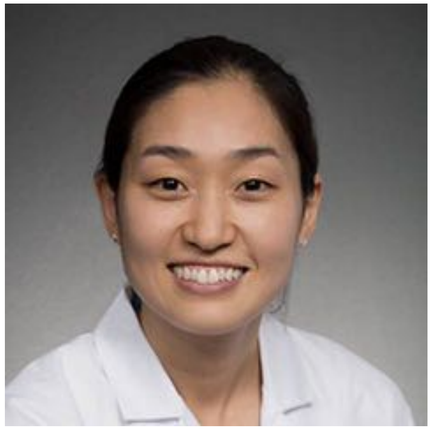
Prognostic Utility of Whole Genome Sequencing and PCR in Post-procedure Endophthalmitis

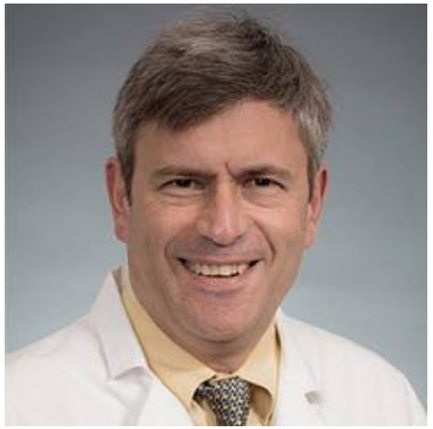
Sunir J. Garg, MD, FACS
Professor of Ophthalmology
MidAtlantic Retina, The Retina Service of Wills Eye Hospital
Thomas Jefferson University
August 2020

Disclosures

- Research Support: Aerpio, Allergan, Apellis, Eyegate, Retina Implant AG
- Consultant: Bausch and Lomb, Johnson & Johnson

- Many thanks to Cecilia Lee, MD and Russ VanGelder, MD, PhD





Summary

- Pathogen-negative and *S. epidermidis* endophthalmitis have better outcome than non-*S. Epidermidis* cases
- Bacterial load identified by WGS in non-*S. Epidermidis* cases are inversely associated with clinical outcome
- TTV is a significant risk factor for needing a secondary PPV
- Molecular data may be important predictors of poor clinical outcome

Introduction

- Approximately 30% of post-CE endophthalmitis is culture-negative
  - qPCR 30% culture negative
- Up to 2/3 post-injection endophthalmitis culture-negative

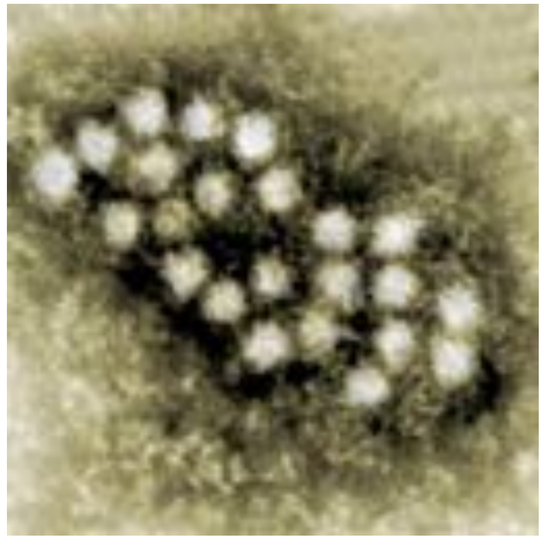
Han et al. AJO 1996
Joseph et al. AJP 2012
Shah et al. Ophthalmology 2011

Emerging techniques for pathogen discovery in endophthalmitis

Bryan K. Hong[1], **Cecilia S. Lee**[2], **Russell N. Van Gelder**[2], and **Sunir J. Garg**[1]

- Culture, 16S PCR, and BRiSK provide complementary information
- Culture-negative endophthalmitis cases do not have detectable bacterial DNA

