Big Data at SCPMG

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Financial Disclosures

- None

"Big data"

- Electronic medical records have revolutionized the ability to perform observational studies.
  - Relatively efficient and fast queries of medical information
- Databases can have breadth and/or depth of information
- Cannot establish cause-and-effect relationships with retrospective data, but large databases can be used to study descriptive statistics, predictive capacity, and/or casual inferences.

Different sources of "big data"

- Kaiser Permanente (KP)
- American Academy of Ophthalmology's Intelligent Research in Sight (IRIS) Registry
- MarketScan Database
- Medicare claims data
- Vestrum
- National Health and Nutrition Examination Survey (NHANES)

What makes KP "big data" unique

- Length of data collection
  - High patient retention
  - Diverse patient population
  - 100 million person-years with electronic medical data are available for research from 1981 to 2017
- Combination of systemic and ocular data
- Pharmacy dispensing database
- "Potential" access to ophthalmic images

What are potential pitfalls of KP data?

- ? Accuracy of billing
- Vision and IOP data can be hard to extract
- Laterality of procedures/interventions/medications difficult to discern

Limitations of "big data" in general

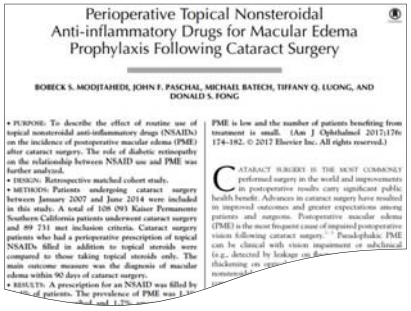
- Variable data quality
- Risk of patient lost to follow-up/transfer of care
- "Exaggerated" statistical significance
  - Large n's can make statistical significance "easy" to find → small and potentially practically meaningless differences may be statistically significant
- Confounding
- Appropriate reporting

What have we studied using KPSC "big data"

- Cataract
- Myopia
- Age related macular degeneration (AMD)
- Plaquenil toxicity
- Glaucoma
- Diabetic retinopathy (DR)

Pre-operative vision and surgeon volume as predictors of visual outcomes following cataract surgery

- Purpose
  - Evaluate the relationship between pre-operative vision and surgeon volume with visual outcomes following cataract surgery
- Methods
  - Retrospective cohort study of patients > 18 years enrolled in KPSC health plan and who underwent cataract surgery
  - Conducted multivariate analysis to determine relationship between surgeon volume and post-op visual acuity, controlling for patient age, pre-op visual acuity, history of diabetes, and history of diabetic retinopathy
- Results
  - Patients whose surgeons performed more surgeries gained significantly more letters, but the difference between the lowest and highest volume groups was ~1.25 letters.



Perioperative Topical Nonsteroidal Anti-inflammatory Drugs for Macular Edema Prophylaxis Following Cataract Surgery

BOBECK S. MODJTAHEDI, JOHN F. PASCHAL, MICHAEL BATECH, TIFFANY Q. LUONG, AND DONALD S. FONG

• PURPOSE: To describe the effect of routine use of topical nonsteroidal anti-inflammatory drugs (NSAIDs) on the incidence of postoperative macular edema (PME) after cataract surgery. The role of diabetic retinopathy on the relationship between NSAID use and PME was further analyzed.
• DESIGN: Retrospective matched cohort study.
• METHODS: Patients undergoing cataract surgery between January 2007 and June 2014 were included in this study. A total of 108 093 Kaiser Permanente Southern California patients underwent cataract surgery and 89 231 met inclusion criteria. Cataract surgery patients who had a perioperative prescription of topical NSAIDs filled in addition to topical steroids were compared to those taking topical steroids only. The main outcome measure was the diagnosis of macular edema within 90 days of cataract surgery.
• RESULTS: A prescription for an NSAID was filled by [illegible] of patients. The prevalence of PME was 1.[illegible] and 1.7%

PME is low and the number of patients benefiting from treatment is small. (Am J Ophthalmol 2017;176:174–182. © 2017 Elsevier Inc. All rights reserved.)

