Demographics and Seasonality of Retinal Detachment, Retinal Breaks, and Posterior Vitreous Detachment from the IRIS® Registry (Intelligent Research In Sight)

Steven S. Saraf, MD, Megan Lacy, MS, Matthew S. Hunt, BS, Cecilia S. Lee, MD, MS, Aaron Y. Lee, MD, MSCI, Yewlin E. Chee, MD, on behalf of IRIS Registry Research Analytic Centers

PII: S2666-9145(22)00034-3
DOI: https://doi.org/10.1016/j.xops.2022.100145
Reference: XOPS 100145

To appear in: Ophthalmology Science

Received Date: 7 September 2021
Revised Date: 8 March 2022
Accepted Date: 14 March 2022

Please cite this article as: Saraf S.S., Lacy M., Hunt M.S., Lee C.S., Lee A.Y., Chee Y.E. & on behalf of IRIS Registry Research Analytic Centers, Demographics and Seasonality of Retinal Detachment, Retinal Breaks, and Posterior Vitreous Detachment from the IRIS® Registry (Intelligent Research In Sight), Ophthalmology Science (2022), doi: https://doi.org/10.1016/j.xops.2022.100145.

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Demographics and Seasonality of Retinal Detachment, Retinal Breaks, and Posterior Vitreous Detachment from the IRIS® Registry (Intelligent Research In Sight)

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Running title: Demographics and Seasonality of Retinal Detachment

The material was presented in part at The Association for Research in Vision and Ophthalmology annual meeting (2021, Virtual Meeting)

Funding sources: NIH/NIA R01AG060942 (Cecilia S. Lee); NIH/NEI K23EY029246 (Aaron Y. Lee), NIA/NIH U19AG066567 (Cecilia S. Lee, Aaron Y. Lee), Research to Prevent Blindness Career Development Award (Aaron Y. Lee); Latham Vision Innovation Award (Cecilia S. Lee, Aaron Y. Lee), and an unrestricted grant from Research to Prevent Blindness (Steven S. Saraf, Cecilia S. Lee, Yewlin E. Chee, Aaron Y. Lee)

Disclosures: Aaron Lee reports support from the US Food and Drug Administration, grants from Santen, Regeneron, Carl Zeiss Meditec, and Novartis, and personal fees from Genentech, Roche, and Johnson and Johnson, outside of the submitted work. This article does not reflect the opinions of the Food and Drug Administration. Matthew S. Hunt: Boston Scientific (Patent, ID: US20180228896A1). The remaining authors have no financial disclosures to report.

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Abstract

Objective:
To investigate the incidence, seasonal variation, and differences among age, sex, and race for rhegmatogenous retinal detachment (RRD) repair, retinal break (RB) treatment, and posterior vitreous detachment (PVD) in the IRIS Registry.

Design:
Retrospective database study

Subjects:
Patients in the IRIS Registry who underwent RRD repair, RB treatment, or cataract surgery (CS) based on CPT codes and PVD diagnosis based on ICD-9/ICD-10.

Methods:
Daily incidence rates within the IRIS Registry were defined as the ratio of number of patients who underwent RRD repair or RB treatment and the number of patients diagnosed with PVD to the total number of patients followed on a given day within the IRIS Registry. The CS group was included as a comparison for seasonal variation given its elective nature. Rates were stratified by decade of life, sex, and race.

Main Outcome Measures:
Time series trends for incidence rates of RRD, RB and PVD.

Results:
A total of 7,115,774 patients were diagnosed with incident PVD during the study period, 237,646 underwent RRD repair, and 359,022 had RB treatment. 5,940,448 patients who underwent CS were also included. The mean daily incidence within the IRIS Registry for RRD repair, RB treatment, PVD diagnosis, and CS were 0.46, 0.70, 13.90, and 11.80 per 100,000 patients,
respectively. Men had higher incidence within the IRIS Registry of RRD repair and RB treatment than women, whereas women had higher incidence within the IRIS Registry of PVD diagnosis.