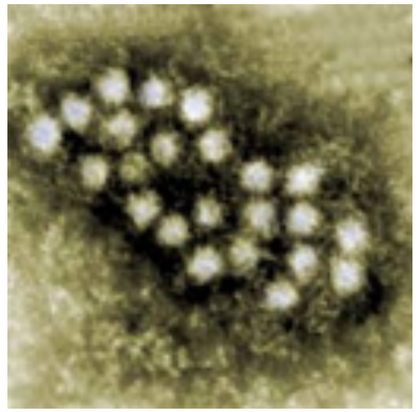
Torque Teno Virus



- Small (3.8 kb), single-stranded DNA anellovirus
- Nearly ubiquitous
  - Viremia 2/3
- Associated with numerous chronic inflammatory conditions
  - MS, SLE, pulmonary fibrosis, asthma
  - SHAPU

Identification of Torque Teno Virus in Culture-Negative Endophthalmitis by Representational Deep DNA Sequencing

Aaron Y. Lee, MD, MSCI,[1] Lakshmi Akileswaran, PhD,[2] Michael D. Tibbetts, MD,[5] Sunir J. Garg, MD,[5] Russell N. Van Gelder, MD, PhD[2,3,4]



- All culture- samples showed at least trace evidence of TTV, as did some culture+
- Viral loads of Torque Teno virus varied but in some cases were extremely high (>10^7/ml)

Purpose

- Is TTV, along with other molecular data, associated with clinical outcome?

Methods

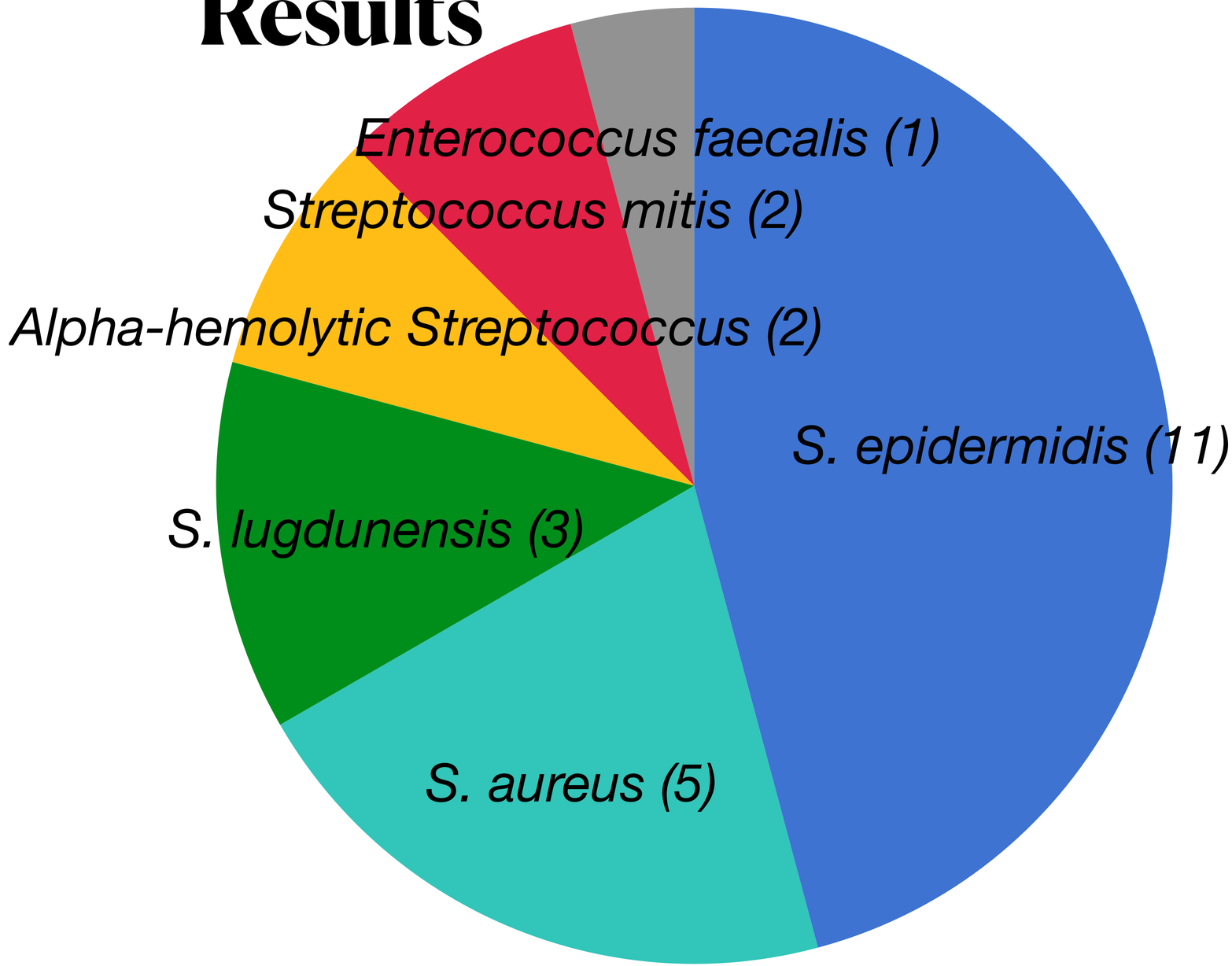
- Post procedure endophthalmitis cases recruited prospectively
- Standard culture, quantitative PCR (qPCR) and whole genome sequencing (WGS) performed
- Outcomes: baseline, week 1, week 4, week 12

