Title
Geographic Distribution of Pediatric Glaucoma Patients and their Outcomes

Author
Chen, Jenny

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Geographic Distribution of Pediatric Glaucoma Patients and their Outcomes

By

JENNY CHEN
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Approved:

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Mark Carroll, Chair

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Nick Anderson

____

Prabhu Shankar

Committee in Charge

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Geographic Distribution of Pediatric Glaucoma Patients and their Outcomes

Abstract

Background:

Pediatric glaucoma is a treatable condition that can cause potential blindness. Social factors such as insurance and loss-to-follow-up visits are rarely addressed as risk factors in studies of visual outcome. To assist in visualizing the data in a novel way, GIS (geographic information system) will be used to visualize patient outcomes by location and other social risk factors.

Methods:

The study is a retrospective cohort study of pediatric glaucoma patients seen at UC Davis. The primary outcome of the study is visual acuity, and basic demographic data as well as social factors were also recorded. The patients were initially mapped to their 3-digit zip code prefix, and statistical analysis was performed to identify significant risk factors to poor visual outcome.

Results:

In the multivariate analysis, the odds of having a good vision score are 53% lower in Females compared to Males (p-value = 0.04). The number of patients, visual outcomes and select risk factors were mapped and shown in the figures in the manuscript, with the highest number of patients in the zip-code prefix 958 and 956.

Conclusions:

Females have a higher risk of having a poor visual outcome in the multivariate analysis, while insurance and race trended towards significance. The mapping of patient outcomes, while a helpful way to represent patient demographics, does not necessarily reflect the data analysis, but still holds a helpful hypothesis generating role.

INTRODUCTION

Glaucoma is a condition that causes blindness by damage to the optic nerve of the eye[1]. The mechanism of the disease is only partially understood, though it is widely accepted that increased intraocular pressure (IOP) causes progressive, often irreversible, damage to the nerve. This results in a phenotypic appearance of the nerve having "cupping" where the center optic nerve head is hollowed out. The degree of cupping is often proportional to the damage endured by the nerve.

Glaucoma is the second leading cause of blindness in the world[2], behind cataracts, but the challenge of the disease is that it is often irreversible. There are multiple subtypes of glaucoma (which will be briefly reviewed), but the focus of this study will be primarily on pediatric glaucoma patients. There are two broad subtypes of glaucoma: open-angle and closed-angle[3]. The angle refers to the anatomical structure of the eye that encompasses the aqueous outflow of the eye. As suggested by its name, the aqueous is fluid that is produced by a structure called the ciliary body that occupies the inside of the eye. Increased IOP, and thus glaucoma, occurs when there is an imbalance between the aqueous production and aqueous, with insufficient outflow resulting in increased pressure. Angle-closure is when the iris blocks the outflow of aqueous by physically occupying the angle[4]. Open-angle glaucoma is when the iris is not blocking the aqueous outflow, but rather the outflow occurs further "downstream" within a structure called the trabecular meshwork and beyond[1].

Glaucoma is often thought of as a disease of the elderly, but pediatric glaucoma, while less common, can cause permanent blindness in children and results in a lifetime of disability. There are multiple subtypes of pediatric glaucoma, ranging from infantile glaucoma to juvenile glaucoma, and glaucoma as a part of a syndromic disease process[5], which can be both open or closed angle. The pathophysiology of all the subtypes of glaucoma is outside of the scope of this paper.

The unifying factors for all these types of pediatric glaucoma are that they always necessitate treatment, whether that be in the form of medication or surgery, and these patients will need a lifetime of consistent and reliable follow-up. Inconsistent follow-up and lack of access to care will likely lead to disability[6]. Additionally, management of pediatric glaucoma is a highly specialized field, and may not be readily available to patients who live outside of a metropolitan area[7].

Outcomes for untreated pediatric glaucoma is grave, and many factors influence the outcome of the patient's sight. This includes their IOP, the types of surgery, the treatment of comorbid conditions, and their follow-up.

Geographic Distribution of Disease

Many studies of risk factors for disease outcome explore patient's intrinsic factors such as age, race, genetic markers, but the location of the patient has always been a more challenging risk factor to consider. This is because location by itself is not a risk factor, but a risk factors exist within that location that predisposes the patient to a disease. For example, a young patient may develop asthma by living next to the freeway, but is that because of increased air pollution or the socioeconomic implications of living next to a freeway? Therefore, location is not a sufficient risk factor, but it can be a hypothesis generating method of exploring patient data, and provide an alternate way to observe disease processes.

