

# Monitoring Adverse Events using an Interactive Web-Based Tool

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<http://graphics.rhoworld.com/tools/aeexplorer/>

## Introduction

Frequent and careful monitoring of adverse events (AEs) is one of the most important responsibilities of medical monitors and safety monitoring committees. For trials with large participant enrollment, severe diseases, or complex treatments, study monitors may be tasked with reviewing thousands of AEs.

Traditional reporting methods require monitors to comb through scores of static displays and summary tables. This method is inefficient and poses the risk that clinically-relevant signals will be obscured by the sheer volume of events.

We created an interactive web-based AE Explorer tool to give monitors the ability to quickly explore adverse event data in real time. The Explorer draws upon common user interface principles (e.g., nested content, tool tips, dynamic filtering) to allow users to instantly search, query, and filter data.

## Status Quo

The traditional adverse event summary provides data that are useable, but far from user-friendly.

Figure 1 shows a single page view of a traditional AE summary table for the Learning Early about Peanut Allergy (LEAP) study, a randomized, open-label, controlled trial with over 8800 AEs.\*

Figure 1: Traditional Static AE Summary Table - Single Page View

	Negative Stratum (n=221)		Positive Stratum (n=68)		Overall (n=289)		P-value [1]	P-value [2]	P-value [3]
	Avoidance Group (n=221)	Consumption Group (n=68)	Avoidance Group (n=68)	Consumption Group (n=221)	Avoidance Group (n=221)	Consumption Group (n=68)			
Number of Events	3552	3763	735	764	4287	4527			
Number of Participants with at Least One Event	288(99.3)	271(99.6)	51(100)	47(100)	218(99.4)	218(99.7)	0.556		0.566
Infections and Infestations	287(98.9)	279(99.3)	51(100)	47(100)	218(99.4)	218(99.7)	0.642		0.659
Upper respiratory tract infection	151(99.6)	151(99.3)	29(59)	31(66)	117(99.3)	117(99.6)	0.852	0.133	0.800
Gastroenteritis	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Rhinitis	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Varicella	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Lower respiratory tract infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Ear infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Nasopharyngitis	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Viral infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Viral upper respiratory tract infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Group infections	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Respiratory tract infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Pharyngitis	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Molluscum contagiosum	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Urinary tract infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Influenza	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006
Eye infection	148(91.9)	171(64.3)	38(56)	28(39)	178(53.6)	283(63.6)	0.002	0.948	0.006

This type of static table has several drawbacks:

- Text-only display: The data are entirely numeric, making it difficult to quickly compare rates between groups or identify signals of interest.
- Lack of interactivity: As a static report, users are unable to sort, filter, or interact with the data.
- Designed for printing, not exploring: AE summaries are produced in page-based file formats (.doc, .rtf, .pdf). Though easy to print, such formats limit the accessibility and usability of the data. For example, Figure 1 shows only the first page of an 18-page table. Comprehensive AE reports can include multiple tables and summaries spanning many dozens, if not hundreds of pages. Comparing data across multiple-page reports of this size is very difficult for users.

## A Vision for Visualization

We created an interactive, web-based AE Explorer to address the many limitations of traditional, static AE reports.

Our guiding principles were to:

