

Incidence of Adenovirus Respiratory Infections and Coinfections in a Longitudinal Birth Cohort

Adam Gailani, MD; Zheyi Teoh, MD; Shannon Conrey, PhD, MS; Rachel Burke, PhD, MPH; Allison R Cline, RN BSN; Marie E. Killerby, VetMB, MPH; Xiaoyan Lu, MS; Claire Mattison, MPH; Monica McNeal, MS; Ardythe Morrow, PhD, MSc; Daniel Payne, PhD, MSPH; Mary Allen Staat, MD, MPH

Background

Adenovirus (AdV) is a common cause of respiratory infections in children. Viral infections have been shown to cause significant burden on children and their families in the form of ill symptoms, days missed from work and school, doctors visits, hospitalizations, and even death. There are, however, relatively few contemporary, community focused cohort studies on Adenovirus. Many previous studies focus on symptomatic and more severe disease, using children who have presented for medical care such as emergency departments and hospitals. Due to the limitations of previous studies, there is an incomplete understanding of Adenovirus infections in children.

Methods

PREVAIL Cohort

The PREVAIL cohort is a CDC sponsored, longitudinal cohort study conducted from 2017-2020 in Cincinnati, OH. 245 mother infant pairs were followed from the 3rd trimester of pregnancy until the child's 2nd birthday. Weekly nasal samples were obtained and tested for common respiratory viruses via PCR testing. Weekly symptom surveys were also obtained. This study uses 101 of the most highly compliant mother infant pairs, defined as those who turned in at least 70% of nasal swabs over the 2 years of the study.

Definitions

Acute Respiratory Infection (ARI) = the presence of fever or cough on symptom survey

Viral Infection = positive nasal swabs by viral PCR no more than 30 days apart for a given virus

Coinfection = presence of an additional distinct virus during a viral infection

Statistical Analysis

Comparisons between single infections and coinfections used Fishers exact tests and Kruskal-Wallis tests. Comparisons between initial infections and subsequent infections used generalized estimating equation logistic models.

Goals and Aims

Prevalence

Describe the prevalence of Adenovirus infection and Adenovirus coinfections in children in the PREVAIL cohort.

Severity

Characterize the differences in symptoms and severity between Adenovirus infection and Adenovirus coinfections in children in the PREVAIL cohort

Time Course

Describe the natural course of Adenovirus infections by analyzing initial and repeat infections in children in the PREVAIL cohort