GIS (Geographic Information System) has long been used by the fields of public health, and institutions such as the Center for Disease Control (CDC)[8]. GIS when used in healthcare is the study of geospatial information and its relationship to disease and health. Examples include studies of disease outbreak, distribution of healthcare providers and how diseases are related to their environment.

However, in the field of ophthalmology, geographic distribution of disease is still underutilized. There have been papers describing distribution of eye care specialists, but fewer studies on patient location and risk factors associated with their environment[7].

Objective

In this paper, I will describe the geospatial distribution of a cohort of pediatric glaucoma patients from UC Davis. The patients will be mapped to their locations with exploration of several potential risk factors, and statistical correlation will be examined.

METHODS

Data Collection

The study is a retrospective cohort study of pediatric glaucoma patients seen at UC Davis between 2000 and 2019. The study was approved by the University of California, Davis Institutional Review Board and abided by the Health Information Portability and Accountability Act and the Declaration of Helsinki. Data is stored on REDCap (Research Electronic Data Capture), which is a secure web application for data storage that is HIPAA compliant.

Inclusion criteria for patients were any pediatric patient with the diagnosis of pediatric glaucoma, or any adult with a prior history of pediatric glaucoma. Pediatric glaucoma is an umbrella term that is used to include subtypes of glaucoma including: primary congenital glaucoma, juvenile open angle glaucoma, glaucoma following cataract surgery, glaucoma of acquired conditions, glaucoma associated with non-acquired ocular disease, and glaucoma associated with non-acquired systemic syndromes. Exclusion criteria for patients was any adult patient (> age 18) who is diagnosed with glaucoma that is not considered pediatric glaucoma.

Basic demographic data was collected; this includes patient age, gender and race. Social data including the patient's first 3 digits of their current zip code, number of "no shows" to clinic, and health insurance information were also collected. Visual acuity is subdivided into categorical variables such as good (VA between 20/20 to 20/25), moderate (20/25 to 20/200), and poor (worse than 20/200) based on World Health Organization's criteria.

The main outcome of interest is visual acuity. The primary risk factors include insurance, age, number of no-show appointments, and gender and race. While the focus of this paper is on geographic distribution of patients, the patient's zip code is not included in the statistical analysis as a risk factor. This is due to high heterogeneity of zip codes among patients, and thus no statistical significance can be meaningfully drawn from this data. However, recall that visualizing patient geography is a hypothesis generating method for underlying causes, and not a sufficient risk factor in and of itself.

Geographic Mapping

I used the software ARCGIS (ESRI, Redlands, California) in order to generate geographic representation of the pediatric glaucoma database. Initially, a publicly available map of the United States delineated by the first 3 digits of the zip code was imported into ARCGIS. A definition query was used so that only California was shown on the map. Subsequently, the data file with the patients' collected data was imported as well.

The patient data was geocoded using the first 3 digits of their zip code as the corresponding point, and a spatial join was used to link the zipcode map of California and the data map. Then using map symbology, patient count per zip code was color coded with darker colors representing a higher patient population[9].

I used the map symbology feature to represent predominant insurances by zip code, and frequency of lost-to-follow up by zip code. Subsequently, maps were made using two sets of features from the dataset, including a map of visual outcomes stratified by lost-to-follow-up frequency, and a map of insurances also stratified by lost-to-follow-up, with larger dots representing a higher rate of loss-to-follow-up.

Statistics

The risk of having a poor visual outcome was calculated using multivariate modeling with lost-to-follow-up, insurance type, age, sex and age as risk factors. Visual loss will be measured as a binary variable as either 'poor' or 'moderate/good.'

All statistical analyses were conducted using SAS 9.4 (SAS Institute). Univariate analysis for vision was conducted by calculating Odds Ratios for predictors with 95% CI while accounting for two eye scores as a random effect. Hypothesis tests were two-sided and evaluated at a significance level of 0.05.

A mixed effect model was performed with subject as a random effect to account for the correlation between each subject's two eyes if both were given.

Results

Summary Patient Characteristics

A total of 177 patients were enrolled into the study in which 233 eyes were included in the study. 91 patients had bilateral disease and 51 patients had unilateral disease. Table 1 shows the baseline characteristics of the population. Table 2. shows the Odds Ratios and 95% Confidence Intervals for patient characteristics and social economic status (SES) predictors to the vision test.

Table 1. Population Summary.