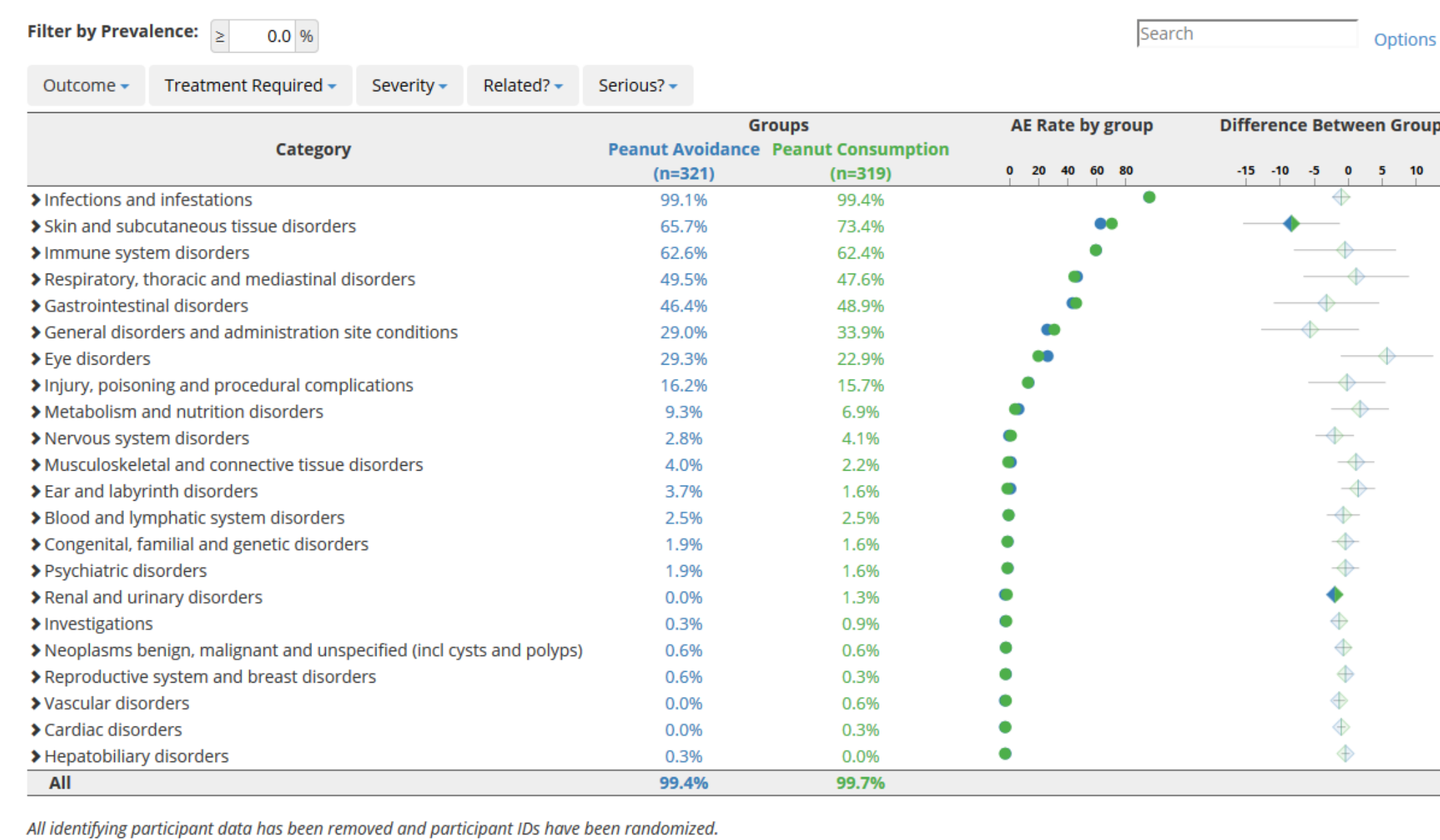
- Create a tool that fulfilled all of the reporting requirements of the traditional static summaries
- Improve accessibility, usability, and understanding of AE data via data visualization and user-oriented navigation
- Equip our end users to focus their time and effort on the key task (medical examination of patient safety) instead of focusing on number crunching, data hunting, and page turning

To achieve these goals, we used universally accessible open-source web-programming conventions (HTML, JavaScript, CSS) to develop an AE Explorer for use in a common web-browser.

Figure 2 shows the default view of our AE Explorer.

\*The LEAP study was conducted by the Immune Tolerance Network (ITN), which is funded by the National Institute of Allergy and Infectious Disease, National Institutes of Health. Primary results from the LEAP study were published in the New England Journal of Medicine in February 2015 (available online here: <http://www.nejm.org/doi/full/10.1056/NEJMoa1414850>).