CATARACT SURGERY IS THE MOST COMMONLY performed surgery in the world and improvements in postoperative results carry significant public health benefit. Advances in cataract surgery have resulted in improved outcomes and greater expectations among patients and surgeons. Postoperative macular edema (PME) is the most frequent cause of impaired postoperative vision following cataract surgery.[1,2] Pseudophakic PME can be clinical with vision impairment or subclinical (e.g., detected by leakage on fl[illegible] thickening on [illegible] nonsurgical [illegible]

Preoperative Topical Nonsteroidal Anti-inflammatory Drugs for Macular Edema Prophylaxis Following Cataract Surgery

- Study Objective
  - Describe the effect of routine use of topical NSAIDs on the incidence of post-op macular edema after cataract surgery
- Methods
  - Retrospective matched cohort study of patients who underwent cataract surgery between Jan. 2007 – Jun. 2014
  - Patients who had a perioperative prescription of topical NSAIDs filled in addition to topical steroids were compared to patients taking topical steroids only

Preoperative Topical Nonsteroidal Anti-inflammatory Drugs for Macular Edema Prophylaxis Following Cataract Surgery

- Results
  - 89,731 patients met study criteria
  - Prevalence of post-op macular edema was 1.3% among patients prescribed NSAIDS, vs. 1.7% among patients not prescribed NSAIDs

	Adjusted Risk (95% CI) of Diabetic Macular Edema by NSAID Use
No Diabetes	0.68 (0.58, 0.78)
Diabetes without Retinopathy	0.51 (0.32, 0.82)
Diabetes with Retinopathy	1.06 (0.81, 1.38)

Public Health Burden and Potential Interventions for Myopia

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Myopia is the most common ocular abnormality in the world.[1,2] Its growing prevalence has resulted in it reaching near ubiquitous status in many East Asian communities, affecting 80% to 90% of young adults in many communities.[1,2] Approximately one third of adult Americans and Europeans are myopic.[1,2] A limitation of both of these estimates is that they used noncycloplegic refractions, which may have overestimated myopia in younger patients because of accommodation.[1,2] The estimated prevalence of myopia (≤−0.75 diopters [D]) among Europeans aged 50 to 54 years is 33.6%, with 2.6% of these in this age group being highly myopic (≤−6 D). Vitale et al[1] estimated the prevalence of myopia (defined as ≤−0.5 D) using the National Health and Nutrition Examination Survey (NHANES) as 50.2% in individuals aged 20 to 39 years and 50.1% in individuals aged 40 to 59 years. The prevalence of severe myopia (≤−5 D) was 7.4% and 7.8% in these age groups, respectively.[1] In an effort to examine trends in myopia prevalence, Vitale et al[1] applied the definition of myopia from the 1971–1972 NHANES to their more contemporary cohort[1] to make these groups comparable. [illegible] older criteria likely overestimate

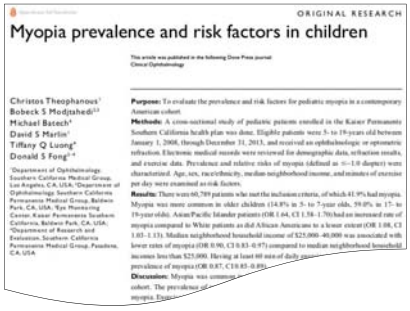
Despite the frequency, increasing prevalence, public health burden, and financial costs of myopia, this problem remains largely underappreciated by the ophthalmic community.

children is projected to increase by 26% in 2060, with 69% of cases being from simple uncorrected refractive error.[1] The ability to reliably estimate visual impairment in preschool children is limited, and these estimates were derived by combining data from 3 different sources, which can lead to inaccuracies. Despite the limitations of these projections, the increasing prevalence of myopia is well established in several populations (especially in East Asia),[1,2,10] and these figures should provide justifiable concern to ophthalmologists even if the exact estimates are imperfect.