Results – Prevalence

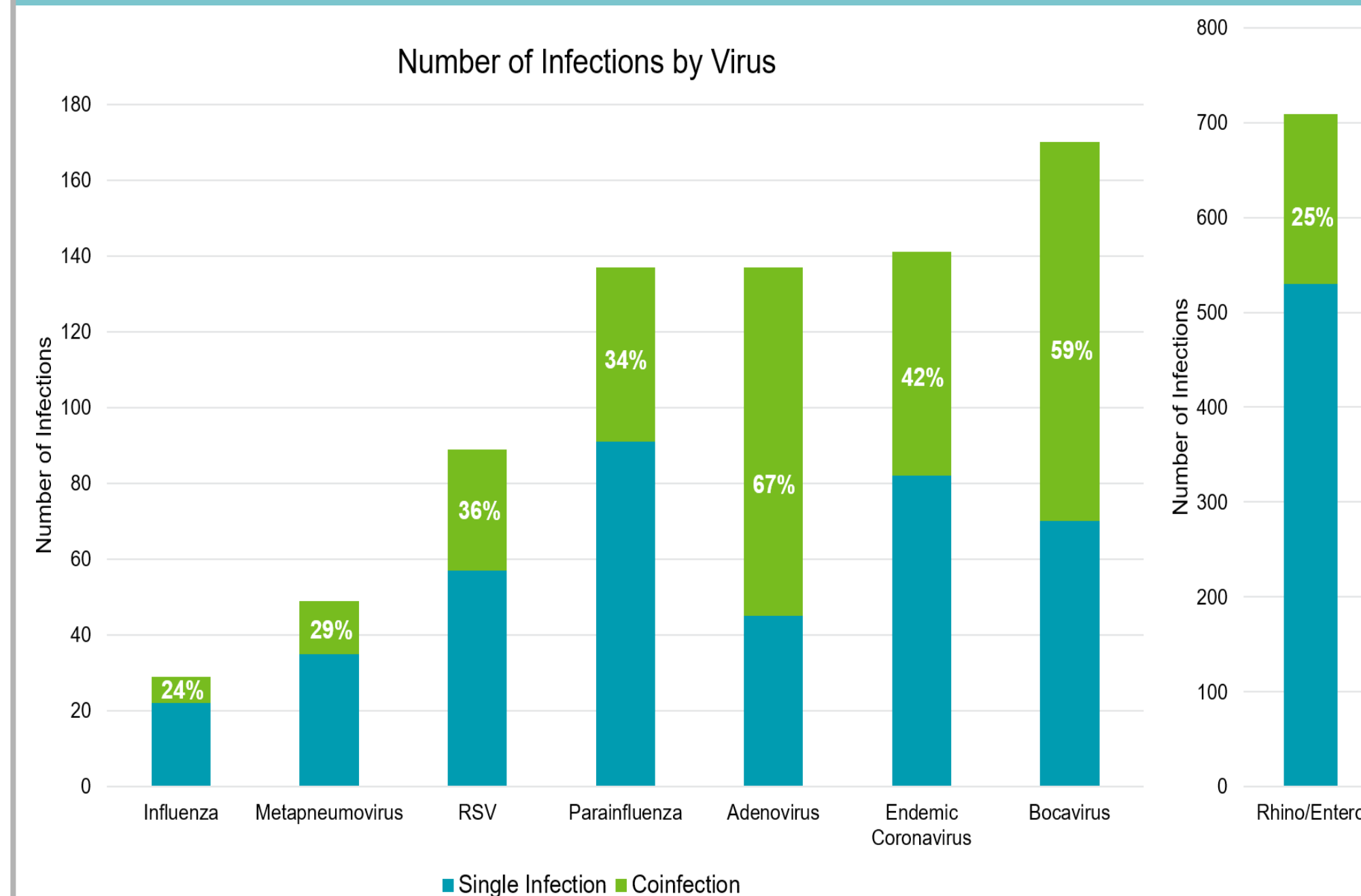


Chart 1. Number of infections by different viruses. There were 1461 infections in total, half of which were rhinovirus/enterovirus infections. 137 (9.3%) of the infections were AdV infections which results in an incidence of 0.84 AdV infections per child year. Coinfections versus single infections are displayed in blue vs green respectively. 67% of AdV infections were coinfections.