Results

50 eyes:

24 culture-positive cases

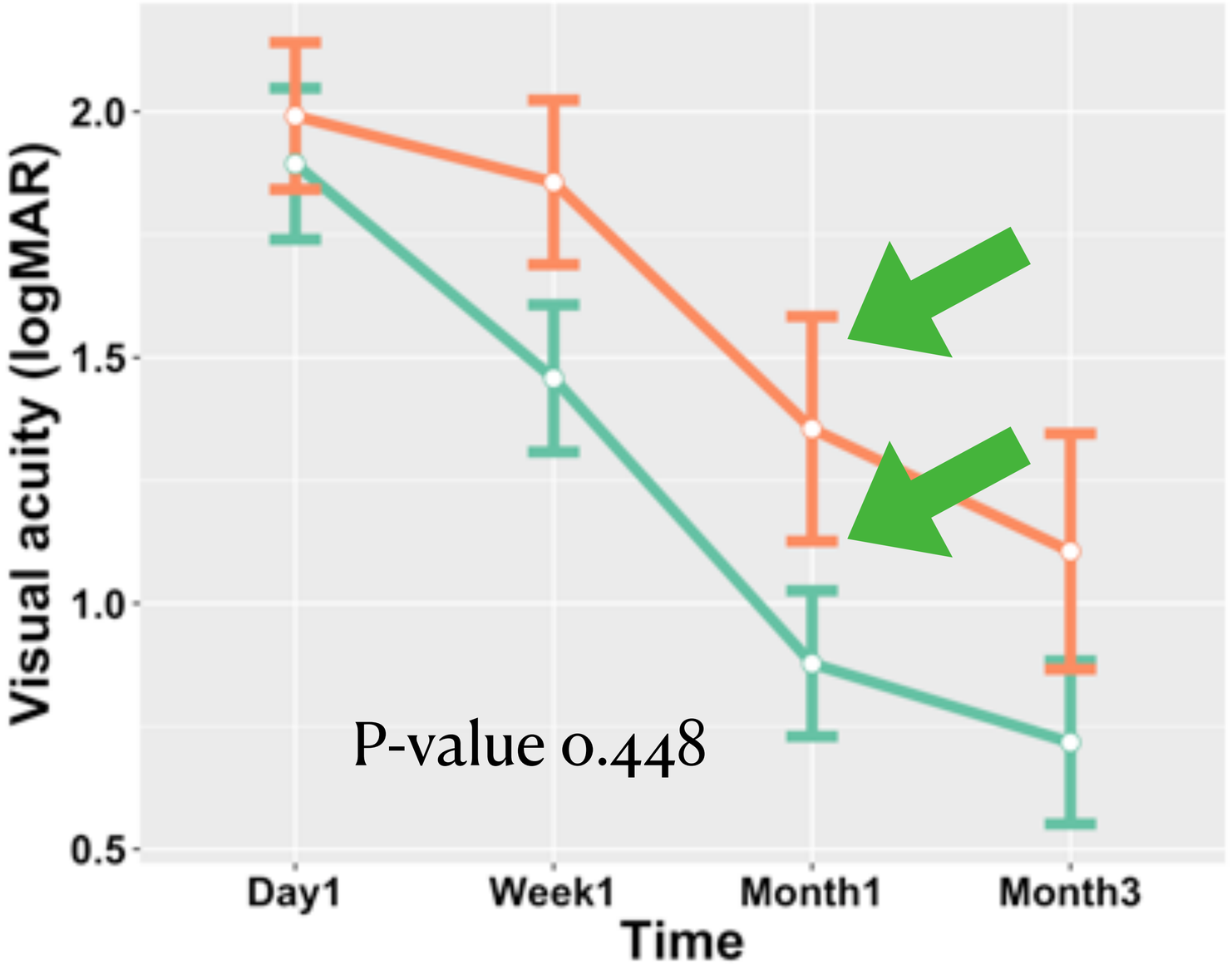
26 culture-negative cases



	Culture positive (n=24)	Culture negative (n=26)	P-value
Mean age (range)	67 (44-85)	72 (36-98)	0.84
Male, n (%)	14 (58)	12 (46)	0.41
Intravitreal injections	16 (67)	14 (54)	0.43
Cataract surgeries	2 (8)	6 (23)	0.43
Median days to presentation (range)	5 (1-30)	8 (1-42)	0.14
Median baseline VA, logMAR	2.4 (HM)	2.4 (HM)	0.74
TTV presence (%)	8/22 (36)	15/25 (60)	0.15

- Of the 24 culture + cases, WGS identified the cultured bacteria in 3/4
- WGS identified potential pathogens in 8/22 (36%) culture-negative cases
  - (*S. epidermidis* (n=7) and *Pseudomonas fluorescens* (n=1))