RRD incidence within the IRIS Registry was higher in Whites compared to others. Seasonal decreases in PVD, RB treatment, RRD repair, and CS corresponded to national holidays with larger decreases in winter months. Kaplan-Meier estimates showed that RRD repair and RB treatment typically occurred within 60 days of PVD diagnosis.

Conclusions:

Within the IRIS Registry, the highest incidence of RRD was in the 6th and 7th decade of life, consistent with prior studies. The higher incidence of RRD repair and RB treatment in men compared to higher incidence of PVD in women may suggest an inherent sex-related risk. The seasonal variation associated with national holidays was less pronounced for RRD repair and RB treatment.
Introduction

Rhegmatogenous retinal detachment (RRD) is a vision-threatening condition with an estimated incidence of 10-18 per 100,000 population per year in the United States.\textsuperscript{1-3} Posterior vitreous detachment (PVD) is a normal age-related anatomic development that can lead to the formation of retinal breaks (RB) at sites of firm vitreoretinal adhesion and subsequent retinal detachment.

RB are identified in 8-16\% of patients with acute symptomatic PVD and may progress to RRD in 30-50\% of cases if untreated.\textsuperscript{4-8} Understanding the relative incidence of these conditions and the timing of RB and RRD following an acute PVD may be important to determine clinical surveillance guidelines.

The estimated incidence of RRD in the United States has been derived from surveys and computer database studies conducted at a local level in Iowa and Minnesota.\textsuperscript{1-3} Similarly, estimated rates of RB formation and PVD have been derived from single-center studies, meta-analyses and autopsy studies.\textsuperscript{4-7,9} Demographic findings from international studies have shown an association with age, with the highest incidence of RRD being reported in the sixth (ages 50-59) and seventh (ages 60-69) decades of life.\textsuperscript{2,3,10-13} More studies report a preponderance of RRD in men compared to women (male to female ratio 1.3:1 to 2.3:1).\textsuperscript{12,14-18} However, it is unclear whether this is due to a higher exposure to ocular trauma, healthcare avoidance, or an inherent sex-related risk. Differences among race with respect to RRD and RB formation have not been reported from study populations in the United States.\textsuperscript{1-3}

PVD onset is known to be associated with increasing age.\textsuperscript{9} Environmental factors have been hypothesized to also contribute, such as light exposure, temperature, and humidity.\textsuperscript{19} Seasonal variation in RRD incidence has been studied in local populations but with conflicting findings. Select studies show a summer peak\textsuperscript{20-23}, no seasonality\textsuperscript{11,15,24}, and a winter peak.\textsuperscript{25} Larger
scale study is necessary to better determine environmental contributions to PVD progression and secondary complications such as RB formation and RRD.

At the time of writing, the American Academy of Ophthalmology IRIS® Registry (Intelligent Research In Sight) is able to provide aggregate data from over 300 million ophthalmology visits from 60 million unique patients in the United States. Our aim is to utilize the IRIS Registry to report on a national scale the daily incidence rate of RRD, RB, and PVD. Furthermore, we aim to use the large IRIS Registry dataset to provide additional insight on questions regarding seasonality, age, sex, and race with respect to these conditions.

Methods

This study was conducted in accordance with the Declaration of Helsinki. Given the use of de-identified patient data, the review was exempted from the University of Washington Institutional Review Board. The methods of data collection and aggregation of the IRIS Registry database have previously been described. Version 2020_07_28 of the IRIS Registry, which was last modified on October 23rd, 2020, was used for this study.