Characteristic		**N**	**%**
Sex	Female	92	52.0
	Male	85	48.0
Race	White	77	43.5
	African American	10	5.7
	Asian	12	6.8
	Other	8	4.5
	Unknown/Not Reported	70	39.6
Insurance	Medicaid	67	37.9
	Private	96	54.2
	Unknown	14	7.9
Characteristic	**N**	**Mean**	**SD**

Age (in months)	177	51.7	69.5
No Shows	177	2.5	4.4

Table 2. **Univariate** Odds ratio estimates and p-values for patient characteristics for predictors of bad vision based on mixed effect logistic regression model.

Comparison	**Estimate**	**95% Confidence Limits**		**P-Value**
Sex: Female vs Male	**0.51**	**0.27**	**0.97**	**0.04**
Race: African American vs. White	*0.26*	*0.06*	*1.09*	*0.07*
Race: Asian vs. White	0.63	0.15	2.59	0.52
Race: Other vs. White	0.43	0.12	1.58	0.20
Race: Unknown/Not Reported vs. White	0.91	0.45	1.85	0.79
Ethnicity: Hispanic/Latino vs. Not Hispanic or Latino	0.61	0.30	1.25	0.17
Ethnicity: Unknown/Not Reported vs. Not Hispanic or Latino	1.98	0.59	6.60	0.26
Insurance: Private vs. Medicaid	*1.92*	*0.99*	*3.71*	*0.053*
Insurance Unknown vs. Medicaid	2.93	0.72	11.94	0.13

unit change of Age from mean	1.00	0.99	1.00	0.11
unit change of 'No Shows' from mean	0.95	0.89	1.01	0.12
unit change of 'Number of Surgeries' from mean	0.99	0.76	1.29	0.96
Effects of continuous variables are assessed as one unit offsets from the mean. The AT suboption modifies the reference value and the UNIT suboption modifies the offsets.				

Notably, of the statistically significant results, the odds of having a good vision score are 49% lower in Females compared to Males (p-value = 0.04). Trending towards statistically significant is that the odds of having a good vision score are 74% lower in AA compared to Whites (p-values = 0.07), and the odds of having a good visual outcome is almost half in Medcaid insurance compared to private.

Table 3. **Multivariate** Odds ratio estimates and p-values for patient characteristics for predictors of bad vision based on mixed effect logistic regression model.

Comparison	**Estimate**	**95% Confidence Limits**		**P-Value**
Sex: Female vs Male	**0.47**	**0.22**	**0.98**	**0.04**
Race: African American vs. White	0.31	0.07	1.43	0.13
Race: Asian vs. White	0.49	0.11	2.26	0.36

Race: Other vs. White	0.85	0.20	3.69	0.82
Race: Unknown/Not Reported vs. White	1.30	0.55	3.06	0.55
Ethnicity: Hispanic/Latino vs. Not Hispanic or Latino	0.60	0.25	1.46	0.26
Ethnicity: Unknown/Not Reported vs. Not Hispanic or Latino	1.51	0.39	5.84	0.54
Insurance: Private vs. Medicaid	*1.98*	*0.93*	*4.21*	*0.08*
Insurance: Unknown vs. Medicaid	2.09	0.46	9.57	0.34
unit change of Age from mean	*1.00*	*0.99*	*1.00*	*0.07*
unit change of 'No Shows' from mean	0.98	0.91	1.06	0.63
Effects of continuous variables are assessed as one unit offsets from the mean. The AT suboption modifies the reference value and the UNIT suboption modifies the offsets.				

After adjusting for other predictors, the odds of having a good vision score are 53% lower in Females compared to Males (p-value = 0.04)