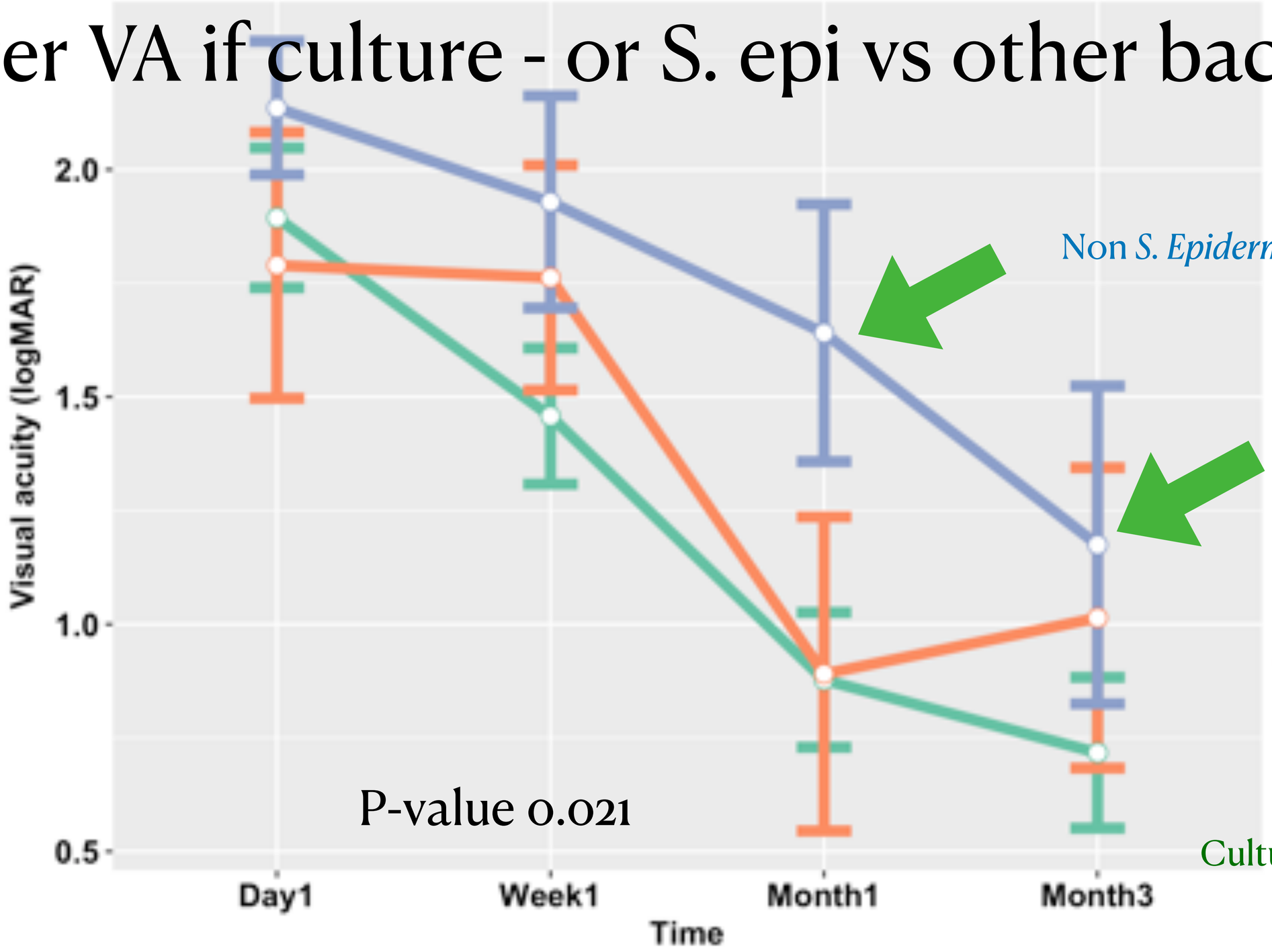
Culture + vs - doesn't predict outcome



Culture positive

Culture negative

Better VA if culture - or S. epi vs other bacteria