Glasses, contact lenses, and refractive surgery can address refractive error; however, myopic patients, especially those with high myopia, are at an increased risk of a host of secondary sequelae, including retinal detachment, glaucoma, cataract, choroidal neovascularization, optic neuropathy, staphyloma, and myopic macular degeneration. Uncorrectable visual impairment is seen in 4% of 75-year-olds with myopia and 39% with high myopia. Cross-

Public Health Burden and Potential Interventions for Myopia

- Key Points
  - Currently, ~1.4 billion people (23%) in the world are myopic
  - By 2050, ~4.8 billion people (50%) expected to have myopia
  - Efforts to reduce the prevalence, progression, and severity of myopia could have a profound public health impact
  - Strategies for preventing myopia include orthokeratology and low-dose atropine
  - Another strategy for consideration is increasing outdoor time



ORIGINAL RESEARCH

Myopia prevalence and risk factors in children

This article was published in the following Dove Press journal:
Clinical Ophthalmology

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Purpose: To evaluate the prevalence and risk factors for pediatric myopia in a contemporary American cohort.

Methods: A cross-sectional study of pediatric patients enrolled in the Kaiser Permanente Southern California health plan was done. Eligible patients were 5- to 19-years old between January 1, 2008, through December 31, 2013, and received an ophthalmologic or optometric refraction. Electronic medical records were reviewed for demographic data, refraction results, and exercise data. Prevalence and relative risks of myopia (defined as ≤−1.0 diopter) were characterized. Age, sex, race/ethnicity, median neighborhood income, and minutes of exercise per day were examined as risk factors.

Results: There were 60,789 patients who met the inclusion criteria, of which 41.9% had myopia. Myopia was more common in older children (14.8% in 5- to 7-year olds, 59.0% in 17- to 19-year olds). Asian/Pacific Islander patients (OR 1.64, CI 1.58–1.70) had an increased rate of myopia compared to White patients as did African Americans to a lesser extent (OR 1.08, CI 1.03–1.13). Median neighborhood household income of $25,000–40,000 was associated with lower rates of myopia (OR 0.90, CI 0.83–0.97) compared to median neighborhood household incomes less than $25,000. Having at least 60 min of daily [illegible] prevalence of myopia (OR 0.87, CI 0.83–0.89).

Discussion: Myopia was common in this contemporary cohort. The prevalence of [illegible] myopia. Expan-

Myopia Prevalence and Risk Factors in Children

- Objective
  - Evaluate the prevalence of and risk factors for pediatric myopia

Myopia Prevalence and Risk Factors in Children

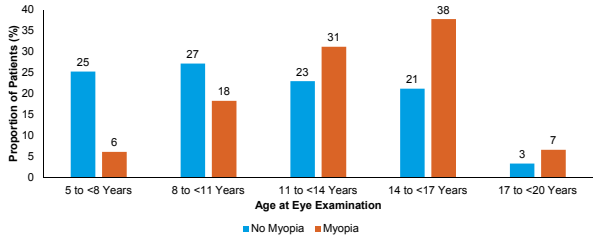
Table 1. Study population demographics

Variables, N (%)	No Myopia 35,326 (58)	Myopia 25,463 (42)	P-value
Age at eye exam			<0.001
5 to < 8 years	8929 (25)	1548 (6)	
8 to <11 years	9610 (27)	4661 (18)	
11 to <14 years	8132 (23)	7941 (31)	
14 to <17 years	7486 (21)	9633 (38)	
17 to <20 years	1169 (3)	1680 (7)	
Female	19032 (54)	13756 (54)	0.72
Race			<0.001
White	14567 (41)	8337 (33)	
African American	3740 (11)	2362 (9)	
Asian/Pacific Islander	3000 (8)	4570 (18)	
Other/Multiple/Unknown	14019 (40)	10194 (40)	
Hispanic	20453 (58)	13768 (54)	
Neighborhood household income (USD)			<0.001
Less than $25,000	710 (3)	568 (3)	
$25,000 - $49,999	9328 (33)	6445 (31)	
$50,000 - $99,999	14896 (53)	11001 (53)	
$100,000 or Higher	3018 (11)	2705 (13)	
Body mass index percentile for age and sex*			0.76
Normal or under weight (<85th)	20367 (60)	14238 (60)	
Overweight (85th to <95th)	6112 (18)	4340 (18)	
Moderately obese (95th to 1.2 x 95th)	6634 (20)	4394 (19)	
Extremely obese (≥1.2 x 95th)	630 (2)	718 (3)	
Exercise per day			<0.001
Less than 60 minutes	14685 (60)	11114 (65)	
At least 60 minutes	9957 (40)	5986 (35)	

USD = United States dollars
*Based on the sex-specific body mass index-for-age growth charts developed by the Centers for Disease Control and Prevention.