Table 4 *Vision for each eye by Zip Code:*

	Vision		
Zip Code	Poor Vision	Not Poor Vision	Total

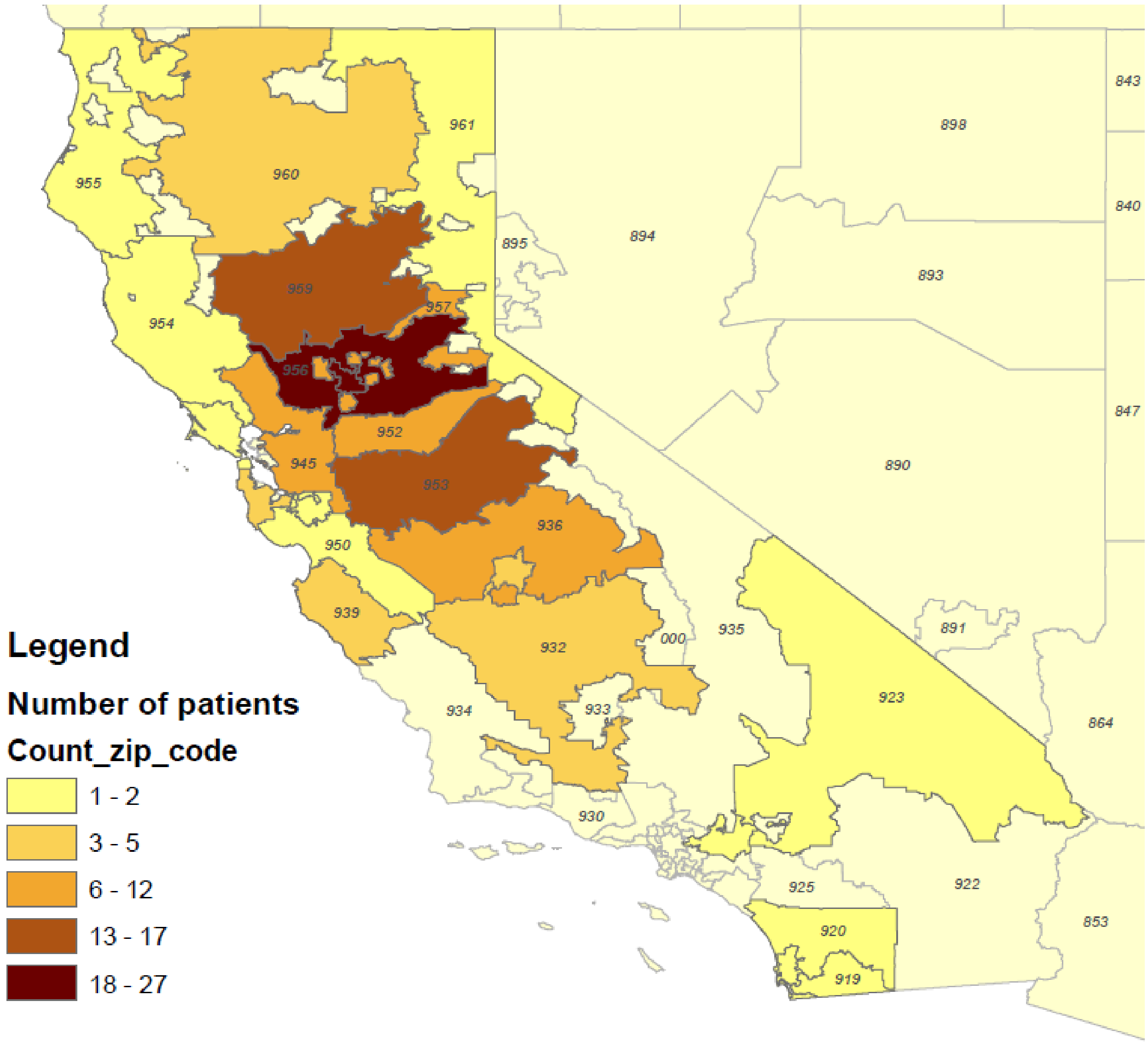
	N (%)	N (%)	N (%)
617	0 (0%)	1 (0.6%)	1 (0.4%)
782	0 (0%)	1 (0.6%)	1 (0.4%)
837	0 (0%)	0 (0%)	0 (0%)
838	0 (0%)	2 (1.2%)	2 (0.9%)
852	1 (1.5%)	0 (0%)	1 (0.4%)
894	0 (0%)	3 (1.8%)	3 (1.3%)
895	2 (3.1%)	12 (7.1%)	14 (6.0%)
897	0 (0%)	4 (2.4%)	4 (1.7%)
917	0 (0%)	0 (0%)	0 (0%)
919	0 (0%)	0 (0%)	0 (0%)
920	1 (1.5%)	2 (1.2%)	3 (1.3%)
921	0 (0%)	0 (0%)	0 (0%)
923	1 (1.5%)	0 (0%)	1 (0.4%)
932	0 (0%)	6 (3.6%)	6 (2.6%)
936	3 (4.6%)	6 (3.6%)	9 (3.9%)
937	3 (4.6%)	4 (2.4%)	7 (3.0%)
939	2 (3.1%)	4 (2.4%)	6 (2.6%)