Patients in the IRIS Registry between 2014 and 2018 were included in this study. First PVD diagnosis was based on ICD-9/10 codes. Laterality information from EMR linked to the ICD-9/10 PVD diagnosis was used to confirm its laterality. First instances of RRD repair, RB treatment, and cataract surgery (CS) were identified based on current procedural terminology (CPT) codes (Supplemental Table 1). The incidence for PVD and CS were calculated as an average daily incidence, dividing the number of identified patients by the total number of patients followed by the IRIS registry on a given day. The CPT code for complex retinal detachment repairs was excluded to recruit a population more consistent with primary RRD repair, rather than recurrent detachments or diabetic tractional retinal detachments. The incidence rate was defined as the
The number of outcomes (RB treatment, RRD repair, or both) by the number of patients who had a previous PVD diagnosis and were therefore at risk. Patients were considered followed and at risk if the day fell between their first and last records in the IRIS Registry and they had no history of the event in question on any date prior to that point.

Overall incidence rates and stratified incidence rates by decade of life, sex, and race were plotted by day per 100,000 patients. The denominator for every substrata was recalculated to ensure that the denominator represented the population at risk throughout all analyses. Given that date of birth is redacted in the IRIS Registry for patients 87 years old or older at the time of data release, patients over 86 years of age were included in the age group 70 and above. Race was categorized as Whites or other races. The CS group was included as our internal comparator group given its elective nature and its expected fluctuations during holidays, weekends, or seasons. Means and Wald 95% confidence intervals for daily incidence rates were reported. Two sample t-tests were used to compare the differences in mean daily incidence rates between males and females and Whites and other races for PVD, RB treatment, and RRD repair.

Kaplan-Meier curves were fit to estimate the time from PVD diagnosis to RRD repair and/or RB treatment. All analyses were performed with R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 7,115,774 patients were diagnosed with incident PVD between the start of 2014 and end of 2018. Patients undergoing RRD repair (n=237,646), RB treatment (n=359,022) and CS (n=5,940,448) during this same time period were also included in the analysis. The mean daily
incidence within the IRIS Registry for RRD repair, RB treatment, PVD, and CS were 0.46, 0.70, 13.9, and 11.8 per 100,000 patients, respectively (Table 2).

Seasonal variation in RRD repair, RB treatment, PVD, and CS demonstrating relative declines in average point incidence that corresponded to national holidays are shown in Figure 1; these fluctuations were more pronounced during winter months. The seasonal variation in the rate of RRD repair, RB treatment, and PVD were similar to seasonal variation in cataract surgery (Figure 1). The average daily incidence within the IRIS Registry of CS was lowest in Q1 at 11.6 per 100,000 patients, 11.8 per 100,000 patients in Q2 and Q3, and highest in Q4 at 12.1 per 100,000 patients. Average daily incidence within the IRIS Registry of PVD per quarter ranged from 13.4 cases per 100,000 patients in Q2 to 15.1 per 100,000 patients in Q4. Average daily incidence within the IRIS Registry of RB treatment ranged from 0.68 to 0.72, and RRD repair incidence ranged from 0.45 to 0.47 per quarter (Table 2).

Time series showing seven day moving average point incidence within the IRIS Registry for RRD repair, RB treatment and PVD by age and sex demographics are shown in Figure 2. The highest incidence of RRD repair was between the ages of 50 to 59 years, and 60 to 69 years, at 0.76 and 0.67 per 100,000 patients, respectively. Men had higher incidence within the IRIS Registry of RRD repair (0.67 vs 0.32 per 100,000 patients, p<0.001) and RB treatment (0.86 vs 0.59 per 100,000 patients, p<0.001) than women. In contrast, women had a higher incidence within the IRIS Registry of PVD than men (14.4 vs 13.2 per 100,000 patients, p<0.001).