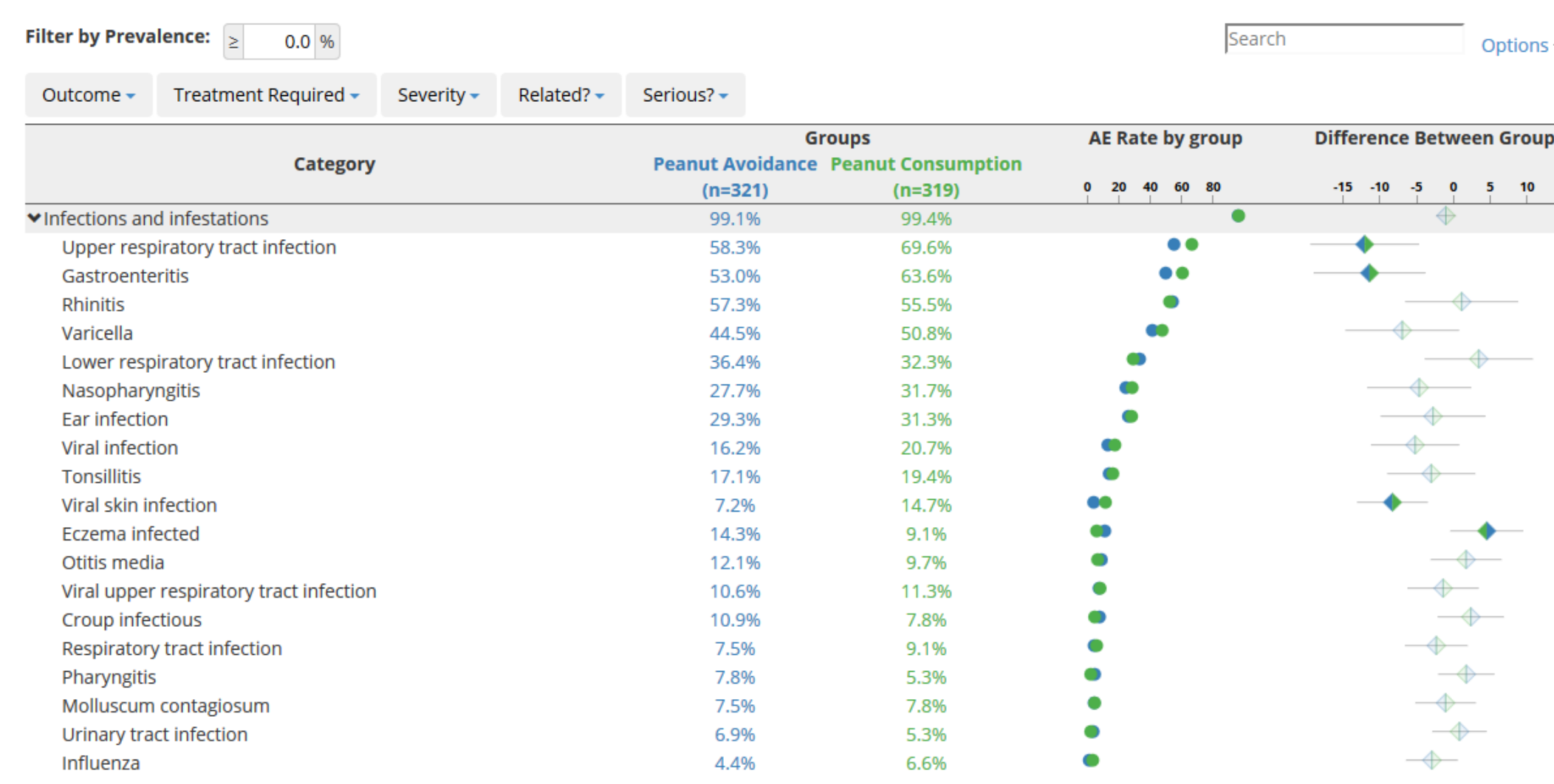
Figure 2: Default AE Explorer Display



## Fidelity to the traditional reporting requirements

The default Explorer view is a single-screen display of AEs grouped by System Organ Class. Unlike the static displays, which also show the nested Preferred Terms for each System Organ Class, our default view hides the Preferred Terms. This allows users to get a high-level summary of the data at first glance. However, a single mouse-click allows the user to expand the report to show the nested Preferred Terms (Figure 3), thus replicating the same view as the static tables.