940	0 (0%)	1 (0.6%)	1 (0.4%)
941	1 (1.5%)	2 (1.2%)	3 (1.3%)
945	4 (6.2%)	9 (5.4%)	13 (5.6%)
949	1 (1.5%)	0 (0%)	1 (0.4%)
950	1 (1.5%)	1 (0.6%)	2 (0.9%)
951	1 (1.5%)	0 (0%)	1 (0.4%)
952	6 (9.2%)	10 (6.0%)	16 (6.9%)
953	6 (9.2%)	13 (7.7%)	19 (8.2%)
954	0 (0%)	3 (1.8%)	3 (1.3%)
955	1 (1.5%)	1 (0.6%)	2 (0.9%)
956	14 (21.5%)	24 (14.3%)	38 (16.3%)
957	1 (1.5%)	7 (4.2%)	8 (3.4%)
958	12 (18.5%)	26 (15.5%)	38 (16.3%)
959	2 (3.1%)	19 (11.3%)	21 (9.0%)
960	2 (3.1%)	4 (2.4%)	6 (2.6%)
961	0 (0%)	2 (1.2%)	2 (0.9%)
996	0 (0%)	1 (0.6%)	1 (0.4%)
Total	**65 (27.9%)**	**168 (72.1%)**	**233 (100%)**

Table 4 shows vision and visual outcome by zip code. No statistical significance was seen between outcomes and their zip-code prefix.

Maps

Figure 1 demonstrates the distribution of patients by the first 3 digits of their zip code



I added an additional layer of data in Figure 2, where in Figure 2 uses color-coded dots to show the predominant visual outcome, with green representing good, yellow moderate and red poor. In Figure 3, an alternative manner of representing visual outcomes were used: by using a heat map where cold colors (blue) represented a low number of poor outcomes, and hot colors (red) represented a high number poor visual outcomes.