Time series showing seven day moving average point incidence within the IRIS Registry for RRD repair, RB treatment and PVD by age and race demographics are shown in Figure 3. RRD, RB, and PVD incidence within the IRIS Registry was higher in Whites compared to other races (0.53 vs 0.31, p<0.001, 0.76 vs 0.59, p<0.001, and 15.9 vs 10.1, p<0.001 per 100,000 patients, respectively).
The proportions of patients diagnosed with PVD that underwent RB treatment and RRD repair over time are shown with Kaplan-Meier curves in Figure 4. At 90 days, 0.4% had undergone RB treatment, 0.4% had RRD repair, and 0.7% had either. In each of the three outcomes (RB treatment, RRD repair, or both), the majority occurred within 60 days after PVD. The probability of requiring either RB treatment or RRD repair 60 days after PVD diagnosis was less than 0.7%.

Discussion
We used the IRIS Registry to calculate a daily incidence rate within the IRIS Registry for RRD repair, RB treatment and PVD. The mean daily incidence for the duration of the study was calculated as 0.46, 0.70, and 13.9 per 100,000 patients, respectively. Given that these figures represent an incidence out of the total number of patients being followed in ophthalmologic care within the IRIS Registry, it is not directly comparable to prior population studies. However, the total number of RRD repair cases in 2018 (62,902) can be used with a 2018 population estimate of nearly 327 million to estimate an annual-incidence lower bound of 19.25 per 100,000 people in the United States, which is higher than estimates from prior studies.1–3 Our results show that these retinal procedures are substantially common and similar to 5% of the annual cataract surgery rate in the US. Our methodology reveals new insights on age, sex, race, and seasonality for these conditions on a scale that has not been previously investigated.

Our findings support that age is a risk factor for both RRD, RB formation, and PVD, consistent with prior studies.2,3,10–13 The incidence within the IRIS Registry of RRD repair was found to peak between the ages of 50-69, with an intermediate incidence between ages 40-49 and 70 and above. The smallest incidence was in the less than 40 age group. As would be expected, the time series for RRD repair and RB treatment correspond closely given that RB formation plays a necessary role in RRD.
Interestingly, the incidence of PVD within the IRIS Registry increases starting at age 50, initially corresponding with RRD repair and RB treatment. However, the incidence of PVD within the IRIS Registry remains high even above age 70, while RRD repair and RB treatment rates decline in this age group. Given that PVD onset confers a risk for RB formation and RRD, we would expect the rate of PVD-related complications to correspond with the PVD time series. A potential reason for this inconsistency is that our study defines PVD based on diagnosis code, which may be more commonly observed and billed in older patients, resulting in the application of the code in the absence of associated PVD symptoms. A physiologic explanation is also possible. Early PVD onset may correspond with a vitreopathy in which eyes undergo faster vitreous syneresis and have firmer vitreoretinal adhesions, predisposing to RB formation and RRD. Conversely, later onset PVD may represent a subset of eyes with a slower rate of syneresis, less associated with firm vitreoretinal adhesions.

Our findings showed a clear difference between men and women in regard to incident RRD repair, RB treatment, and PVD. Men consistently showed a higher incidence of RRD repair and RB treatment through all age groups within the IRIS Registry, with the largest differences being noted at ages 50-69, during the peak decades for incident RRD repair and RB treatment. On the other hand, women had a higher incidence of PVD within the IRIS Registry between ages 50-69, a finding that became less pronounced above age 70. Prior studies have similarly shown higher rates of PVD in women, although other studies have found no difference. The higher incidence of PVD in women with a lower incidence of RRD repair and RB treatment again demonstrates that the relationship between PVD and RRD is complex and additional factors are likely contributing.

The disparity between men and women in relation to RRD repair and RB formation has been noted in multiple prior studies. The reasons for a higher incidence of these complications in men are unclear. Men are at higher risk for ocular trauma, which either acutely or remotely
could contribute to RB formation and RRD. Men are also thought to avoid healthcare contact more than women, which may delay the presentation of men until they have suffered vision loss from RRD, whereas women may undergo more prophylactic RB treatments due to earlier presentation. Our dataset does not allow us to investigate the contribution of trauma to our findings. However, if healthcare avoidance were playing a role, then we would expect RB treatment and PVD rates to be lower in men compared to women. The higher rates of both RRD repair and RB treatments in men support an inherent sex-related risk for these conditions. The unexpected disparities between men and women warrant further study to better understand the relationship between PVD and the risk for RB formation and RRD.