Figure 3: AE Explorer with Nested Preferred Terms Displayed



## Effective use of data visualization

Dot plots portray the prevalence in the different treatment groups, which provides users with a simple graphical display of the relative rate of AEs, as well as relative differences between treatment groups. A *Difference Between Groups* column adds further visual information by showing which differences between groups are statistically significant (opaque diamonds) versus those where the difference is not statistically significant (translucent diamonds).

## Interactive navigation

Users can interact with the display in real time to:

- show/hide nested rows (Figure 3)
- search by term of interest (Figure 4)
- filter events based on a minimum prevalence threshold (Figure 5)
- filter according to severity and relatedness to treatment (Figure 6)
- drill down to participant-specific data (Figure 7)

Figure 4: Using the Search Feature to Find AEs with the Term "Viral"

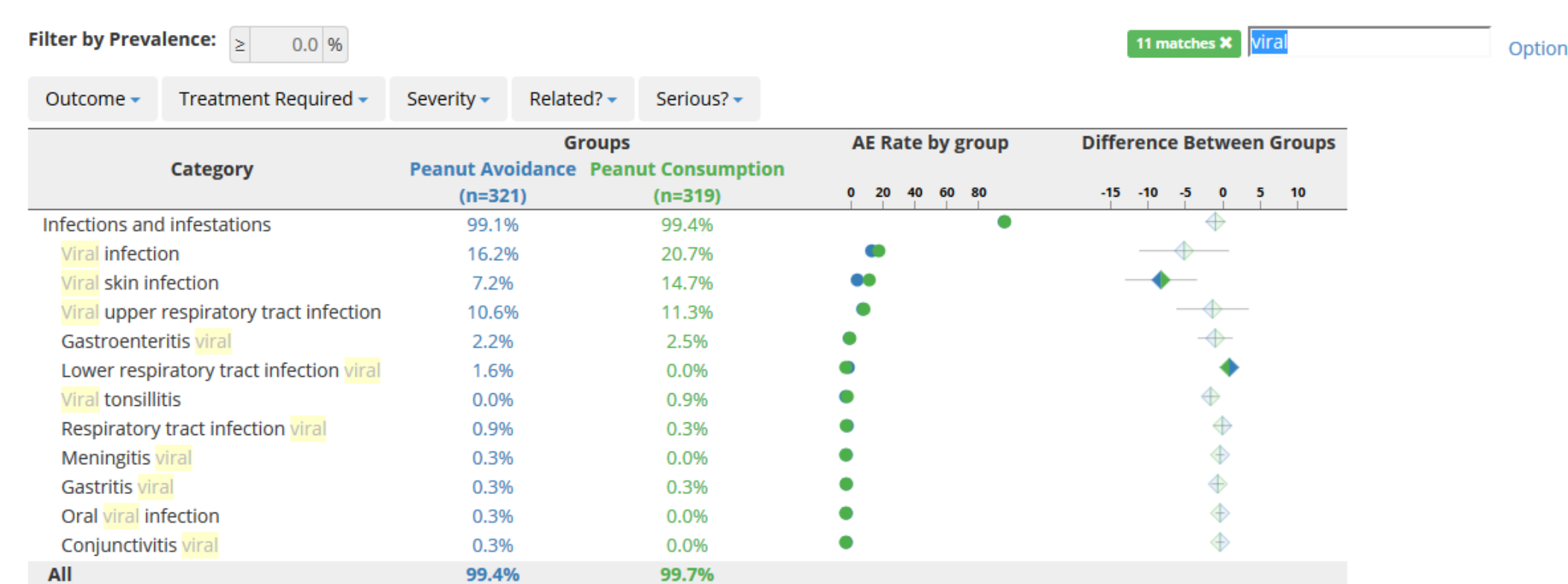


Figure 5: Filtering out AEs Below a Prevalence Threshold of 5.0%

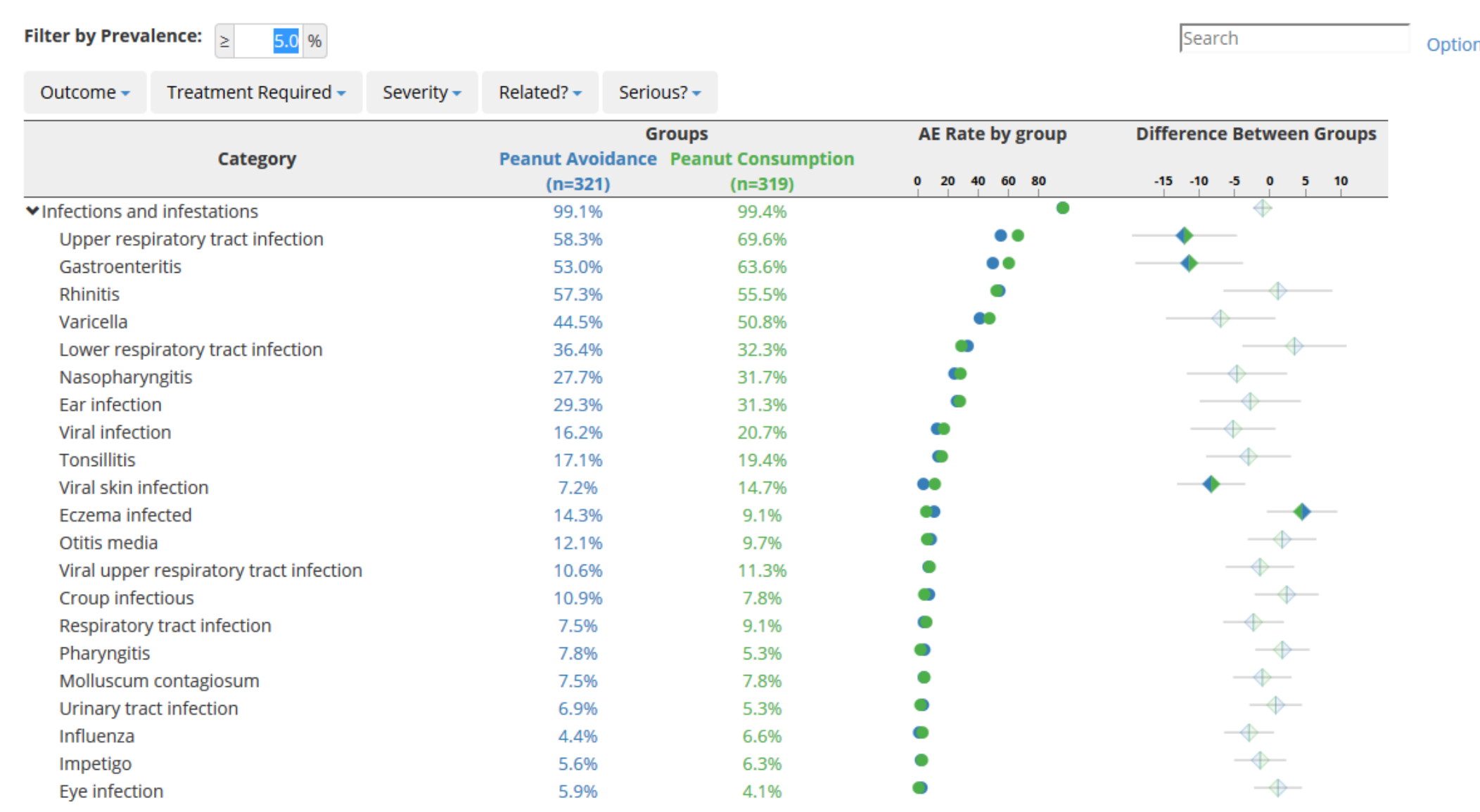


Figure 6: Filtering by Severity

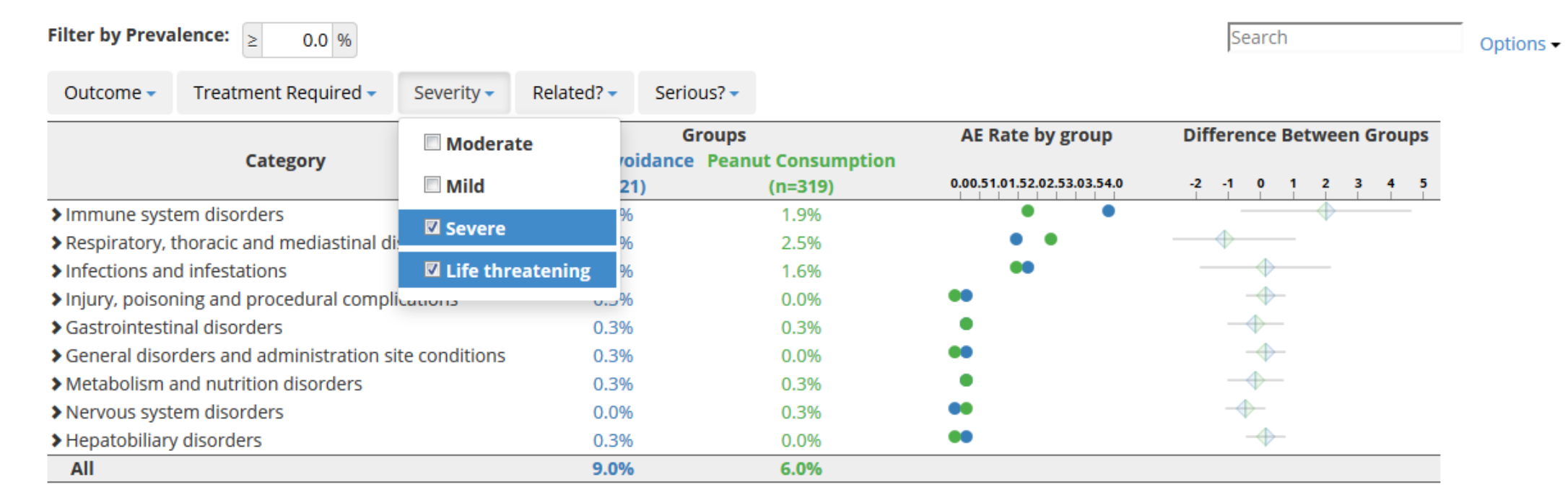


Figure 7: Drilling Down to Participant-Specific Data

#	Verbatim Name	Preferred Term	System Organ Class	Outcome	Severity	Treatment Area	Race/Ethnicity
1	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIROMETRY FORM.	Respiratory tract infection	Infections and infestations	Not Applicable	No	Intervention	Other/Missing
1	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIROMETRY FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Intervention	Other/Missing
1	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIROMETRY FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic
2	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIROMETRY FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic
2	Pneumonia	Pneumonia	Infections and infestations	Complete recovery	Yes	Control	Hispanic
2	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIRO FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic
2	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIRO FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic
2	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIRO FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic
2	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIRO FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic
2	RESPIRATORY INFECTIONS, COLDS, OR BRONCHITIS, PER SPIRO FORM.	Respiratory tract infection	Infections and infestations	Don't Know	No	Control	Hispanic

## A Practical Example

The AE Explorer gives users the ability to find quick answers to complex questions about the data. Consider how easy it would be to answer the following data request using the AE Explorer versus the traditional static summary.