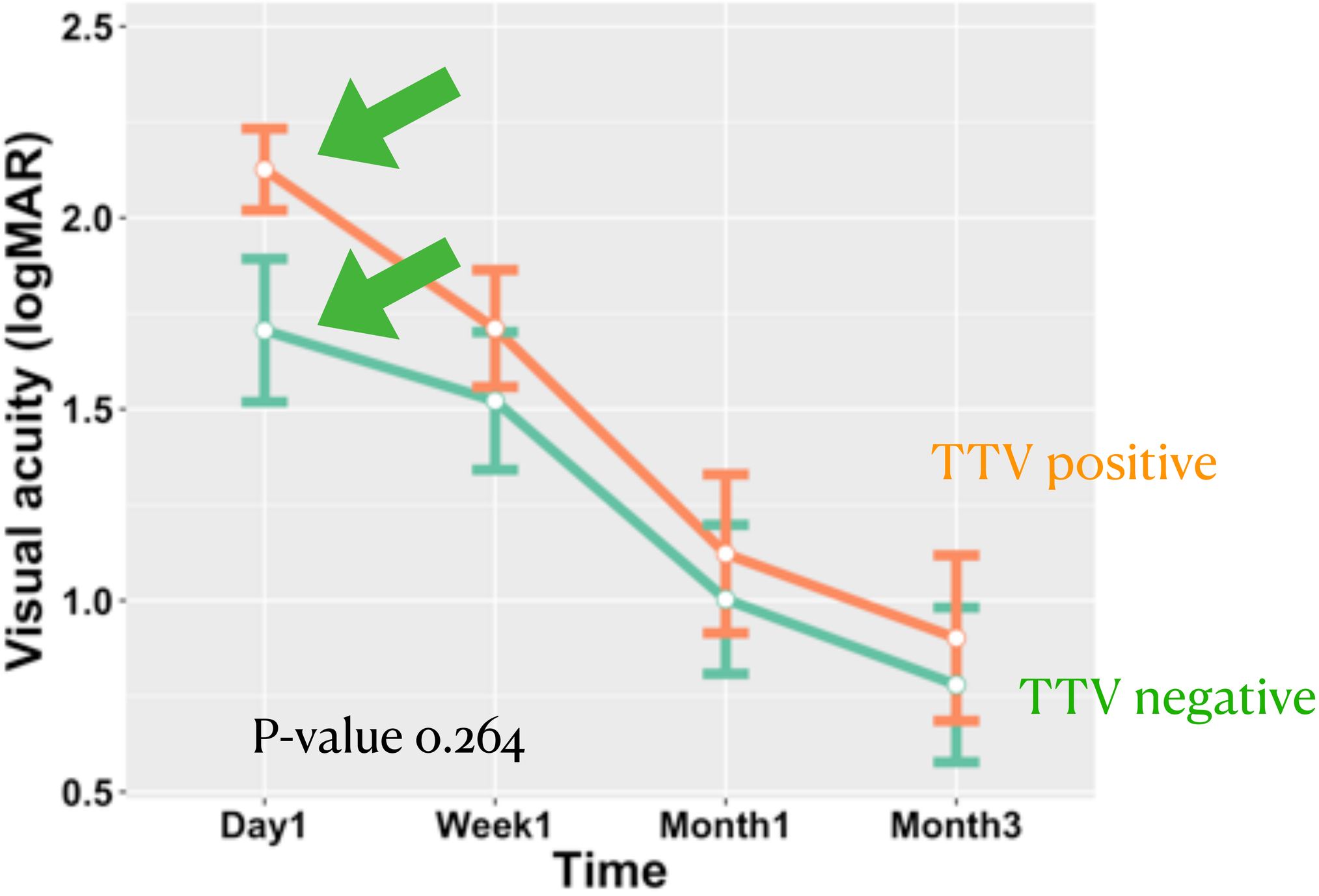


Pathogen Load

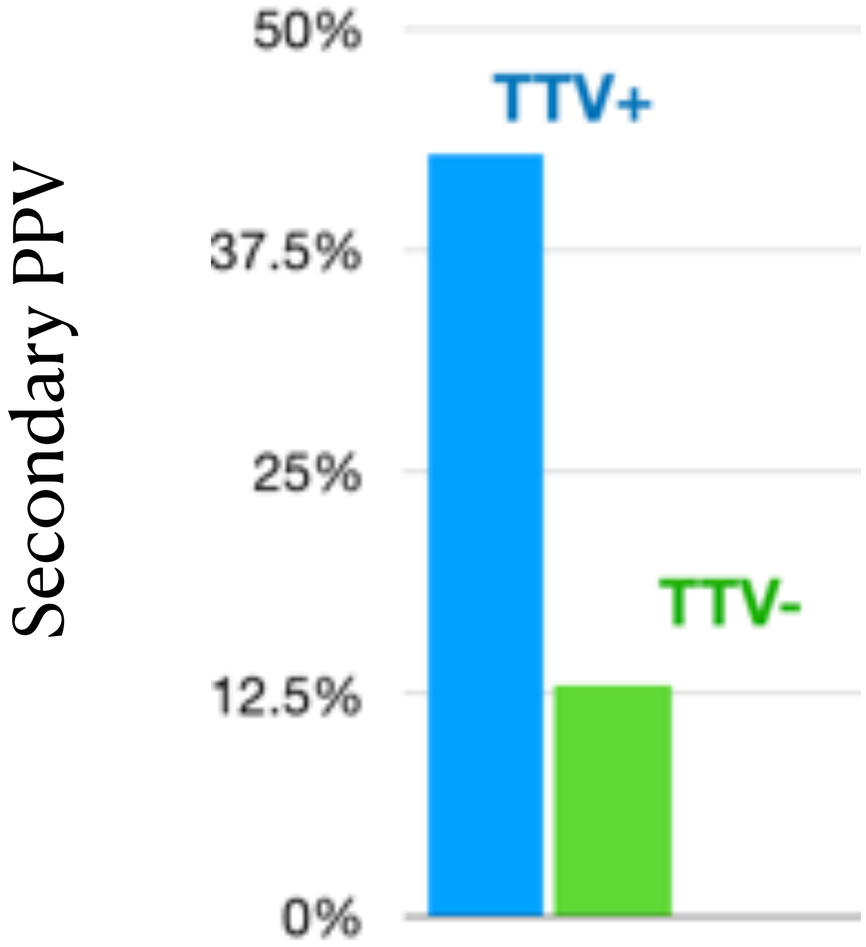
- Pathogen load for S. epi did not impact visual acuity
- However, higher baseline pathogen load for non S. epi was associated with worse vision at month 1 and 3

Torque Teno Virus

- TTV present in 8/22 (36%) of culture-positive and in 15/25 (60%) of culture-negative cases (p=0.147)