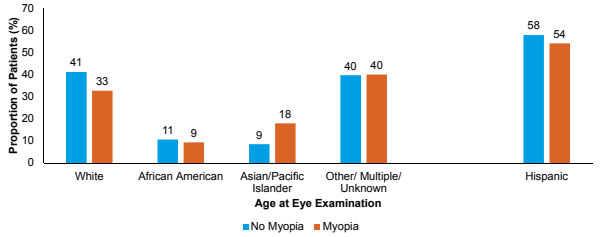
Myopia Prevalence and Risk Factors in Children

Patients with myopia tend to be older than patients with no myopia (p<0.001)



Myopia Prevalence and Risk Factors in Children

Distribution of race & ethnicity



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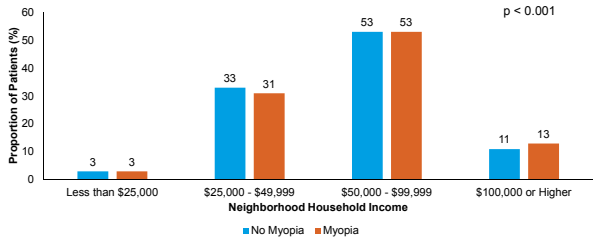
Myopia Prevalence and Risk Factors in Children

Distribution of neighborhood household income by myopia status



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Myopia Prevalence and Risk Factors in Children

Multivariable adjusted Poisson odds-ratio estimates for myopia

Variables	Adjusted OR (95% CI)	Variables	Adjusted OR (95% CI)
Race		**Neighborhood household income (in USD)**	
White	Reference	< $25,000	Reference
African American	1.08 (1.03 – 1.13)	$25,000 to < $50,000	0.90 (0.83 – 0.97)
Asian/Pacific Islander	1.64 (1.58 – 1.70)	$50,000 to < $100,000	0.93 (0.86 – 1.01)
Other/Multiple/Unknown	1.18 (1.14 – 1.22)	$100,000 or higher	1.03 (0.94 – 1.12)
Hispanic (vs. Not Hispanic)	0.99 (0.96 – 1.03)	**Exercise per day**	
Female (vs. Male)	1.00 (0.97 – 1.02)	Less than 60 minutes	Reference
		At least 60 minutes	0.87 (0.85 – 0.89)

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Effect of IOP-Lowering Glaucoma Medications in Patients with Exudative AMD

- Study Objective:
  - Determine if intraocular pressure (IOP)-lowering glaucoma medications reduce the need for anti-VEGF injections in patients with exudative AMD
- Methods
  - Retrospective, matched cohort of patients with exudative AMD and who received anti-VEGF injection(s) in 2010-2015
  - Used medication dispenses to assess whether patient was prescribed an IOP-lowering medication
  - Data on visual acuity, IOP, and number of anti-VEGF injections were abstracted from patient charts

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Effect of IOP-Lowering Glaucoma Medications in Patients with Exudative AMD

	Medication Non-Users (N=127)	Medication Users (N=127)
Baseline IOP Mean (SD) Median (IQR)	 15.1 (3.6) 15 (13, 18)	 15.6 (4.4) 15 (12, 18)
Switched anti-VEGF agents, N (%)	22 (17%)	29 (23%)
No. injections with bevacizumab before switch Mean (SD) Median (IQR)	 4.4 (2.0) 4 (3, 7)	 4.8 (1.7) 4 (4, 5)
Total no. injections Mean (SD) Median (IQR)	 6.2 (3.0) 6 (4, 8)	 6.2 (2.8) 6 (4, 8)

- Number of anti-VEGF injections were similar between glaucoma medication users vs. non-users among exudative AMD patients.
- Additional studies may be needed to assess whether use of glaucoma medications is associated with decreased number of anti-VEGF injections.