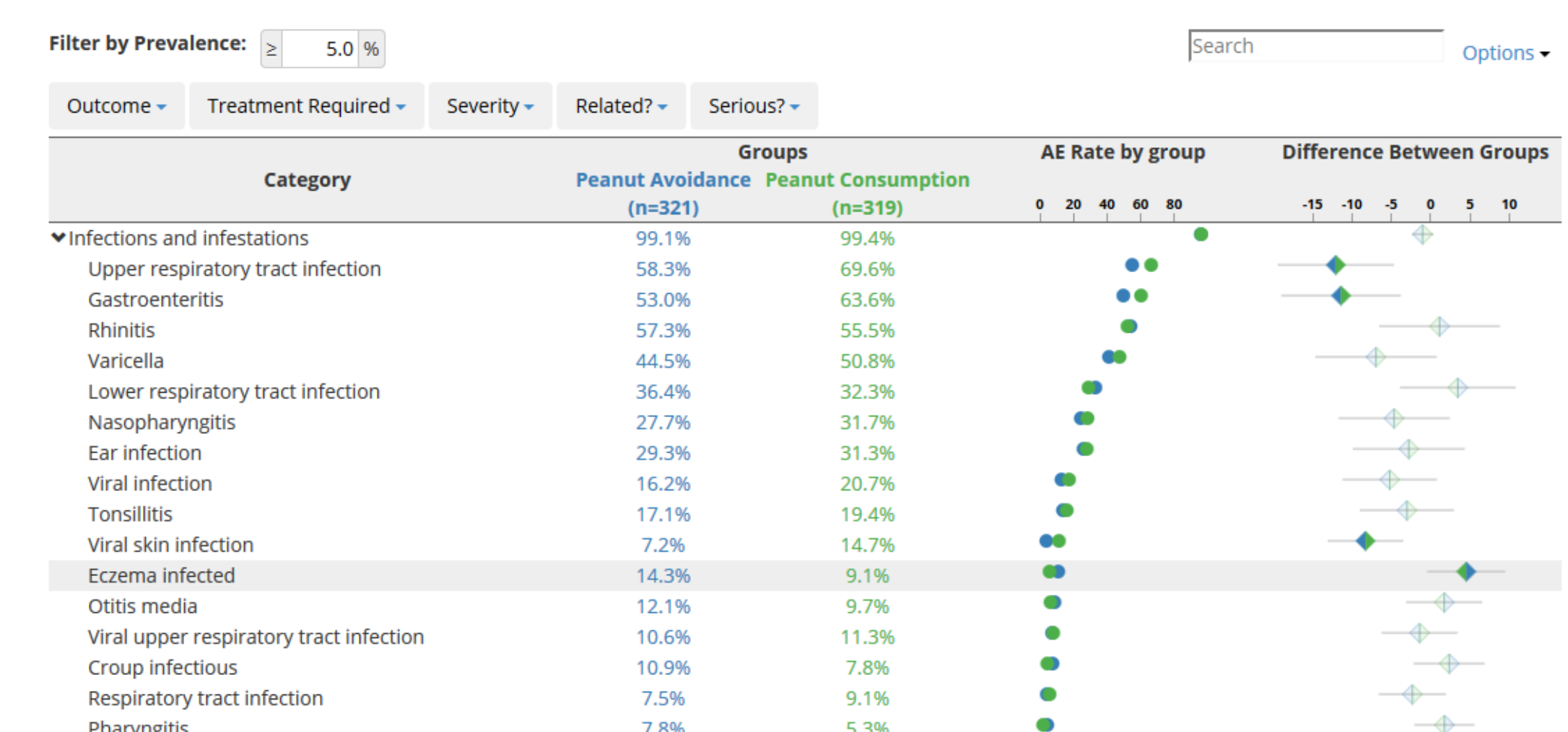
Find the adverse event(s) in the Infections and Infestations System Organ Class where:

- prevalence is at least 5.0 %
- rate of incidence is higher in the Avoidance Group than the Consumption Group
- the difference is statistically significant

Figure 8 shows how easily we can interact with the AE Explorer to find the answer.

With the AE Explorer we can set our prevalence variable at 5.0%, scan the AE Rate by group column for cases where the blue dot is greater than the green dot, and the difference between groups diamond is opaque. In a matter of seconds, we can see that *Eczema infected* is the only AE that meets our criteria. We can answer this question using the single page summary shown in Figure 1, but how long would it take to find this same answer?

Figure 8: Using the AE Explorer to Quickly Answer Complex Questions



End users of our AE Explorer routinely report how much they enjoy the tool and how much time it saves them when reviewing AE reports.

## Conclusions

The objective of Adverse Event reporting and monitoring is to protect patient safety. Traditional reporting methods succeed in providing exhaustive and transparent reporting, but at what expense? Long tables are tedious to read and difficult to navigate, which increases the likelihood that important data will be overlooked.

Web-based technology allows us to improve upon this paradigm by applying common interactive browsing functionality (searching, filtering, clickable navigation) to AE reporting.

Our Adverse Event Explorer applies these web-based design principles to help users gain a better understanding of AE data, without sacrificing the elements of transparency or comprehensive reporting. As a result, medical experts can more efficiently and reliably assess product safety.

Try out the AE Explorer for yourself any time by accessing it on our website: <http://graphics.rhoworld.com/tools/aeexplorer/>

We also provide open access to our source code via GitHub:

<https://github.com/RhoInc/aeexplorer>

