A Contemporary Retrospective Analysis of Endophthalmitis Following Cataract Surgery Using the IRIS® Registry (Intelligent Research in Sight)

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Financial Disclosures

- Michael H. Goldstein, Jamie L. Metzinger, Srilatha Vantipalli, and Nicole Oliynyk are employees of Ocular Therapeutix, Inc.
- Andrew A. Moshfeghi is a consultant for Ocular Therapeutix Inc.
- Helene B. Fevrier is an employee of Verana Health
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Background

Endophthalmitis after cataract surgery is a rare but vision-threatening event that requires a large sample size to conduct meaningful studies:

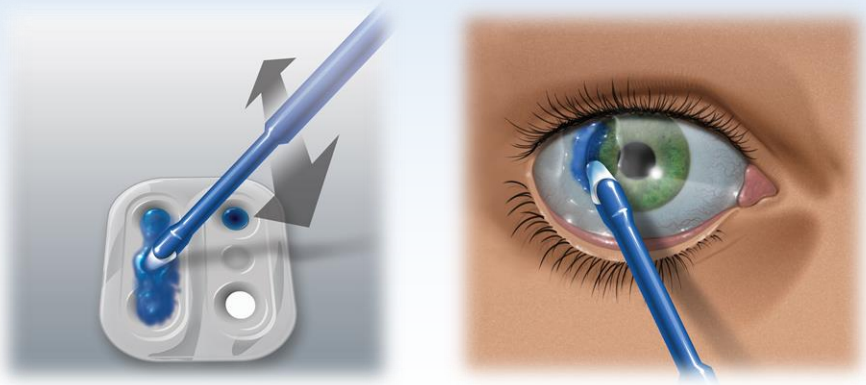
- Incidence ranges from 0.5 to 3.0 per 1,000 surgeries[1-9]
- Data from the AAO IRIS Registry between 2013 and 2017 identified an incidence of 0.42 per 1,000 surgeries[10]

American Academy of Ophthalmology IRIS® (Intelligent Research In Sight) Registry is an ideal database to access rare events such endophthalmitis following cataract surgery

- Clinical registry with aggregated real-world data from nearly 60 million unique patients contributed by ~16,000 eye care clinicians through electronic health records[11]

ReSure Sealant

A hydrogel sealant that creates an in situ temporary, soft surface barrier to prevent wound leakage from clear corneal incisions (up to 3.5 mm) after cataract surgery[12]



Rendering of mixing and applying ReSure Sealant

References: 1. Freeman EE, et al. *Arch Ophthalmol.* 2010;128(2):230-234. **2.** Hatch WV, et al. *Ophthalmology.* 2009;116(3):425-430. **3.** Javitt JC, et al. *Arch Ophthalmol.* 1991;109(8):1085-1089. **4.** Lundstrom M, et al. *Acta Ophthalmol Scand.* 2002;80(3):248-257. **5.** Morlet N, et al. *Br J Ophthalmol.* 2003;87(5):574-576. **6.** Norregaard JC, et al. *Br J Ophthalmol.* 1997;81(2):102-106. **7.** Somani S, et al. *Can J Ophthalmol.* 1997;32(5):303-310. **8.** Stein JD, et al. *Ophthalmology.* 2011;118(9):1716-1723. **9.** Stein JD. *Curr Opin Ophthalmol.* 2012;23(3):219-225. **10.** Pershing S, et al. *Ophthalmology.* 2020;127(2):151-158. **11.** IRIS Registry Data Analysis. American Academy of Ophthalmology. https://www.aao.org/iris-registry/data-analysis/requirements. Accessed October 15, 2021. **12.** ReSure Sealant. Instructions for Use. LCN 80-1004-011 Rev C. Ocular Therapeutix, Inc., Bedford, MA.

Key Objectives

Primary Objective

- To compare the incidence of endophthalmitis within 30 days of any cataract surgery between sites with and without access to ReSure Sealant

Secondary Objective

- To identify the incidence of endophthalmitis within 30 days of any cataract surgery in the United States