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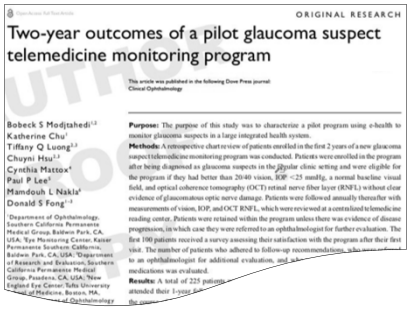

ORIGINAL RESEARCH

Two-year outcomes of a pilot glaucoma suspect telemedicine monitoring program

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Two-Year Outcomes of a Pilot Glaucoma Suspect Telemedicine Monitoring Program

About the Program

Enrollment
- To be eligible, patient must have:
- >20/40 vision
- IOP <25 mmHg
- Normal baseline visual field
- Normal OCT

Follow-Up
- Patients are followed annually with measurements of vision, IOP, and OCT RNFL

If Progress
- Patients are referred to an ophthalmologist for further evaluation

Two-Year Outcomes of a Pilot Glaucoma Suspect Telemedicine Monitoring Program

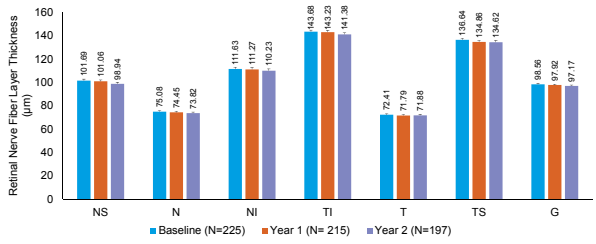
- Paper currently in press
- Study Objective:
  - Characterize the patients enrolled in the first two years of a pilot program that monitors glaucoma suspects in a large, integrated health care system
- Methods
  - Retrospective cohort
  - Collected information on vision, IOP, whether patient was referred

Two-Year Outcomes of a Pilot Glaucoma Suspect Telemedicine Monitoring Program

- Results
  - A total of 225 patients were enrolled
  - 97.3% patients attended their 1-year follow-up visit
  - 92.5% patients attended their 2-year follow-up visit
  - Over the course of two years, five patients were referred for further clinic evaluation due to concern of RNFL loss
  - No patients were referred to the clinic for vision loss or elevated IOP

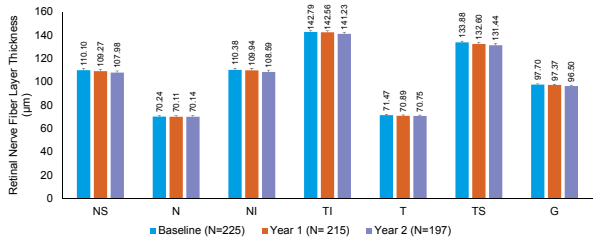
Two-Year Outcomes of a Pilot Glaucoma Suspect Telemedicine Monitoring Program

OCT measurements for the right eye were stable across the two years



Two-Year Outcomes of a Pilot Glaucoma Suspect Telemedicine Monitoring Program

OCT measurements for the left eye were stable across the two years



Coding Patterns by Ophthalmologists for Hydroxychloroquine Toxicity

- Paper currently in press
- Study Objective:
  - Characterize the ICD-9 coding patterns used by ophthalmologists in clinical practice for hydroxychloroquine (HCQ) retinal toxicity
- Methods
  - Retrospective cohort study of patients enrolled in KPSC health plan who were dispensed HCQ between 2001-2014
  - Patients' were identified by ICD-9 codes for toxic maculopathy, non-exudative AMD, Drusen (degenerative), and/or (other) background retinopathy
  - The charts of these patients were manually reviewed to validate the diagnosis

Coding Patterns by Ophthalmologists for Hydroxychloroquine Toxicity

- Results
  - 23,362 patients were dispense HCQ between 2001-2014
  - 678 (2.9%) patients were diagnosed with at least one of the aforementioned ICD codes
  - Only 53 patients were confirmed to have HCQ toxicity on chart review
- Discussion
  - Study underscores the imprecise nature of ICD coding
  - Future work can focus on uniform coding standards among clinicians, particularly for rare conditions
  - Study illustrates the limitations of relying on ICD codes only when conducting research utilizing electronic databases