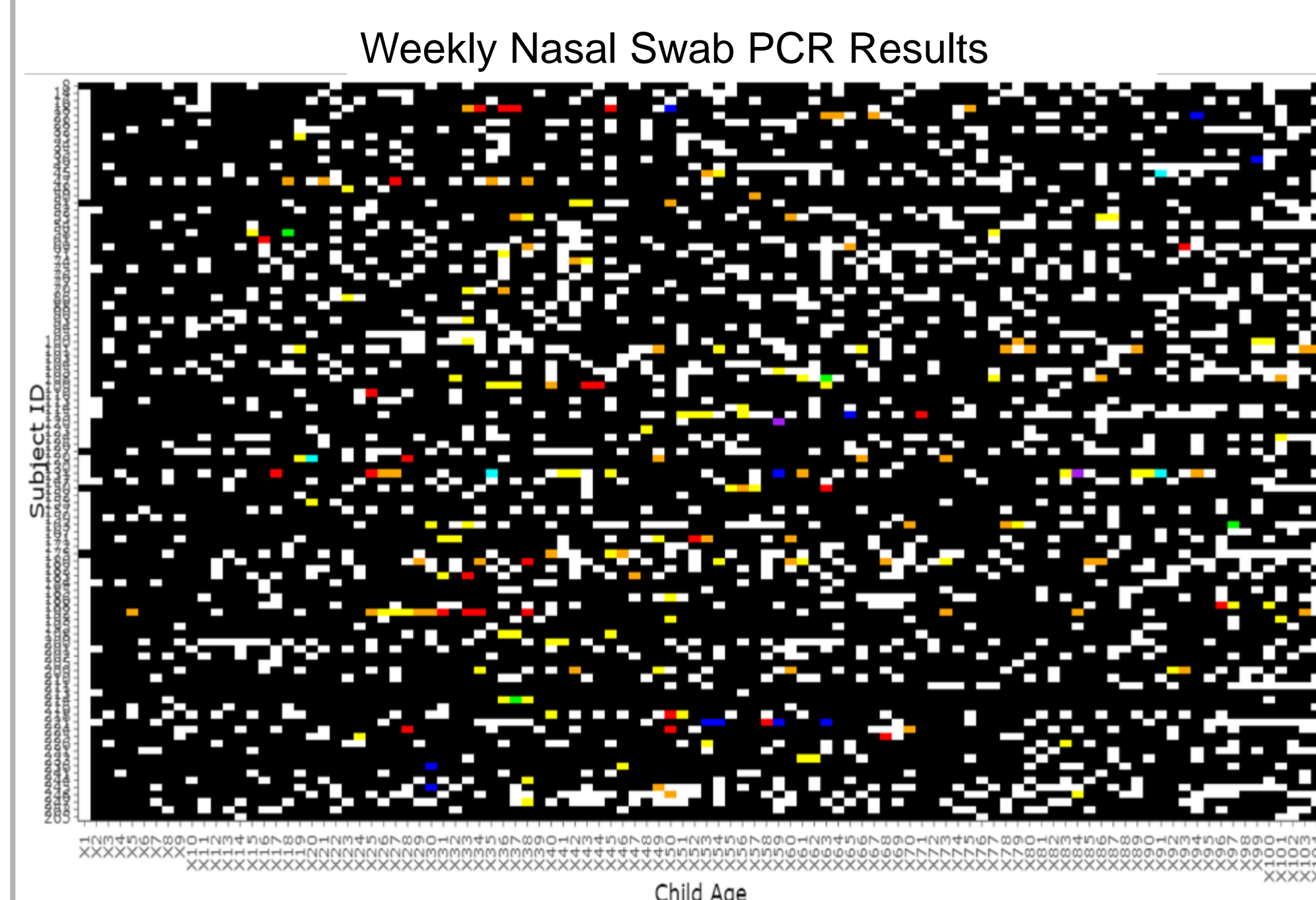


Chart 2. This heat map shows the Adenovirus positive swabs. The x axis represents the children's age in weeks and the y axis indicates each child's ID number. Each row can be seen as the life time of the child in weeks from birth to age 2 years old. The different colors indicate whether Adenovirus was found in that swab, and if it was detected with another virus (see the key above). White blocks indicate that no swab was returned that week. This heat map shows that Adenovirus and Adenovirus coinfections are present throughout the first 2 years of life in the children in this analysis. It is also interesting to note the relative lack of Adenovirus infections prior to week 24, which may represent the waning of maternal antibodies or increase in social interaction of newborns and their families