Study Design

Key Inclusion Criteria

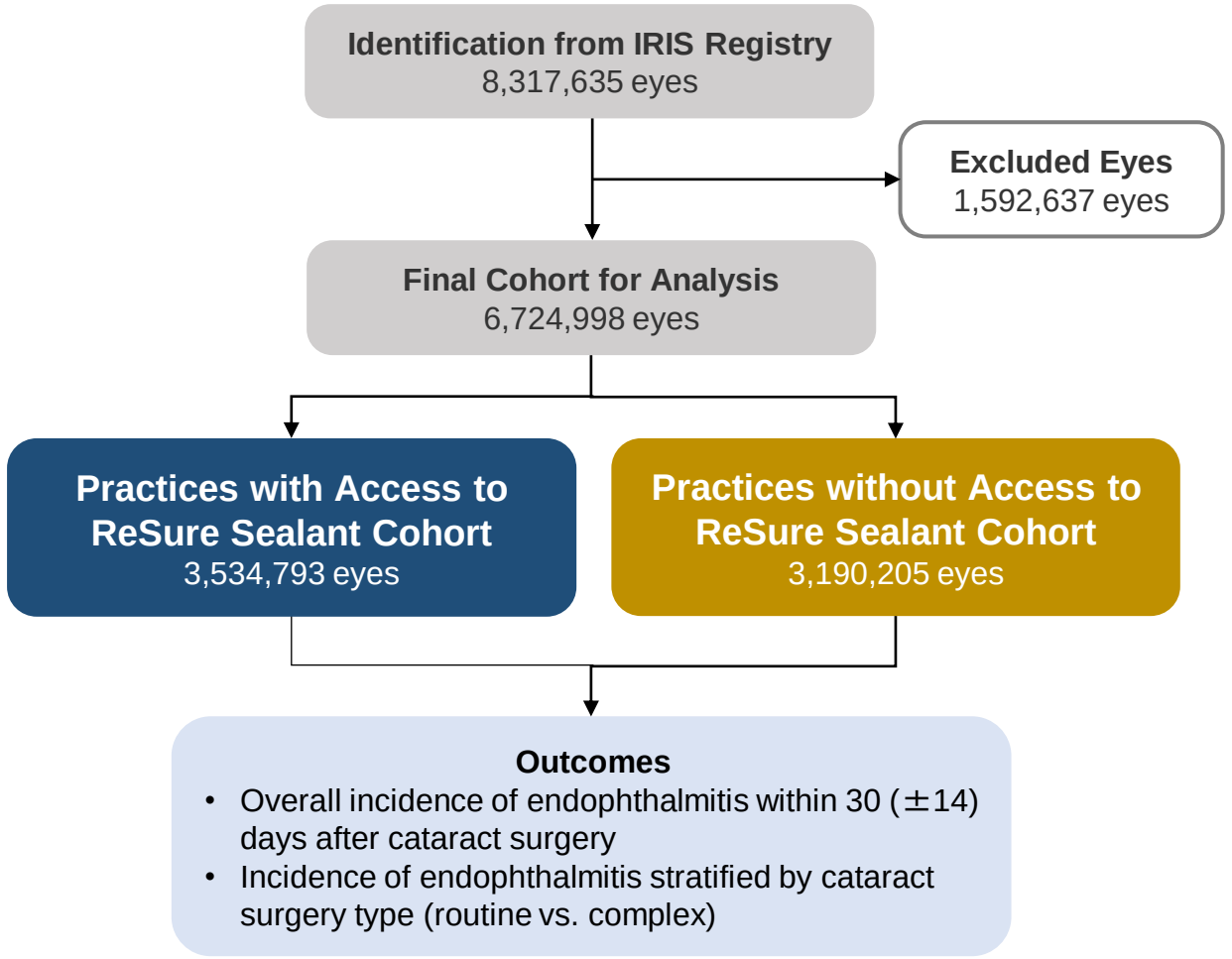
- Extracapsular cataract removal with insertion of intraocular lens prosthesis between January 1, 2016 and December 1, 2019
- Patients ≥22 years old and have ≥1 visits within 30 (±14) days after surgery
- Practices must have provided data for ≥30 days after each surgery

Key Exclusion Criteria

- Practices with <30 days of data following cataract surgery
- Patients with incomplete demographic information
  Physicians that are incompletely documented

Data Source and Analysis

- Data was collected from AAO's IRIS Registry with analyses conducted by Verana Health
- Given the large sample size, the *P* value for statistical significance was *P*<0.001
- Pre-specified level for clinical significance was doubling of observed incidence