Two-Year Incidence of Retinal Intervention in Patients with Minimal or No Diabetic Retinopathy

- Presented as an abstract at AAO 2017
- Study Objective
  - Determine the two-year incidence of retinal intervention in patients with minimal or no diabetic retinopathy
- Methods
  - Retrospective chart review of patients who had non-widefield DR screening photographs
  - Patients were identified by CPT codes for vitrectomy, intravitreal injections, and retinal lasers
  - Chart review was performed to validate procedures

Two-Year Incidence of Retinal Intervention in Patients with No Diabetic Retinopathy

Retinal Intervention	Year 1 DED-Related	Year 1 Not DED-Related	Year 2 DED-Related	Year 2 Not DED-Related	Total
Intravitreal injection	**2**	**0**	**1**	**2**	**5**
Anti-VEGF for branch retinal vein occlusion with macular edema	0	0	0	1	1
Anti-VEGF for macular edema	0	0	1	0	1
Anti-VEGF for non-clearing vitreous hemorrhage	2	0	0	0	2
Ocriplasmin for macular hole	0	0	0	1	1
Laser	**3**	**4**	**4**	**2**	**13**
Focal macular laser	1	0	1	0	2
Pan-retinal photocoagulation	2	1	3	0	6
Retinopexy	0	3	0	2	5
Pars Plana Vitrectomy	**2**	**15**	**4**	**27**	**48**
CMV retinitis / rhegmatogenous retinal detachment	0	0	0	1	1
Epiretinal membrane	0	0	0	4	4
Lymphoma	0	1	0	0	1
Macular hole	0	4	0	7	11
Macular hole / epiretinal membrane	0	1	0	3	4
Melanoma	0	0	0	1	1
Non-clearing vitreous hemorrhage	2	1	4	4	11
Posterior scleritis	0	0	0	1	1
Rhegmatogenous retinal detachment	0	8	0	4	12
Rhegmatogenous retinal detachment / epiretinal membrane	0	0	0	1	1
Vitritis	0	0	0	1	1

CMV = cytomegalovirus; DED = diabetic eye disease; VEGF = vascular endothelial growth factor
11 patients required intervention for DED during first 2 years; 2 patients required both PPV and Laser, 1 patient required both PPV and Injection, 1 patient required PPV, Laser, and Injection.
44 patients required intervention for non-DED during first 2 years; 5 patients required both PPV and Laser, 1 patients required both PPV and Injection.
Three patients required interventions in both eyes (bilateral PPV) and were only counted once in the above table.

Two-Year Incidence of Retinal Intervention in Patients with Minimal Diabetic Retinopathy

Retinal Intervention	Year 1 DED-Related	Year 1 Not DED-Related	Year 2 DED-Related	Year 2 Not DED-Related	Total
Intravitreal Injection	**3**	**2**	**1**	**0**	**6**
Anti-VEGF for exudative age-related macular degeneration	0	1	1	0	
Anti-VEGF for macular edema	3	1	0	0	2
Laser	**5**	**1**	**2**	**0**	**8**
Focal macular laser	0	0	1	0	1
Pan-retinal photocoagulation	5	0	1	0	1
Retinopexy	0	1	0	0	1
Pars Plana Vitrectomy	**2**	**2**	**0**	**1**	**5**
Epiretinal membrane	0	1	0	1	1
Non-clearing vitreous hemorrhage	1	0	0	0	1
Rhegmatogenous retinal detachment	0	1	0	0	1
Tractional retinal detachment	1	0	0	0	1

DED = diabetic eye disease; VEGF = vascular endothelial growth factor
11 patients required intervention for DED during first 2 years; 1 patient required both PPV and Laser, 1 patient required both Laser and Injection.
5 patients required intervention for non-DED during first 2 years; 1 patient required both PPV and Laser.

