

# Reducing Adenoviral Patient Infected Days (RAPID): Prevalence of Polymerase Chain Reaction (PCR) Confirmed Adenovirus Among Patients Presenting With Acute Conjunctivitis

Mary K Migneco<sup>a</sup>; Mathew Margolis<sup>a</sup>; Christina Morettin<sup>b</sup>; Ellen Shorter<sup>c</sup>; Julie Huecker<sup>a</sup>; Andrew Hartwick<sup>d</sup>; Spencer Johnson<sup>e</sup>; Jennifer Harthan<sup>b</sup>; Meredith Whiteside<sup>f</sup>; Chrystal Rosemann<sup>g</sup>; Christian K. Olson<sup>g</sup>; Tavé van Zyl<sup>h</sup>; Tim Bossie<sup>i</sup>; Tammy Than<sup>j</sup>; Mae O. Gordon<sup>a</sup>.

<sup>a</sup>Washington University, St. Louis; <sup>b</sup>Illinois College of Optometry; <sup>c</sup>Illinois Eye and Ear Infirmary; <sup>d</sup>Ohio State University; <sup>e</sup>Northeastern State University; <sup>f</sup>University of California Berkeley School of Optometry; <sup>g</sup>Brooke Army Medical Center; <sup>h</sup>Harvard Medical School; <sup>i</sup>New England College of Optometry; <sup>j</sup>University of Alabama-Birmingham.

## Introduction

The Reducing Adenoviral Patient Infected Days (RAPID) is a double-masked randomized pilot trial investigating the efficacy of a one-time administration of 5% ophthalmic Povidone-Iodine (PVP-I 5%; betadine) for the treatment of qPCR confirmed adenoviral conjunctivitis.