Results – Severity

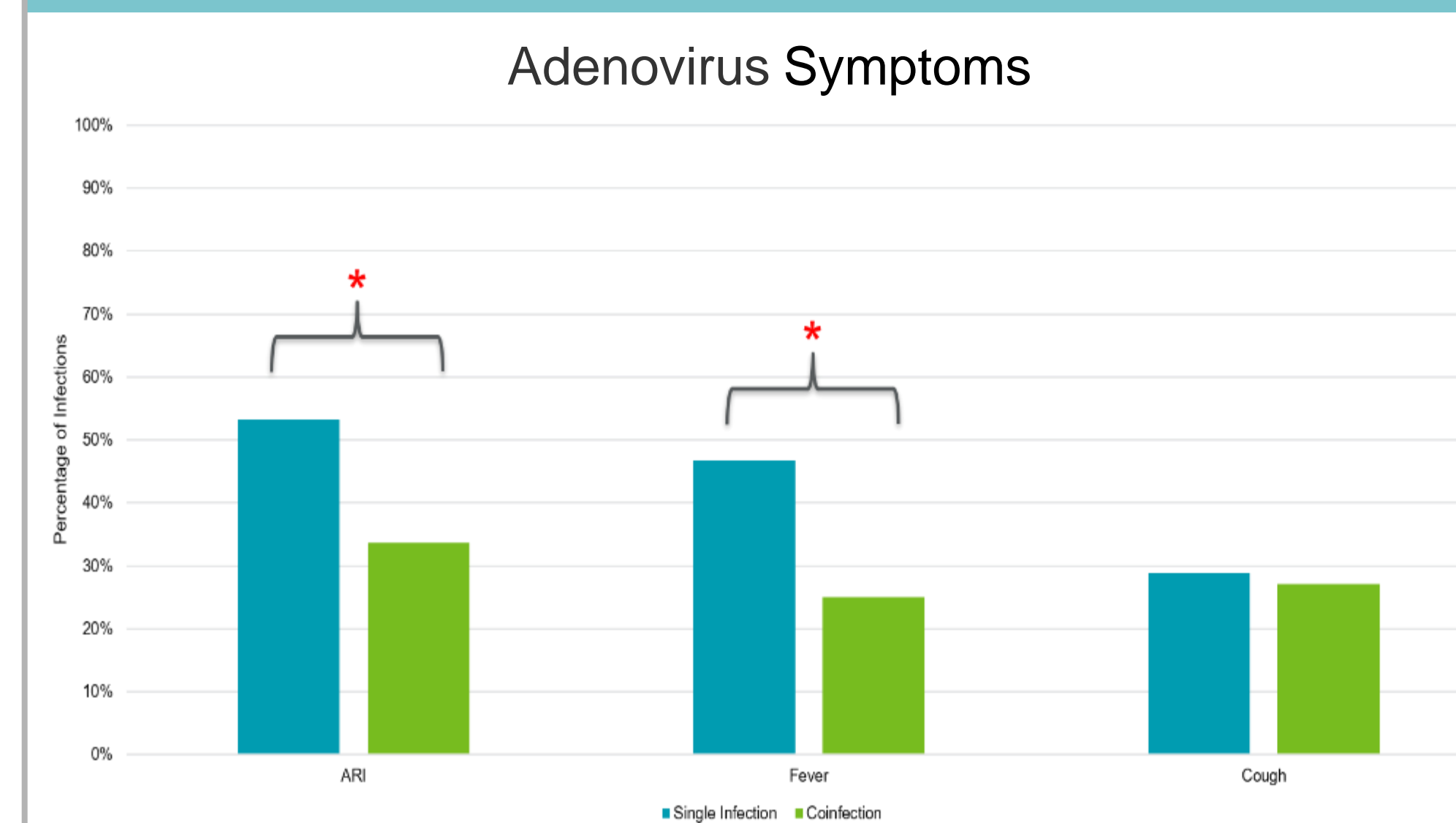


Chart 3. Symptom differences between AdV single infections (blue) and coinfections (green). Red asterisks indicate statistical significance ($p < 0.05$). AdV single infections were more likely to meet ARI criteria and have fever present than coinfections.