TREATMENT PATTERNS AND 2-YEAR VISION OUTCOMES WITH BEVACIZUMAB IN DIABETIC MACULAR EDEMA

An Analysis From a Large U.S. Integrated Health Care System

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Purpose: To assess health care utilization and vision outcomes over 2 years in patients receiving bevacizumab treatment in clinical practice for diabetic macular edema.
Methods: Patients with newly diagnosed diabetic macular edema who received an intravitreal bevacizumab injection within 12 months of initial diagnosis were identified from Kaiser Permanente's 350,000 patients with diabetes mellitus treated between 2008 and 2013. Snellen best-corrected visual acuity (BCVA), number of intravitreal injections, and patient characteristics were abstracted from the electronic record. The main outcome measure was change in BCVA.
Results: Three hundred and nine patients met the inclusion criteria and had 2 years of follow-up after their first bevacizumab injection. These patients had a mean of 3.1 [illegible] (range, 1–17) during the 2-year follow-up. Mean BCVA improvement [illegible] months and 5.3 letters at 24 months. Only 29.8% of [illegible] vision improvement from baseline, whereas 12.3% [illegible] at 24 months.
Conclusion: This is the [illegible]

Treatment Patterns and 2-Year Vision Outcomes with Bevacizumab in Diabetic Macular Edema

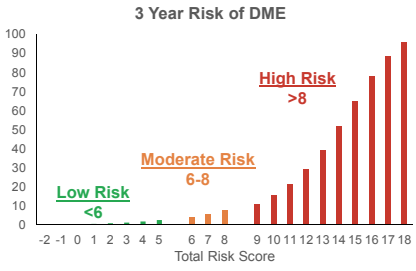
- Study Objective
  - Assess the health care utilization and vision outcomes over two years in patients receiving bevacizumab treatment in clinical practice for diabetic macular edema (DME)
- Methods
  - Patients with newly diagnosed DME who received an intravitreal injection with bevacizumab within 12 months of diagnosis
- Results
  - 309 patients met the inclusion criteria and had 2 years of follow-up
  - Patients had a mean of 3.1 injections (range, 1-17) during the two-year follow-up
  - Mean BCVA improvement was 5.4 letters at 12 months; 5.3 letters at 24 months
  - 30% patients had ≥3 lines of vision improvement from baseline vs. 12% patients with ≥3 lines of vision loss

A Model to Predict the 3-Year Risk of Needing Treatment for Diabetic Macular Edema

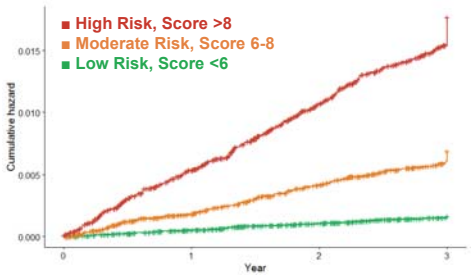
- Presented at ASRS 2018
- Study Objective
  - Predict who will develop DME
- Methods
  - Retrospective cohort of patients from the Diabetes Case Identification Database who were: ≥18 years of age, ≥3 years of follow-up, no prior history of DME, no severe DR on baseline retinal photos
  - Outcomes: (1) diagnosis of DME, (2) diagnosis of DME with anti-VEGF injection
  - Employed a Cox proportional hazard model to calculate DME risk
  - Used model-fitted values to set thresholds for risk calculator

Points Based Scoring System Using Framingham Framework

Characteristic	Risk Score
Age Group	
50-59	3
60-69	5
70-79	7
80+	9
Male	1
Black Race	-1
≥9 Years of Diabetes	1
Age x Duration of Diabetes	
379 – 462	-1
462 – 531	-2
>531	-4
% HbA1c	
8 – 9	1
9 – 10	4
>10	6
Insulin Use	1
CKD Stage	
3 or 4	1
5	2
Retinopathy Status	
Mild	3
Moderate	7
Unable to diagnosis	2
N/A	3



3-Year Cumulative Hazard of DME



A Model to Predict the 3-Year Risk of Needing Treatment for Diabetic Macular Edema

- Conclusions
  - Further modeling can be done to explore additional risk factors and add more granular detail
    - » Time-dependent variables / repeated measures were not used in this model
  - Risk stratification could be integrated into electronic medical records
  - High risk patients may benefit from more intense systemic management and closer ophthalmic monitoring