Demographics and Baseline Characteristics

	All patient eyes (N=6,724,998)	Eyes at practices with access to ReSure (n=3,534,793)	Eyes at practices without access to ReSure (n=3,190,205)
Mean age (SD), years	70.91 (8.95)	70.79 (9.03)	71.03 (8.87)
Sex, n (%)			
Male	2,762,441 (41.1%)	2,081,026 (58.9%)	1,881,531 (59.0%)
Female	3,962,557 (58.9%)	1,453,767 (41.1%)	1,308,674 (41.0%)
Race, n (%)			
White	4,927,456 (73.3%)	2,545,213 (72.0%)	2,382,243 (74.7%)
Black	429,787 (6.4%)	227,936 (6.4%)	201,851 (6.3%)
Asian	151,199 (2.2%)	80,624 (2.3%)	70,575 (2.2%)
Native American/other Pacific	34,833 (0.5%)	20,897 (0.6%)	13,936 (0.4%)
Multirace	27,539 (0.4%)	14,393 (0.4%)	13,146 (0.4%)
Unknown	1,154,184 (17.2%)	645,730 (18.3%)	508,454 (15.9%)

SD, standard deviation

Demographics and Baseline Characteristics

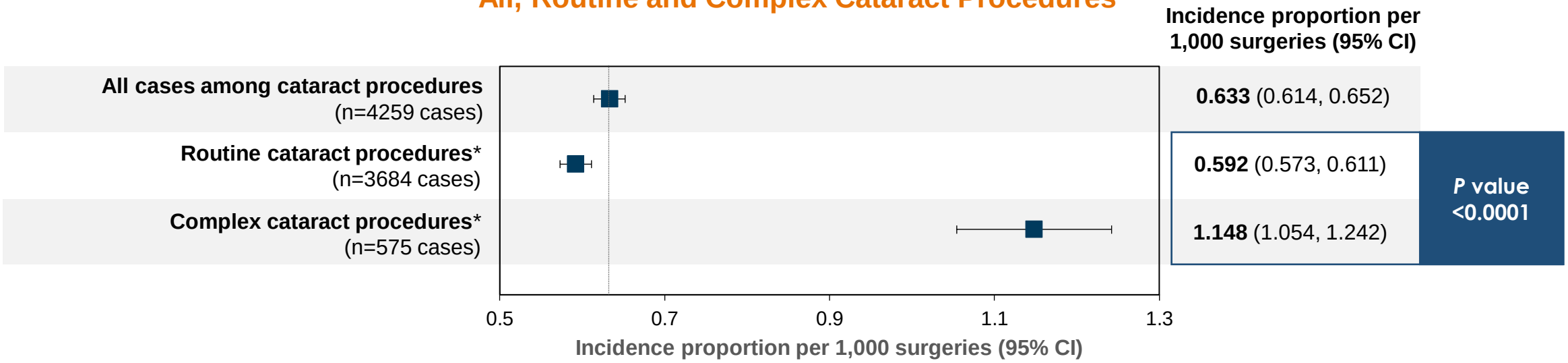
	All patient eyes (N=6,724,998)	Eyes at practices with access to ReSure (n=3,534,793)	Eyes at practices without access to ReSure (n=3,190,205)
Cataract Surgery Type, n (%)			
Routine	6,224,189 (92.6%)	3,276,860 (92.7%)	2,947,329 (92.4%)
Complex	500,809 (7.4%)	257,933 (7.3%)	242,876 (7.6%)
Cataract Type, n (%)			
Congenital Cataract	1,219 (0.02%)	687 (0.0%)	532 (0.0%)
Cortical Cataract	808,103 (12.0%)	396,585 (11.2%)	411,518 (12.9%)
Traumatic Cataract	8,770 (0.1%)	5,705 (0.2%)	3,065 (0.1%)
Nuclear Sclerotic Cataracts	4,485,219 (66.7%)	2,323,841 (65.7%)	2,161,378 (67.8%)
Posterior Subcapsular Cataracts	524,435 (7.8%)	253,503 (7.2%)	270,932 (8.5%)
Concurrent procedures, n (%)			
Glaucoma procedures	241,840 (3.6%)	139,901 (4.0%)	101,939 (3.2%)
Vitreous procedures*	30,591 (0.5%)	20,149 (0.6%)	10,442 (0.3%)
History of diabetes, n (%)	1,528,966 (22.7%)	774,921 (21.9%)	754,045 (23.6%)
Nonproliferative diabetic retinopathy	247,918 (3.7%)	124,859 (3.5%)	123,059 (3.9%)
Proliferative diabetic retinopathy	88,381 (1.3%)	47,104 (1.3%)	41,277 (1.3%)
Diabetic macular edema	112,280 (1.7%)	58,887 (1.7%)	53,393 (1.7%)