Figure 2 shows distribution of the most predominant visual acuity outcomes

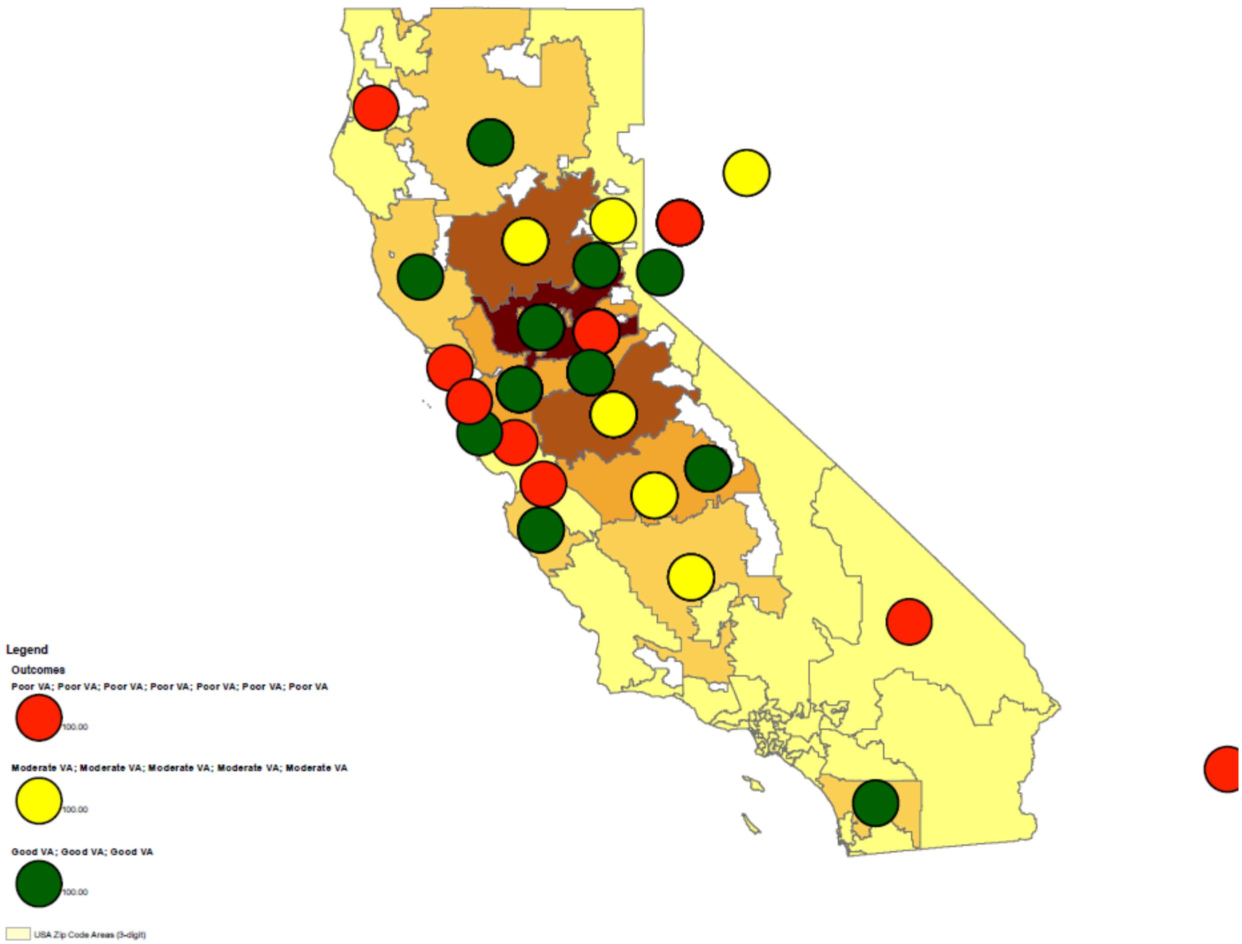
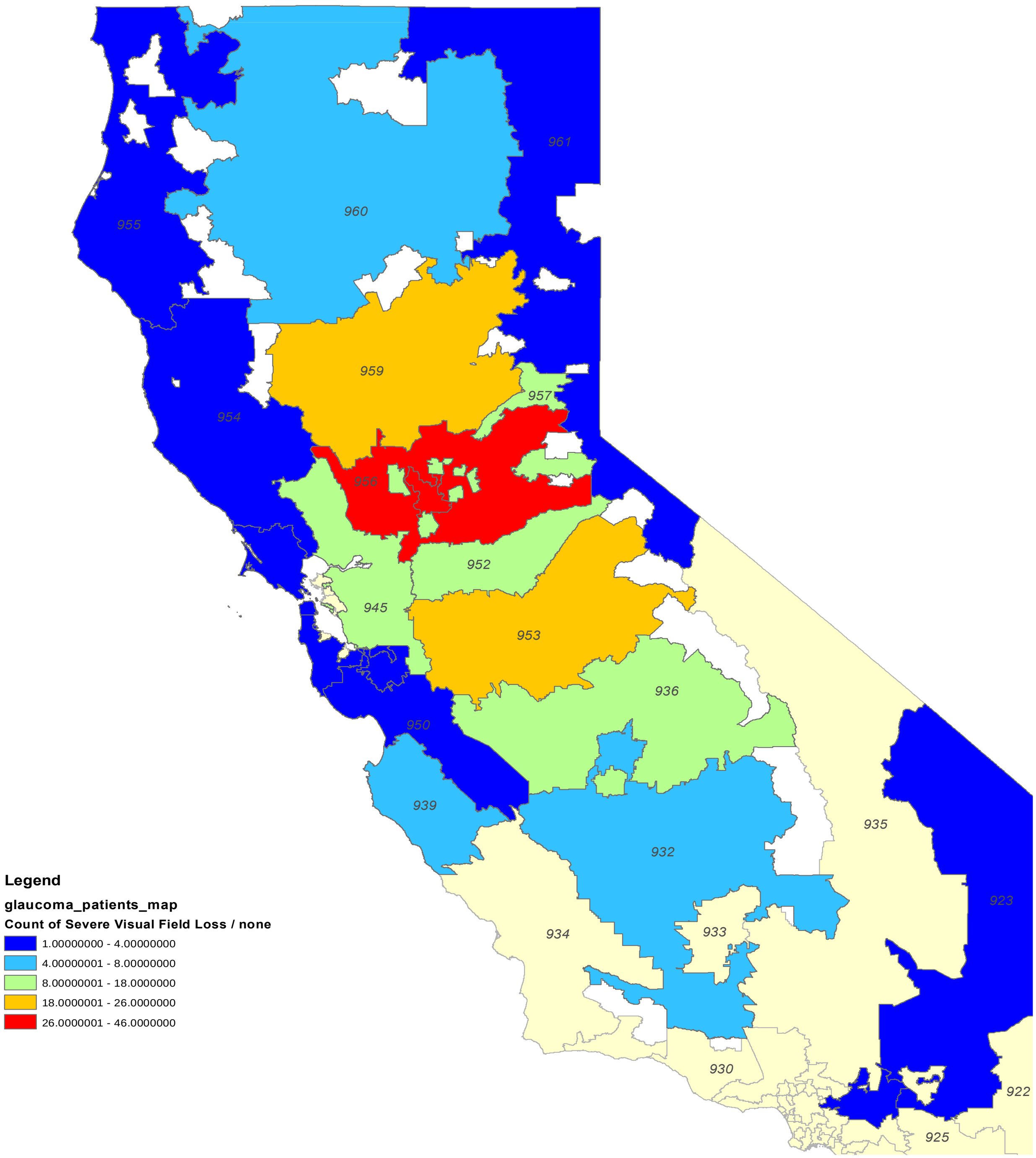