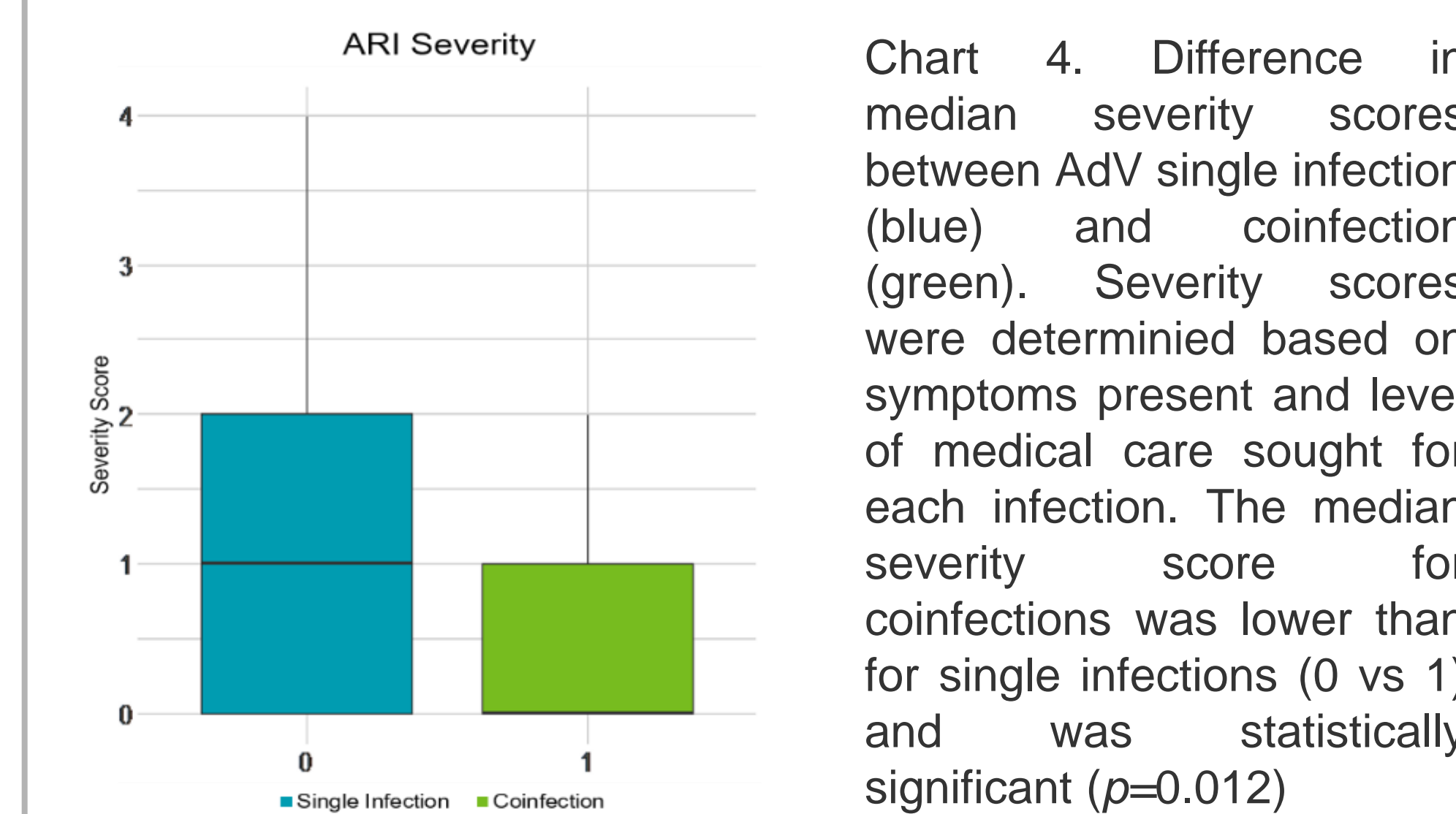


Chart 4. Difference in median severity scores between AdV single infection (blue) and coinfection (green). Severity scores were determined based on symptoms present and level of medical care sought for each infection. The median severity score for coinfections was lower than for single infections (0 vs 1) and was statistically significant ($p = 0.012$)