* Includes anterior vitrectomy and pars plana vitrectomy

Incidence of Endophthalmitis

- Overall incidence of endophthalmitis was low at 0.633 cases per 1,000 cataract surgeries (95% CI: 0.614, 0.652)
- When stratified by cataract surgery type, incidence of endophthalmitis was significantly greater following complex cataract procedures compared to routine procedures (1.148 vs 0.592 cases per 1,000 surgeries; P<0.0001)

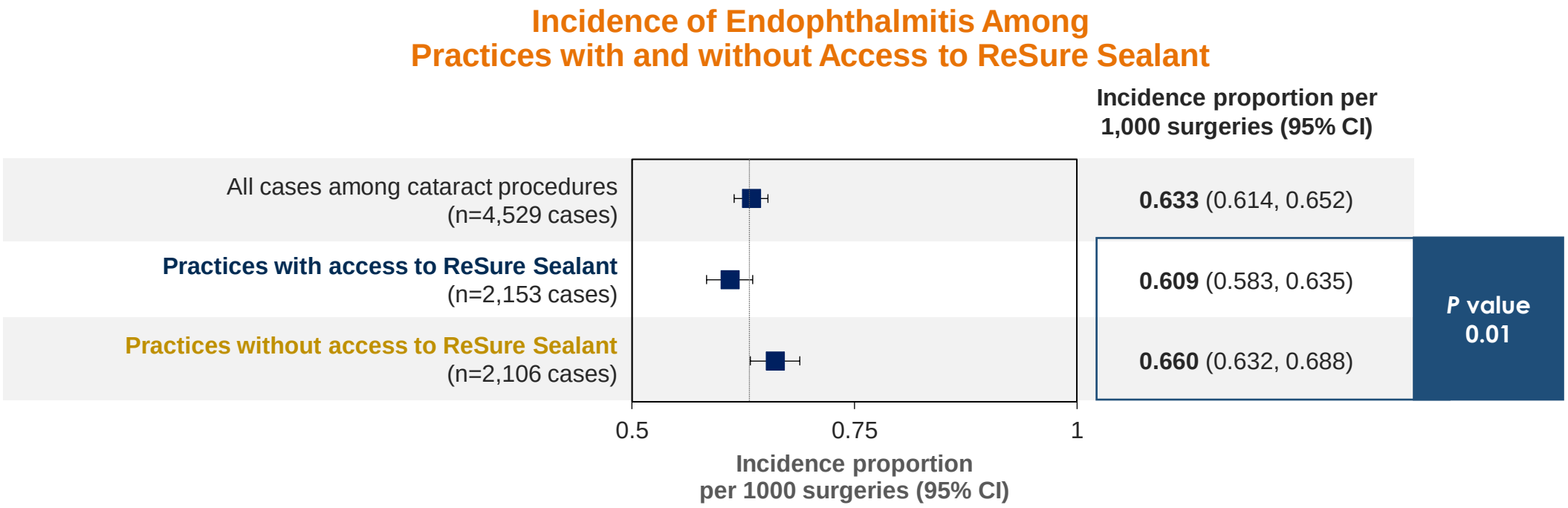
Incidence of Endophthalmitis Among All, Routine and Complex Cataract Procedures