Figure 3 shows an alternate way of presenting distribution of visual acuity outcomes


961
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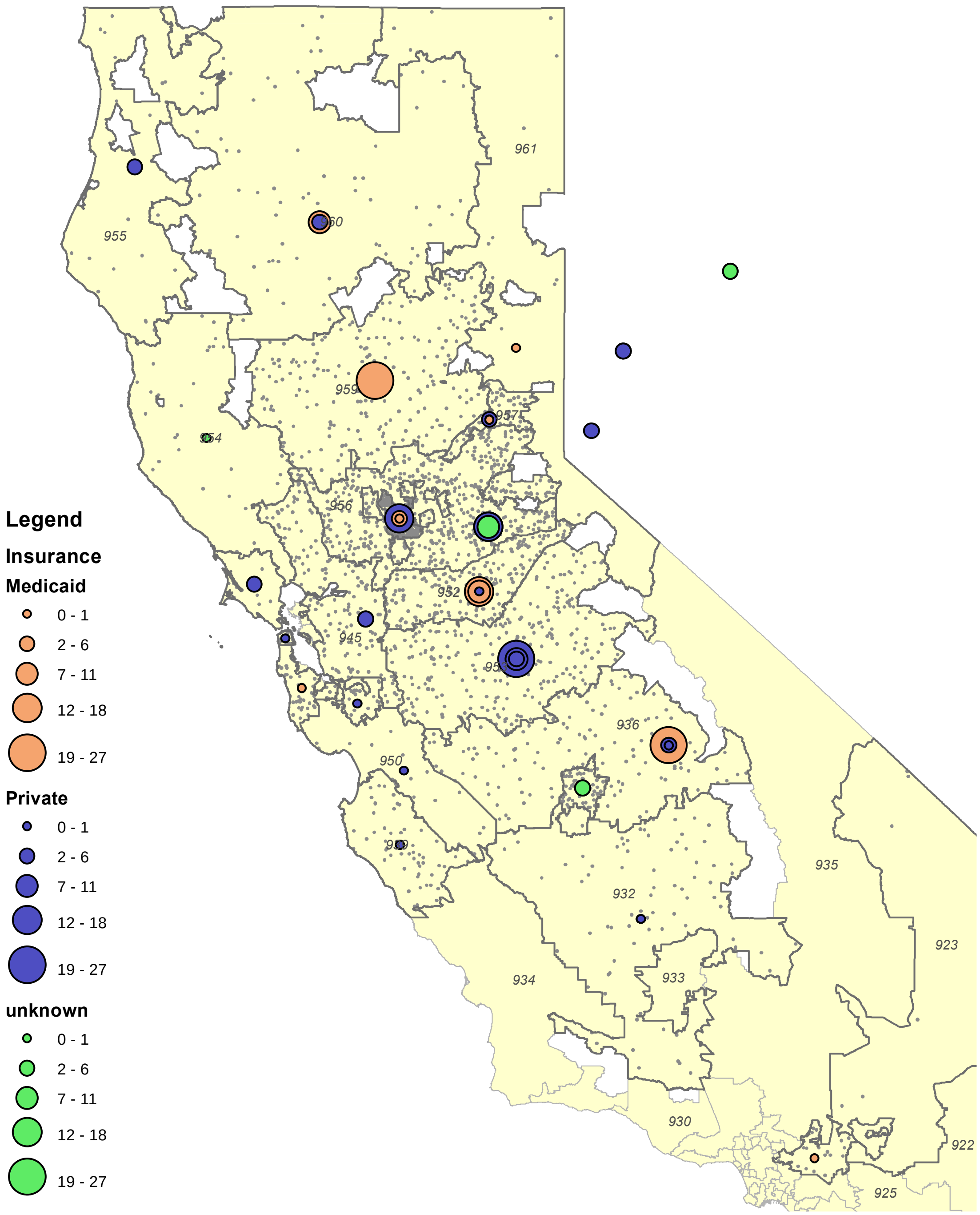
923
934
933
930
922
925
Legend
glaucoma_patients_map
Count of Severe Visual Field Loss / none
1.00000000 - 4.00000000
4.00000001 - 8.00000000
8.00000001 - 18.0000000
18.0000001 - 26.0000000
26.0000001 - 46.0000000