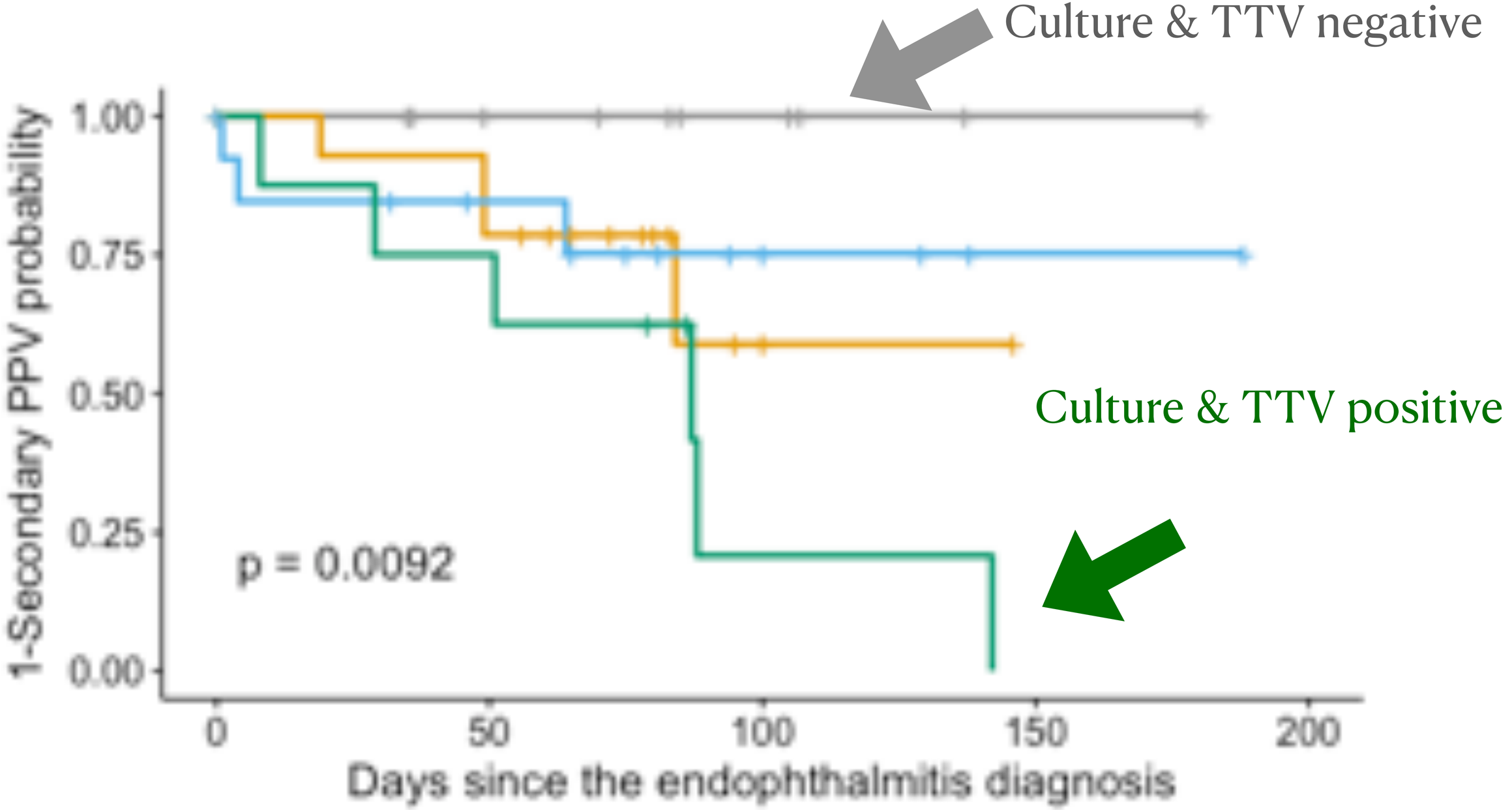

2.5
2.0
1.5
1.0
0.5
Visual acuity (logMAR)
Day1
Week1
Month1
Month3
Time
TTV positive
TTV negative
P-value 0.264

TTV and Secondary PPV



- 10/23 (43%) in TTV + group
- 3/24 (13%) in TTV - group
- **OR 5.2** (95%CI 1.07, 34.82, p=0.02)

All 5 cases that developed RD were TTV+


Culture & TTV negative
Culture & TTV positive
1-Secondary PPV probability
1.00
0.75
0.50
0.25
0.00
p = 0.0092
0
50
100
150
200
Days since the endophthalmitis diagnosis

Conclusions

- Pathogen-negative and *S. epidermidis* endophthalmitis have better outcome than non-*S. Epidermidis* cases
- Bacterial load identified by WGS in non-*S. Epidermidis* cases are inversely associated with clinical outcome
- TTV is a significant risk factor for needing a secondary PPV
- Molecular data may be important predictors of poor clinical outcome

Acknowledgements/Funding

Endophthalmitis Study Group

Christopher Aderman, MD; Katherine Talcott, MD; Murtaza K Adam, MD; David S Ehmann, MD; Ferhina Ali, MD; James P. Dunn, MD; David H. Fisher, MD; Omesh Gupta, MD; Allen C. Ho, MD; Jason Hsu, MD; Michael Klufas, MD; Sonia Mehta, MD; Carl Park, MD; Carl D. Regillo, MD; Arunan Sivalingam, MD; Marc J. Spirn, MD; James Vander, MD, Kasra Rezaei, MD; Lisa Olmos de Koo, MD, MBA; Yewlin Chee, MD

Funding Sources (U of Washington)

NIH/NEI K23EY024921; NIH/NEI P30EY001730; Research to Prevent Blindness; Mark J. Daily, MD Research Grant

Research to Prevent Blindness

National Eye Institute

Thank you!