* Among 4,259 endophthalmitis cases identified
CI, confidence interval

Incidence of Endophthalmitis with and without Access to ReSure Sealant

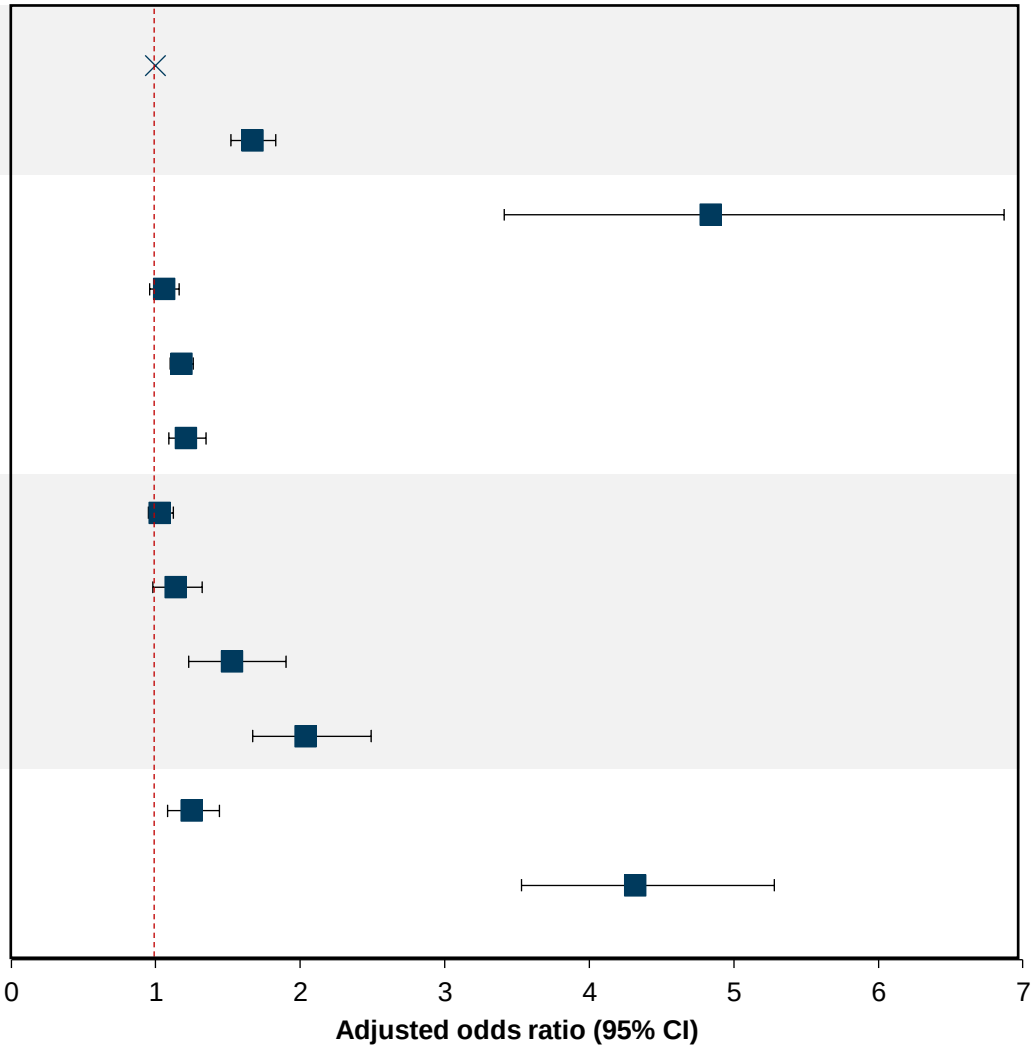
- No clinically meaningful or statistically significant difference in incidence of endophthalmitis at practices with or without access to ReSure Sealant (0.609 vs 0.660; P=0.01). Incidence was numerically lower at practices with access to ReSure Sealant