Figure 4 This map demonstrates number of patients per zip code with types of insurance delineated by color, with larger spots indicating a larger proportion of patients having that insurance



Discussion

The purpose of this paper is to demonstrate the ability of maps to serve both as a hypothesis generating methodology which can subsequently be investigated with statistical analysis, but also as a powerful tool to represent data visually.

Analysis and limitations of mapping patient outcomes:

Figure 1 of the study demonstrates the raw number of patients in each 3-digit zip code region, and unsurprisingly, as the tertiary referral center is UC Davis in the 3-digit zip code zone of 958, both 958 and 956 showed the highest number of patients. This can also be due to a more densely populated urban region. This is corroborated by Table 3 in which the zip codes prefix 956 and 958 each both have 38 patients in its population. This type of map is helpful for the practitioner to visualize their patient population.

Figures 2 adds additional information by superimposing visual outcome onto each zip code. This demonstrates regional differences in demographics and also outcomes in separate maps. In figure 2, no clear patterns in visual outcomes could be drawn. Additionally, Figure 2 may be visually confusing as two sets of color codes were used to represent two patient factors. Therefore, Figure 3 was created to represent only number of patients with poor visual outcomes. Again, Figure 3 might be misleading, because there are a higher number of patients in zip codes 956 and 958, so naturally they would also have a higher number of patients with poor vision, and thus the region does not represent additional risk of having a poor visual outcome.

Similarly, with Figure 4 there is no apparent pattern in insurance and outcome while it trended towards statistically significant in our dataset. Again, this is likely due to private insurances being overrepresented on the map and therefore is inconsistent with the overall findings in statistical analysis. This is also because the area codes 956 and 958 are likely more heavily represented in the statistical analysis. In other words, while it represents merely 2 "dots" on the map, it accounts for 32% of the data.

Lastly, no statistical significance in visual outcomes could be seen when comparing individual zip codes. This is because each zip code prefix contains only a small number of patients (if any), and that does not generate enough power to distinguish any differences between zip codes. Using individual zip codes or even their prefixes is not powerful enough to discern any useful patterns. Therefore, zip codes need to be grouped by shared characteristics instead, or alternatively, a much larger number of N would be necessary to generate statistical significance. For example, we could potentially include zip code prefixes into 3 categories of "near", "moderate" and "far" distance from the medical center. By categorizing individual zip codes, we generate a more powerful analysis of location and patient outcome.

Comparisons to existing research on pediatric glaucoma

In the univariate analysis, being female increased the risk of a poor visual outcome, while African American and insurance type trended towards significance in terms of poor visual outcomes. Only female sex remained as a significant risk factor for poor visual outcomes in a multivariate analysis. Most studies in pediatric glaucoma specifically observe surgical outcomes, but one study by Khitri et al. reported that unilateral disease, multiple surgeries, poor vision at diagnosis were associated with poor outcome[10]. Gender was not a risk factor for poor visual outcome, and our study did not see a correlation between more surgeries and poor visual outcomes.

To my knowledge, this is the first study in pediatric glaucoma to include social factors for poor outcomes (insurance type, location and loss to follow-up). While insurance was a risk factor to poor outcome in the univariate analysis, it was not the case in the multivariate analysis. The number of visits that were missed were also not associated with poorer outcomes, though perhaps the time elapsed between visits due to follow-up loss would have been a better predictor. This was observed in a separate study of pediatric patients who develop glaucoma post-cataract surgery[6].

Conclusions

In this study of pediatric glaucoma patients' visual outcome, we found that females have a higher risk of having a poor visual outcome in the multivariate analysis, while insurance and race trended towards significance. The mapping of patient outcomes, while a helpful way to represent patient demographics, does not necessarily reflect the data analysis, but still holds a helpful hypothesis generating role.

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