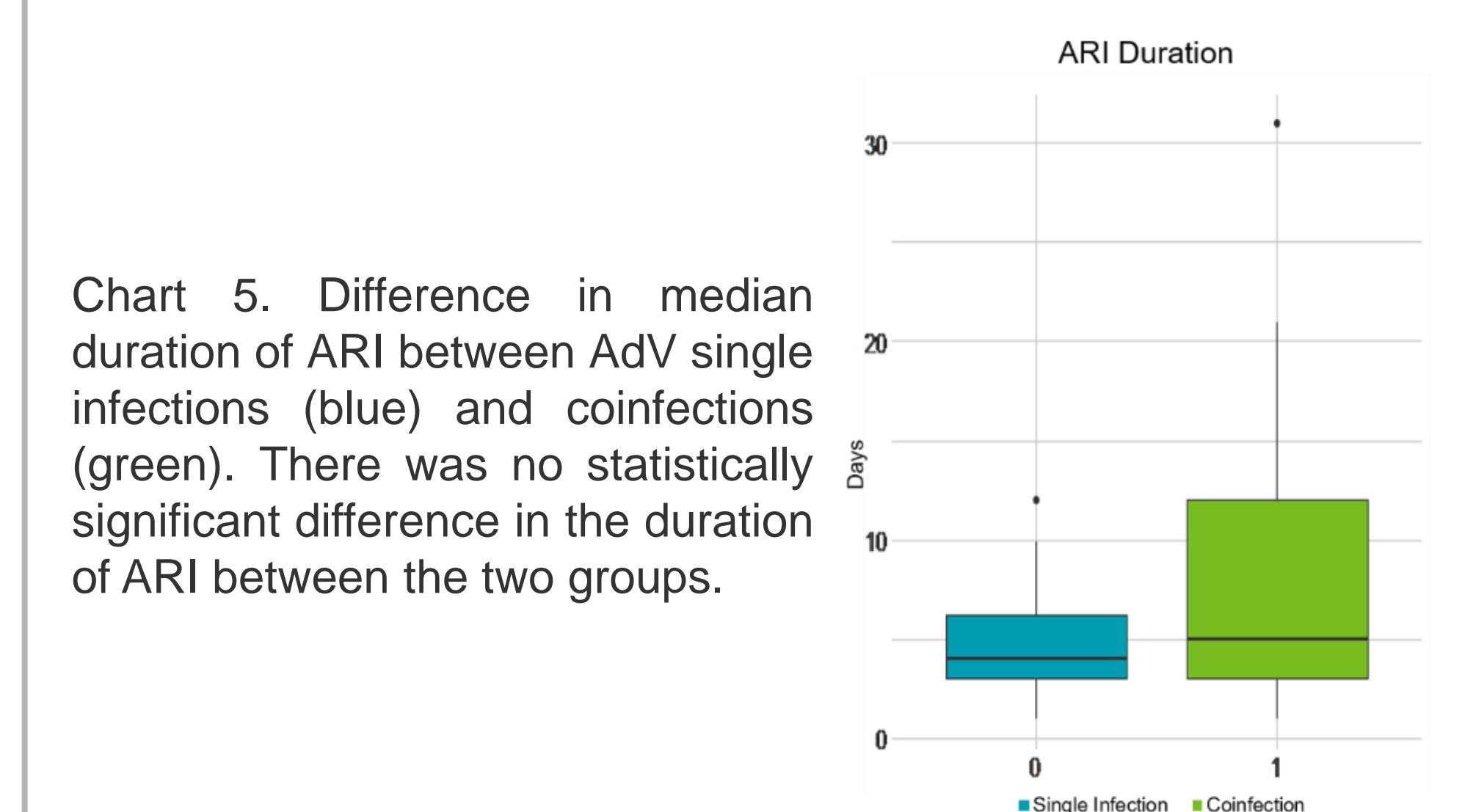


Chart 5. Difference in median duration of ARI between AdV single infections (blue) and coinfections (green). There was no statistically significant difference in the duration of ARI between the two groups.