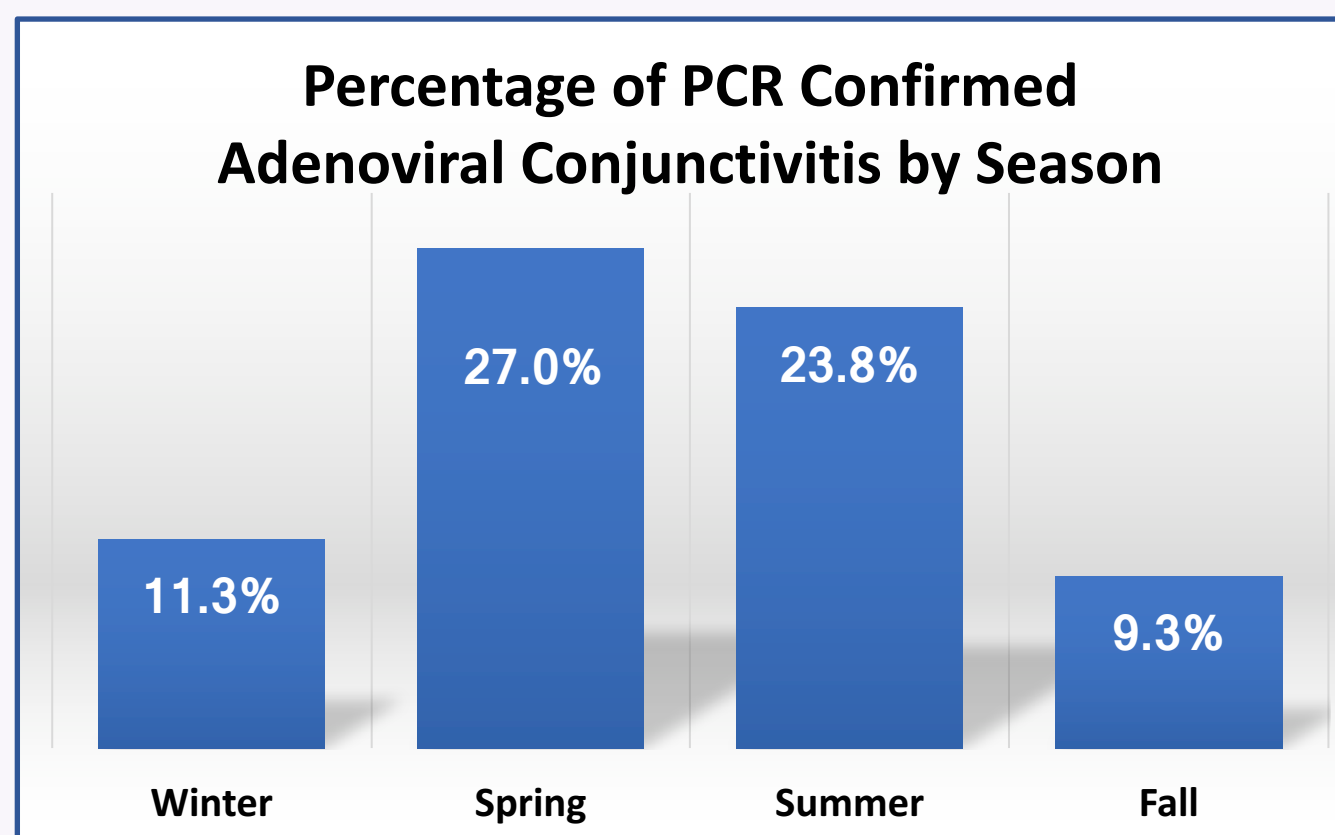
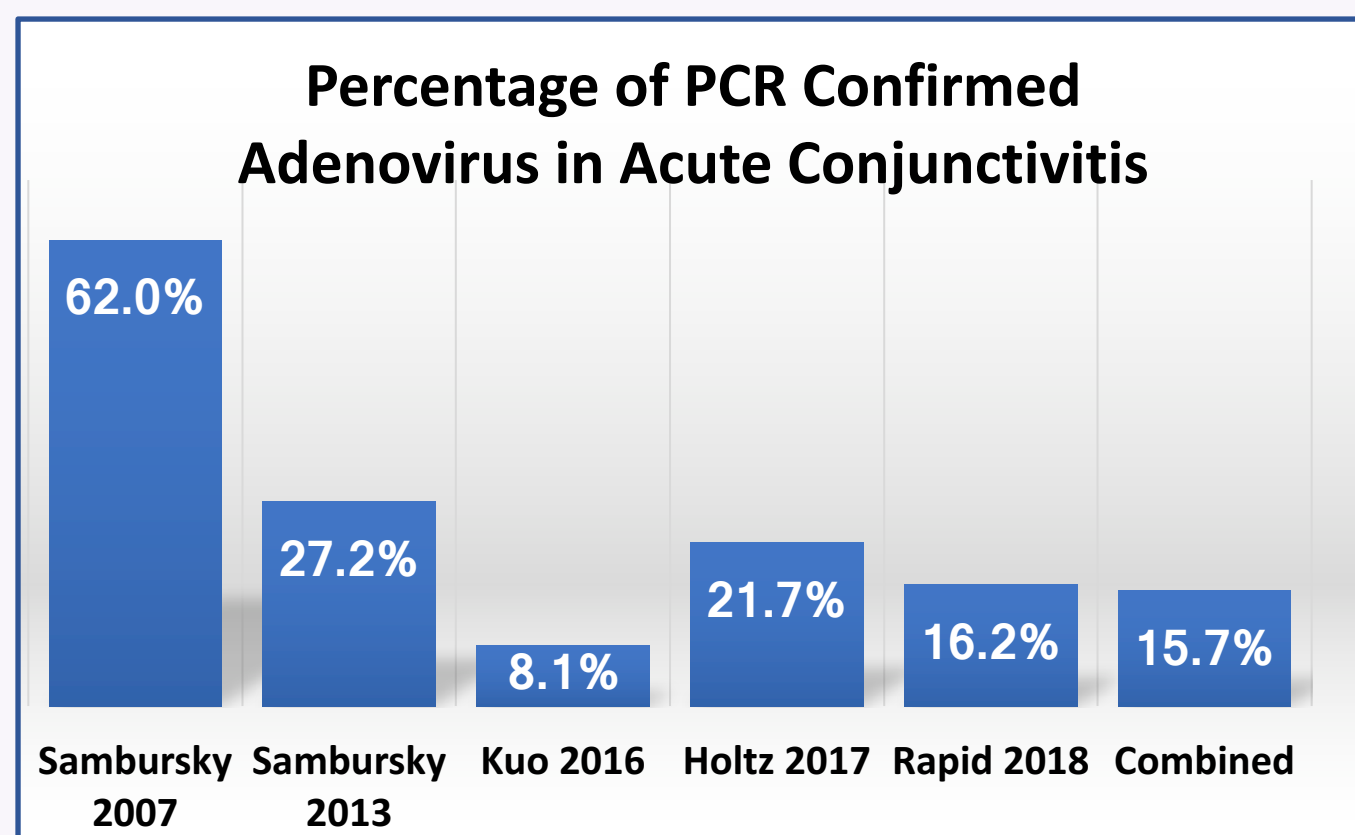
- This contagious eye disease makes up a substantial percent of visits to primary care, urgent care, and eye practitioners alike<sup>[1-2]</sup>.
- Prevalence of PCR confirmed adenovirus in cases of acute conjunctivitis within the United States has ranged from 8% to 62%<sup>[3-6]</sup>.
- Breakdown by location and season are rarely provided, however understanding these trends is important in the accurate diagnosis and treatment of the disease.

The RAPID group documents the prevalence of PCR confirmed adenoviral conjunctivitis by location and season, and reviews the literature regarding adenoviral prevalence in the United States.

## Methods

- From October 2015 to March 2018, eight centers in seven geographically diverse regions in the United States screened patients presenting with clinical signs of acute conjunctivitis for eligibility in the RAPID pilot study.
- Patients  $\geq$  18 years of age with symptom onset  $\leq$ 4 days prior to presentation were screened; all were included in analysis regardless of eligibility for randomization.
- Tear samples were collected from the first affected eye and evaluated by qPCR.