Investigating differences in race with respect to RRD repair, RB treatment, and PVD was challenging due to incomplete demographic information. Our analysis was simplified to compare Whites to other races and found higher rates of RRD repair in Whites compared to other races. RB treatment was found to be higher in Whites compared to other races, especially at ages 50-59, 60-69 and greater than 70. Rates of PVD were similarly higher in Whites in these age groups. Prior study comparing the incidence of RRD among races is limited, especially in the United States where epidemiologic studies have been conducted in predominantly White populations yielding 10-18 per 100,000. In the United Kingdom, Mowatt et. al reported a three-fold lower rate of retinal detachment in Asians compared to Whites. On the other hand, international studies show both lower and similar RRD incidence rates to the United States such as in Singapore (10.5 per 100,000), Beijing (7.98 per 100,000) and Shanghai (14.4 per 100,000). Multiple prior studies have shown Blacks to have a lower incidence of RRD compared to Whites. Further study is needed to understand the observed differences in race and investigate whether additional confounders are at play, such as barriers to healthcare access.
To assess seasonality of RD repair, RB treatment and PVD, we compared the incidence within
the IRIS Registry of these conditions to that of CS. CS was selected due its elective nature,
which would provide an understanding of seasonal fluctuations in ophthalmologic care dictated
by non-medical factors. Our findings showed that seasonal variations in CS corresponded highly
with national holidays. Similarly, RD repair, RB treatment, and PVD were influenced by national
holidays, especially in the winter months. This effect was expectedly less pronounced in RRD
repair and RB treatment, as these conditions represent ophthalmic emergencies that require
prompt attention. No summer or winter peaks were noted for the investigated conditions. The
winter months where holidays were more frequent corresponded to the lowest rate of all
investigated procedures, suggesting this finding represents an artifact, though a true winter
decline in RD repair and RB treatment during these months remains possible. Due to our
methodology of utilizing billing codes to assess seasonality, our findings are likely biased toward
office-based care and may omit instances of care received through emergency departments,
which may ultimately limit our ability to assess seasonality. Seasonal dips in office-based care
may also correspond to spikes in care at tertiary referral centers that may not be captured due
to potential sampling bias of the practices enrolled in the IRIS Registry. However, information on
the types of eyecare centers participating in the IRIS Registry is not currently available to
investigate these types of questions. The association of CS with subsequent PVD has been
well-demonstrated in the literature but we used CS as a control condition to delineate the
holiday-related fluctuations in the frequency of non-urgent surgical care such as CS. 39

We investigated the timing of progression to RB treatment and RRD repair after PVD diagnosis.
The majority of RB treatments and RRD repairs occurred within 6-8 weeks of PVD diagnosis,
which is consistent with the findings of prior studies that have evaluated the timing of these
events. In our analysis of IRIS Registry data, the probability of requiring either treatment of RB
or repair of RRD was less than 0.7% when greater than 60 days after PVD. This was lower than
other published studies except one, which found no new retinal breaks in 105 patients on follow-up examination after PVD. The incidence of delayed RB or RRD after PVD diagnosis in other past studies ranged from 1.5% to 3.9%. One potential reason for the relatively lower probability of RB treatment or RRD repair after PVD in our analysis was the inclusion of all patients with a new diagnosis of PVD in the IRIS Registry, which may not necessarily signal a newly symptomatic PVD, but rather the first use of the PVD billing code. Past studies included patients with clinical complaints consistent with an acute, symptomatic PVD, which may explain the higher likelihood of RB treatment or RRD repair found in these studies.