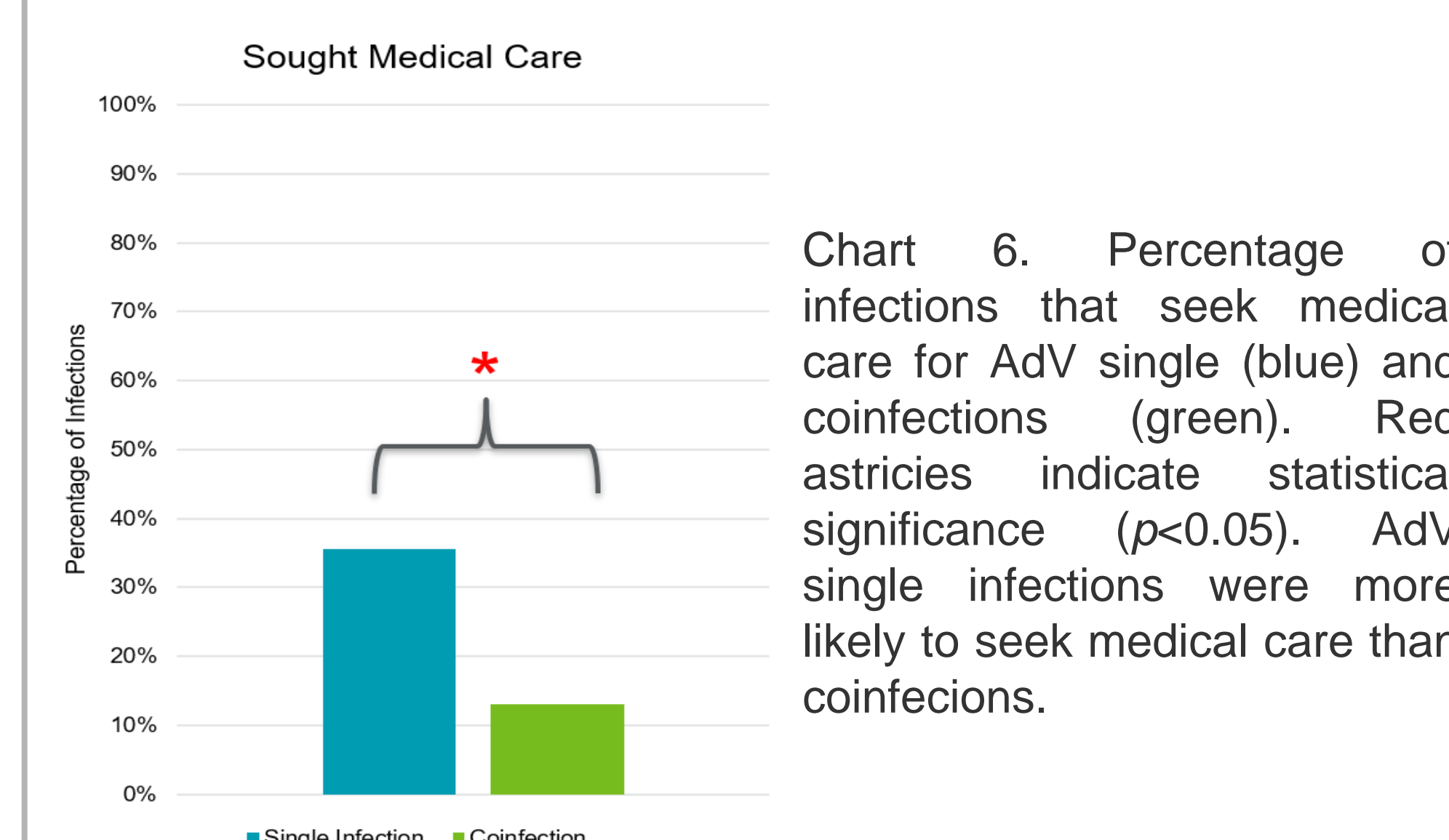


Chart 6. Percentage of infections that seek medical care for AdV single infection (blue) and coinfections (green). Red asterisks indicate statistical significance ($p < 0.05$). AdV single infections were more likely to seek medical care than coinfections.

Results – Time Course

Repeat Infections				
Adenovirus	Initial Infection	Subsequent Infection	Odds Ratio	95% CI
Coinfection	32 (53%)	60 (80%)	2.43	0.69-8.60
ARI	31 (52%)	24 (31%)	0.72	0.28-1.90
Sought Medical Care	19 (32%)	9 (12%)	0.53	0.07-4.23
ED or Hospitalization	4 (7%)	1 (1%)	0.15	0.01-2.40

Table 1. Comparison of first time AdV infections with subsequent AdV infections. There was no statistical difference between the two in regards to coinfection rate, ARI rate, or rate of seeking medical care. However, the overall trend was that subsequent AdV infections were more likely to be coinfections and less likely to meet ARI criteria or seek medical care.