## Results



Site Location	Percent qPCR Positive
Illinois College of Optometry – Chicago; IL	46.2% (6/13)
Northeastern State University – Tahlequah; OK	35.7% (5/14)
University of Alabama – Birmingham; AL	28.6% (2/7)
Illinois Eye & Ear Institute – Chicago; IL	20.0% (2/10)
Mass Eye & Ear Institute – Boston; MA	14.3% (1/7)
Washington University – St. Louis; MO	12.8% (5/39)
Brooke Army Medical Center – Fort Sam Houston; TX	6.3% (3/48)
University of California – Berkeley; CA	6.3% (1/16)

- In total, 25/154 (16.2%) of patients screened were qPCR positive for adenoviral conjunctivitis.
  - 11.3% (6/53) Winter, 27.0% (10/37) Spring, 23.8% (5/21) Summer, and 9.3% (4/42) Fall.
- In 4 prior reports, the prevalence's of PCR confirmed adenovirus in the USA were found to be:
  - 62.0% (31/50); July-October; Philadelphia, PA<sup>5</sup>.
  - 27.2% (34/125); 24 months duration; 8 ophthalmology practices/centers within the USA<sup>4</sup>.
  - 8.1% (44/542); 36 months duration; Baltimore, MD<sup>3</sup>.
  - 21.7% (10/46); June-September; Rochester, MN<sup>6</sup>.
- Overall qPCR determined prevalence across 5 USA studies including RAPID was 15.7% (144/917).

## References

- Sheldrick JH, Wilson AD, Vernon SA, Sheldrick CM. Management of ophthalmic disease in general practice. The British journal of general practice : the journal of the Royal College of General Practitioners. 1993;43(376):459-62. Epub 1993/11/01. PubMed PMID: 8292417; PubMed Central PMCID: PMC1372484.
- McDonnell PJ. How do general practitioners manage eye disease in the community? Br J Ophthalmol. 1988;72(10):733-6. Epub 1988/10/01. PubMed PMID: 3191073; PubMed Central PMCID: PMC1041572.
- Kuo IC, Espinosa C, Forman M, Valsamakis A. A Polymerase Chain Reaction-Based Algorithm to Detect and Prevent Transmission of Adenoviral Conjunctivitis in Hospital Employees. Am J Ophthalmol. 2016 Mar;163:38-44
- Sambursky R, Trattler W, Tauber S, Starr C, Friedberg M, Boland T, McDonald M, DellaVecchia M, Luchs J. Sensitivity and specificity of the AdenoPlus test for diagnosing adenoviral conjunctivitis. JAMA Ophthalmol. 2013 Jan;131(1):17-22.
- Sambursky RP, Fram N, Cohen EJ. The prevalence of adenoviral conjunctivitis at the Wills Eye Hospital Emergency Room. Optometry. 2007 May;78(5):236-9.
- Holtz K, Townsend K, Furst W, Myers J, Binnicker M, Quigg S, Maxson J, Espy M. An Assessment of the AdenoPlus Point-of-Care Test for Diagnosing Adenoviral Conjunctivitis and Its Effect on Antibiotic Stewardship. Mayo Clin Proc Inn Qual Out 2017;1(2):170-175.

## Discussion

Adenoviral conjunctivitis has been reported as one of the leading causes of acute conjunctivitis. Our study, as well as a review of the literature reveals the following:

- The prevalence of PCR confirmed adenovirus in patients presenting with acute conjunctivitis in the United States has been shown to be lower than previously reported.
  - At 8 sites nationwide, RAPID prevalence was 16.2%.
  - Meta-analysis prevalence was 15.7% (133/917).
- The prevalence of PCR confirmed adenovirus varies considerably by season and clinic location.
  - Highest prevalence was in spring, however considerable variation was seen year-to-year.
  - Greatest number of cases of acute conjunctivitis occurred in winter, however a lower proportion of patients were adenovirus positive by qPCR.

Understanding the prevalence of adenoviral conjunctivitis both in relation to season and location is important in the accurate diagnosis and treatment of the condition. The RAPID group welcomes further investigation into the prevalence of adenoviral conjunctivitis across optometric, ophthalmologic, and all other types of healthcare practices within the United States.

## Acknowledgements & Support

The Reducing Adenoviral Patient-Infected Days (RAPID) Study is funded by: National Eye Institute grant 1R34EY023633-01A1; National Eye Institute Center Core Grant (P30EY002687); An unrestricted grant to the Department of Ophthalmology and Visual Sciences from Research to Prevent Blindness.

RAPID would like to thank DiaSorin Molecular LLC (Cypress, CA) for loaning the study a Liaison MDX Instrument and reagents for qPCR analysis.

Clinical Trial Registration: <https://clinicaltrials.gov/ct2/show/NCT02472223>