Our study has additional limitations. Multiple possible CPT codes were used to define RRD repair. However, the CPT code for complex retinal detachment repair was excluded as it is also used for diabetic tractional retinal detachment repair and recurrent RRD repair. Excluding the CPT code for complex retinal detachments likely excluded a subset of patients who presented late after primary RRD. However, we believe the benefit of excluding these patients was worthwhile in order to also exclude a likely large cohort of patients who underwent diabetic tractional retinal detachment repair, which if included would make our study less clinically applicable to primary RRD repair. We defined eyes at risk for RB treatment and RRD repair as those coded previously as having a PVD. A limitation of our study is that this may not capture patients who may experience retinal breaks or detachments in the absence of a PVD. The sharp increase in PVD rates shown in Figure 1 that occurred in October 2015 also highlights a limitation of the use of diagnosis codes. This increase occurred during the transition from ICD-9 to ICD-10 codes and likely represents an artifact in billing than an actual increase in PVD incidence between 2015 and 2016. It is possible the new ICD-10 code being implemented in billing was counted as “new” by our methodology. We chose to use CPT codes as they are a more robust approach to identify a procedure date or surgery date. ICD codes can be re- implemented on multiple clinic visits (both before and after the true procedure date), making
pinpointing an exact procedure date challenging. However, inconsistencies in IRIS registry participation, such as an office-based center working out of a surgery center that is not an IRIS Registry participant may introduce inconsistencies to the dataset.

While there are inherent limitations to conducting a large study based solely on billing and procedure codes, we believe our findings contribute valuable insights to the epidemiology of RRD, RB formation and PVD on a scale that has not previously been examined. Future directions of study should be aimed both to understand the implications of the differences observed between demographic groups and expand datasets such as the IRIS Registry to collect more granular information that could help improve future investigations.
References


Figure legends

**Figure 1.** Stacked time series 2014-2018 showing 7 day moving average point incidence for cataract surgery (CS), posterior vitreous detachment (PVD), retinal break (RB) treatment, and rhegmatogenous retinal detachment (RRD) repair. National holidays shown in gray dashed lines in the following order: New Year's Day, Martin Luther King Jr. Day, President's day, Memorial Day, Independence Day, Labor Day, Veterans Day, Thanksgiving, and Christmas.

**Figure 2.** Time series showing 7 day moving average point incidence by sex and age for rhegmatogenous retinal detachment (RRD) repair, retinal break (RB) treatment, and posterior vitreous detachment (PVD) diagnosis.

**Figure 3.** Time series showing 7 day moving average point incidence by race and age for rhegmatogenous retinal detachment (RRD) repair, retinal break (RB) treatment, and posterior vitreous detachment (PVD) diagnosis.