CI, confidence interval

Clinical Risk Factors

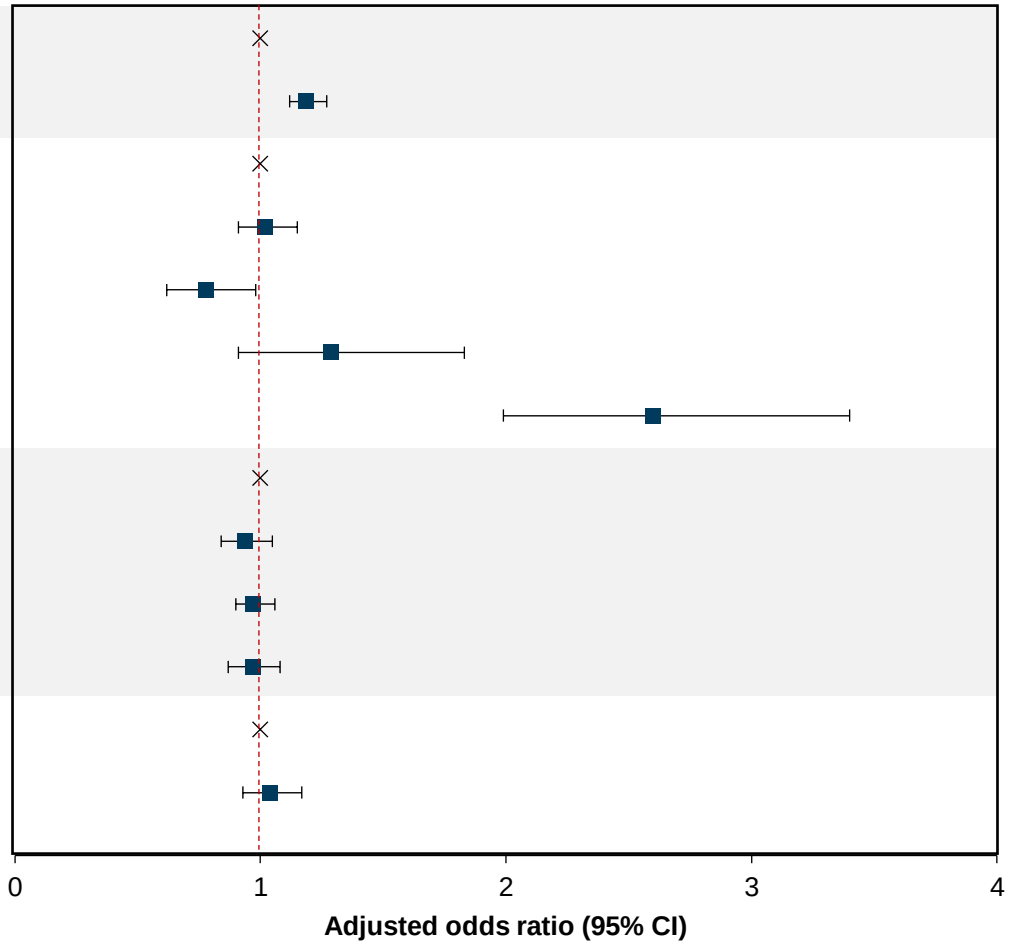
		Adjusted Odds Ratio (95% CI)	P value
Cataract surgery type	Routine (reference)	-	-
	Complex	**1.67 (1.52, 1.83)**	***<0.0001***
Cataract type	**Traumatic cataract**	**4.84 (3.41, 6.87)**	***<0.0001***
	Cortical cataract	1.06 (0.96, 1.16)	0.23
	Nuclear sclerotic cataract	**1.18 (1.1, 1.26)**	***<0.0001***
	Posterior subcapsular cataract	**1.21 (1.09, 1.35)**	***<0.0001***
History of diabetes	Diabetes	1.03 (0.95, 1.12)	0.47
	Background diabetic retinopathy	1.14 (0.98, 1.32)	0.09
	Proliferative diabetic retinopathy	**1.53 (1.23, 1.9)**	***<0.0001***
	Diabetic macular edema	**2.04 (1.67, 2.49)**	***<0.0001***
Concurrent procedures	Glaucoma procedures	1.25 (1.08, 1.44)	0.003
	Vitreous procedures*	**4.32 (3.53, 5.28)**	***<0.0001***



* Includes anterior vitrectomy and pars plana vitrectomy
Bolded risk factors were associated with statistically significantly higher rates of endophthalmitis (P<0.0001)
CI, confidence interval

Demographic Risk Factors

		Adjusted Odds Ratio (95% CI)	*P* value
Sex	Female (reference)	-	-
	Male	**1.19 (1.12, 1.27)**	***<0.0001***
Race	White (reference)	-	-
	Black	1.02 (0.91, 1.15)	0.72
	Asian	0.78 (0.62, 0.98)	0.03
	Native American and other Pacific*	1.29 (0.91, 1.83)	0.15
	Multiracial*	**2.60 (1.99, 3.40)**	***<0.0001***
Region	Midwest (reference)	-	-
	North	0.94 (0.84, 1.05)	0.28
	South	0.97 (0.90, 1.06)	0.54
	West	0.97 (0.87, 1.08)	0.56
Setting	Urban (reference)	-	-
	Rural	1.04 (0.93, 1.17)	0.46



* Represents ≤0.5% of study population
Bolded risk factors were associated with statistically significantly higher rates of endophthalmitis (P<0.0001)
CI, confidence interval

Conclusions

- These data represent one of the largest recent analyses (N=6,724,998 eyes) of acute postoperative endophthalmitis following cataract surgery
- The overall incidence of post-cataract surgery endophthalmitis between 2016 to 2019 was low 0.633 per 1,000 surgeries (95% CI: 0.614, 0.652)
- Incidence of endophthalmitis following complex cataract surgery was significantly higher compared to routine cataract surgery (1.148 vs. 0.592 per 1,000 cataract surgeries, respectively; $P<0.0001$)
- Incidence of endophthalmitis in eyes treated at practices with access to ReSure Sealant was numerically lower than eyes treated at practices without access to ReSure Sealant (0.609 vs 0.660; $P=0.01$). This difference was not clinically meaningful or statistically significant.
- Traumatic, nuclear sclerotic, or posterior subcapsular cataracts, concurrent vitreous procedures, history of diabetic macular edema or proliferative diabetic retinopathy and complex cataract surgeries were identified as risk factors and associated with statistically significantly higher rates of endophthalmitis ($P<0.0001$)