret_all;
TITLE2 'by Screening Location';
TABLES DiabetesType*screening_location / fisher;
RUN;

***************************** Continuous Variables ***************************;

PROC UNIVARIATE data=ret_all NORMAL;
VAR age_at_screen age_at_dx duration total_insulin_dose BMI BMI_percentile
mean_bps p_sbp_score mean_bpd p_dbp_score day_of_screening_hba1c__poc_
Triglycerides Total_Cholesterol HDL LDL;
RUN;
```

```
PROC MEANS data=ret_all MAXDEC=2 NMISS MIN Q1 MEDIAN Q3 MAX QRANGE MEAN STD CLM;
TITLE2 'Overall';
VAR age_at_screen age_at_dx duration total_insulin_dose BMI BMI_percentile
mean_bps p_sbp_score mean_bpd p_dbp_score day_of_screening_hba1c__poc_
Triglycerides Total_Cholesterol HDL LDL;
RUN;

PROC MEANS data=ret_chponly MAXDEC=2 NMISS
MIN P10 Q1 MEDIAN Q3 MAX QRANGE MEAN STD CLM;
TITLE2 'by Screening Result';
CLASS RetinExam;
VAR age_at_screen age_at_dx duration total_insulin_dose BMI BMI_percentile
mean_bps p_sbp_score mean_bpd p_dbp_score day_of_screening_hba1c__poc_
Triglycerides Total_Cholesterol HDL LDL;
RUN;

PROC npar1way data=ret_chponly anova wilcoxon plots=anovaboxplot;
TITLE2 'Nonparametric test to compare diagnostic groups';
CLASS retinExam;
VAR age_at_screen age_at_dx duration total_insulin_dose BMI BMI_percentile
mean_bps p_sbp_score mean_bpd p_dbp_score day_of_screening_hba1c__poc_
Triglycerides Total_Cholesterol HDL LDL;
RUN;

PROC MEANS data=ret_all MAXDEC=2 NMISS
MIN P10 Q1 MEDIAN Q3 MAX QRANGE MEAN STD CLM;
TITLE2 'by Screening Location';
CLASS screening_location;
VAR age_at_screen age_at_dx duration total_insulin_dose BMI BMI_percentile
mean_bps p_sbp_score mean_bpd p_dbp_score day_of_screening_hba1c__poc_
```

```
Triglycerides Total_Cholesterol HDL LDL;
RUN;

PROC npar1way data=ret_all wilcoxon plots=wilcoxonboxplot;
TITLE2 'Nonparametric test to compare between screening locations';
CLASS screening_location;
VAR age_at_screen age_at_dx duration total_insulin_dose BMI BMI_percentile
mean_bps p_sbp_score mean_bpd p_dbp_score day_of_screening_hba1c__poc_
Triglycerides Total_Cholesterol HDL LDL;
RUN;

************************** Retinopathy Prevalence ***************************;
TITLE 'Retinopathy Prevalence';
PROC FREQ data=ret_all;
TABLES retinExam / binomial(level=2);
RUN;

TITLE 'CHP Retinopathy Prevalence';
PROC FREQ data=ret_chponly;
TABLES retinExam / binomial(level=2);
RUN;

DATA ret_out;
SET ret_all;
IF screening_location=2;
RUN;


TITLE 'Outside Retinopathy Prevalence';
PROC FREQ data=ret_out;
```

```
TABLES retinExam / binomial(level=2);
RUN;


***************************** Kappa concordance ******************************;
TITLE 'Screening Result Concordance';

DATA retk;
SET ret_all;
IF (retinopathy_exam_samanth=-999) THEN retinopathy_exam_samanth=.;
IF screening_location=1;
RUN;

PROC FREQ data=retk;
TABLES retinopathy_exam_samanth*retinopathy_exam_nischal / KAPPA;
RUN;


PROC LOGISTIC data=ret_all;
CLASS race diabetestype sex;
MODEL screening_location = race diabetestype sex day_of_screening_hba1c__poc_
duration age_at_dx age_at_screen triglycerides total_cholesterol;
RUN;


ODS PDF CLOSE;
```

BIBLIOGRAPHY

[1] C. for Disease Control, Prevention, *et al.*, "National diabetes statistics report: estimates of diabetes and its burden in the united states, 2014," *Atlanta, GA: US Department of Health and Human Services*, 2014.

[2] N. D. D. Group *et al.*, "Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance," *Diabetes*, vol. 28, no. 12, pp. 1039–1057, 1979.

[3] G. Schernthaner, S. Hink, H. Kopp, B. Muzyka, G. Streit, and A. Kroiss, "Progress in the characterization of slowly progressive autoimmune diabetes in adult patients (lada or type 1.5 diabetes).," *Experimental and clinical endocrinology & diabetes: official journal, German Society of Endocrinology [and] German Diabetes Association*, vol. 109, pp. S94–108, 2000.

[4] S. for Diabetes in Youth Study Group *et al.*, "The burden of diabetes mellitus among us youth: prevalence estimates from the search for diabetes in youth study," *Pediatrics*, vol. 118, no. 4, pp. 1510–1518, 2006.

[5] J. Vislisel and T. Oetting, "From one medical student to another," 2010.

[6] Y. H. Cho, M. E. Craig, S. Hing, P. H. Gallego, M. Poon, A. Chan, and K. C. Donaghue, "Microvascular complications assessment in adolescents with 2-to 5-yr duration of type 1 diabetes from 1990 to 2006," *Pediatric diabetes*, vol. 12, no. 8, pp. 682–689, 2011.

[7] M. C. Eppens, M. E. Craig, J. Cusumano, S. Hing, A. K. Chan, N. J. Howard, M. Silink, and K. C. Donaghue, "Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes," *Diabetes care*, vol. 29, no. 6, pp. 1300–1306, 2006.

[8] A. D. Association *et al.*, "11. children and adolescents," *Diabetes Care*, vol. 39, no. Supplement 1, pp. S86–S93, 2016.