**Figure 4.** Kaplan-Meier curve showing time from onset of posterior vitreous detachment to treatment of retinal break (RB), repair of rhegmatogenous retinal detachment (RRD), or either. The estimated probability of RB and/or RRD following the diagnosis of PVD is depicted as the proportion of patients with PVD who have not had the specified event over time.
<table>
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<tr>
<th>Demographic Factor</th>
<th>Cataract Surgery (N=5,940,448)</th>
<th>Posterior Vitreous Detachment (N=7,115,774)</th>
<th>Retinal Break (N=359,022)</th>
<th>Rhegmatogenous Retinal Detachment (N=237,646)</th>
<th>IRIS® Registry Population (N=52,227,553)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean (SD)</td>
<td>69.49 (8.86)</td>
<td>67.81 (10.25)</td>
<td>58.36 (13.83)</td>
<td>59.46 (13.37)</td>
<td>51.36 (21.13)</td>
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<tr>
<td>&gt;86 n(%)</td>
<td>368,183 (6.20)</td>
<td>634,088 (8.91)</td>
<td>3,550 (0.99)</td>
<td>5,684 (2.39)</td>
<td>3,244,824 (6.21)</td>
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<tr>
<td>Missing Age</td>
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<td>3,241</td>
<td>70</td>
<td>52</td>
<td>481,689</td>
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<td>Sex n(%)</td>
<td>Female</td>
<td>3,434,341 (57.81)</td>
<td>4,305,477 (60.51)</td>
<td>175,558 (48.9)</td>
<td>95,398 (40.14)</td>
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<td>Male</td>
<td>2,486,064 (41.85)</td>
<td>2,786,320 (39.16)</td>
<td>181,779 (50.63)</td>
<td>140,939 (59.31)</td>
<td>22,094,347 (42.3)</td>
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<td>Race n(%)</td>
<td>White</td>
<td>4,376,056 (73.67)</td>
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<td>Black or African American</td>
<td>385,556 (6.49)</td>
<td>331,049 (4.65)</td>
<td>22,556 (6.28)</td>
<td>11,535 (4.85)</td>
<td>3,780,524 (7.24)</td>
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<tr>
<td>Asian</td>
<td>136,810 (2.3)</td>
<td>188,618 (2.65)</td>
<td>12,966 (3.61)</td>
<td>5952 (2.5)</td>
<td>1,559,546 (2.99)</td>
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<td>Other</td>
<td>60,213 (1.01)</td>
<td>56,053 (0.79)</td>
<td>4,682 (1.3)</td>
<td>3,002 (1.26)</td>
<td>456,534 (0.87)</td>
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<td>Unknown</td>
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<td>1,178,805 (16.57)</td>
<td>60,386 (16.82)</td>
<td>33,060 (13.91)</td>
<td>12,729,910 (24.37)</td>
</tr>
</tbody>
</table>

IRIS Registry population represents all patients eligible to fulfil at least one diagnosis or procedure code during the study period (2014-2018).
Table 2. Mean daily incidence, 95% confidence intervals (CI), and demographic factors for rhegmatogenous retinal detachment (RRD) repair, retinal break (RB) treatment, and posterior vitreous detachment (PVD).

<table>
<thead>
<tr>
<th></th>
<th>Rhegmatogenous Retinal Detachment</th>
<th>Retinal Break</th>
<th>Posterior Vitreous Detachment</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean Daily incidence</td>
<td>95% CI</td>
<td>Mean Daily incidence</td>
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<tr>
<td>All participants</td>
<td>0.461</td>
<td>0.459-0.462</td>
<td>0.703</td>
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<tr>
<td>Q1</td>
<td>0.448</td>
<td>0.445-0.451</td>
<td>0.683</td>
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<tr>
<td>Q2</td>
<td>0.473</td>
<td>0.470-0.476</td>
<td>0.704</td>
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<tr>
<td>Q3</td>
<td>0.471</td>
<td>0.468-0.474</td>
<td>0.709</td>
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<tr>
<td>Q4</td>
<td>0.45</td>
<td>0.446-0.454</td>
<td>0.717</td>
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<tr>
<td>Age</td>
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<td>0.584</td>
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<td>0.753-0.761</td>
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<td>60 - 69</td>
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<td>0.669-0.675</td>
<td>1.139</td>
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<td>70+</td>
<td>0.31</td>
<td>0.309-0.312</td>
<td>0.378</td>
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<td>Sex</td>
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<tr>
<td>Male*</td>
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<td>0.314-0.316</td>
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<td>Race</td>
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<tr>
<td>White**</td>
<td>0.534</td>
<td>0.532-0.536</td>
<td>0.761</td>
</tr>
<tr>
<td>Other**</td>
<td>0.312</td>
<td>0.310-0.314</td>
<td>0.586</td>
</tr>
</tbody>
</table>

*p<0.001 for the difference in mean daily incidence between males and females for each of PVD, RB, and RRD; **p<0.001 for the difference in mean daily incidence between white and those of other races for each of PVD, RB, and RRD.
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Precis
Differences exist among age, sex, and race in large-scale study of retinal detachment repair, retinal break treatment, and posterior vitreous detachment diagnosis. Seasonal decreases in the reported incidence of these conditions correspond with national holidays.