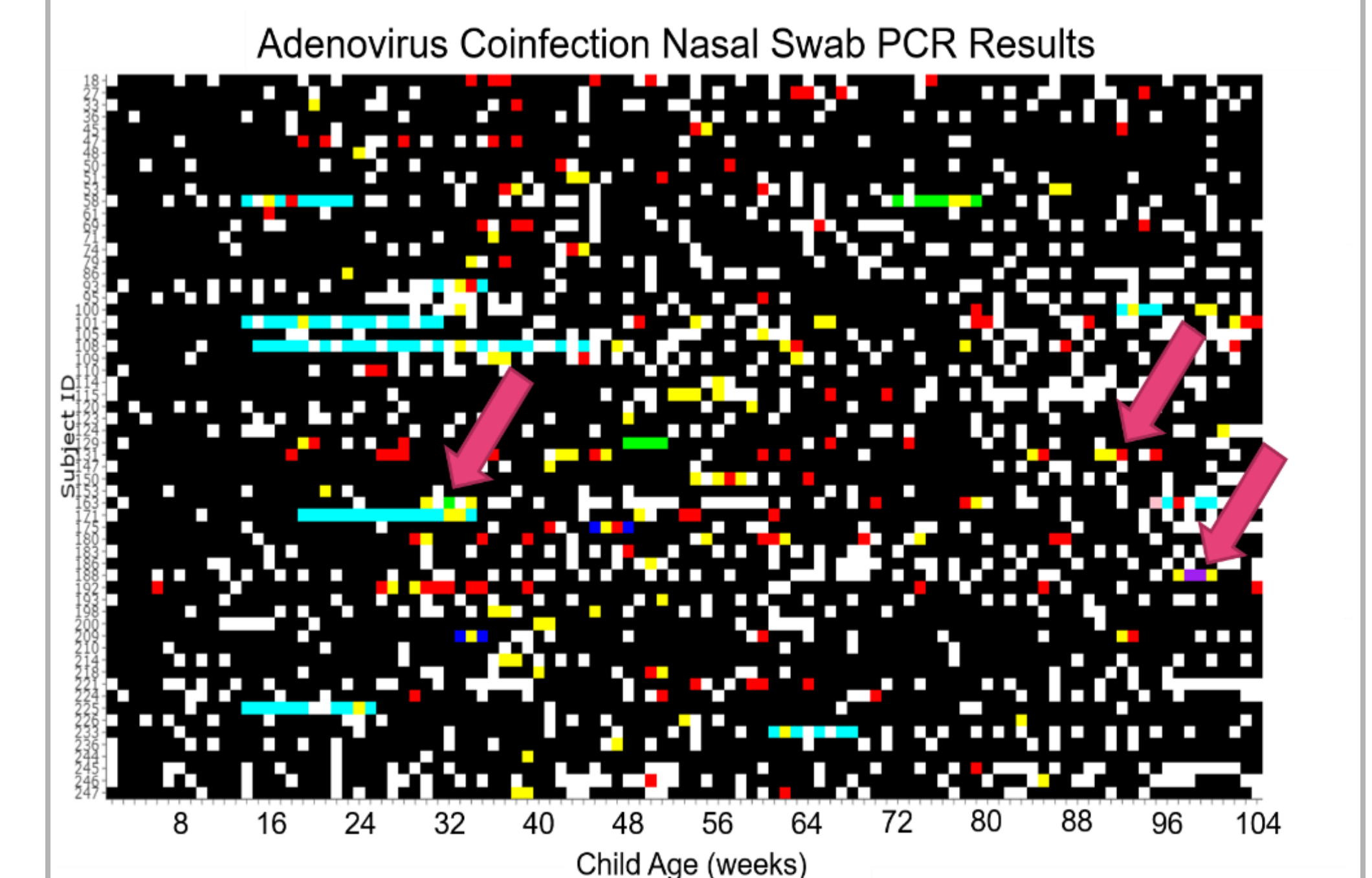


Chart 7. Heat map depicting all AdV positive swabs and coinfection swabs. The x axis represents the children's age in weeks and the y axis indicates each child's ID number. Black is no AdV detected, white is no swab returned, red is AdV + another virus, and all other colors are swabs positive for other viruses. The other virus positive swabs were included in this chart if they were part of an AdV coinfection. This map allows us to see the time course of developing a AdV coinfection. Of note, only 3 times (pink arrows) did an AdV coinfection start with AdV detected first. All other coinfections with AdV had AdV detected at the same time as the other virus or after the other virus.

Summary

Adenoviruses are a common cause of respiratory infections in children. These infections are frequently mild with little to no symptoms. They are also commonly detected as coinfections with other viruses

Adenovirus coinfections do not result in more severe illness compared with single adenovirus infections. This study indicates that these coinfections may actually be less severe compared to single infections. Adenovirus coinfections appear more likely to be detected as subsequent infections than initial infections. Coinfections with Adenovirus typically involve infection with another virus prior to or simultaneously with Adenovirus, and rarely have Adenovirus detected first.