HEALTHCARE COSTS ASSOCIATED WITH PATIENTS EXPERIENCING MILD-TO-MODERATE OR SEVERE ANAPHYLAXIS PRESCRIBED AUVI-Q VS. OTHER EPINEPHRINE AUTO-INJECTORS IN A U.S. COMMERCIAL CLAIMS DATABASE STUDY

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Introduction

Severity of an anaphylactic event may impact healthcare costs across the continuum of care in outpatient, emergency department (ED) and hospital settings. Auvi-Q® (epinephrine injection, USP) is an epinephrine auto-injector (EAI) designed with audible and visible cues for use, a compact size, and an auto-retractable needle. Health-economic consequences of patients with anaphylaxis who were previously prescribed Auvi-Q vs. a different EAI have not been studied. Additionally, studies have not evaluated the impact of anaphylaxis severity on healthcare resource use and healthcare costs. This study aims to address these research gaps.

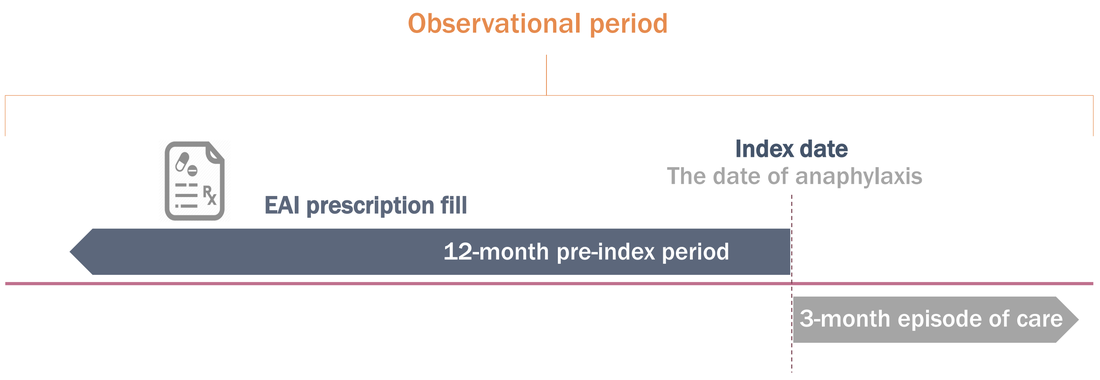
Objective

To compare real-world costs of care for propensity score-matched (PSM) patients who experienced mild-to-moderate (I, IIA, IIB) or severe (IIIA, IIIB, IIIC) anaphylaxis and had been previously prescribed Auvi-Q or another EAI.

Materials and Methods

The IBM MarketScan® Commercial Claims and Encounters Database (January 01, 2016–October 31, 2019) was used to identify patients who experienced anaphylaxis based on a previously validated algorithm of Harduar-Morano.[1] To identify the events of anaphylaxis in the database, ICD-9 and ICD-10 codes were used. The date of initial anaphylactic episode was set as the index date. Continuous medical and pharmacy coverage were required 12 months pre-index and 3-months post-index, and a filled EAI prescription was required in the pre-index period. Patients were assigned to a treatment cohort (Auvi-Q or Other EAIs) based on the last prescribed EAI before the index date. Anaphylaxis severity was evaluated using a previously defined grading system proposed by Niggemann.[2] The 3-month post-index healthcare resource consumption and healthcare costs independent of prescription costs were compared between the Auvi-Q and Other EAIs cohorts.

Figure 1. Study design



Outcomes were summarized and reported as mean and standard deviation (SD) for continuous variables, while counts and percentages were reported for categorical variables. The independent t-test was performed to determine the difference between the cohorts for continuous variables, while the chi-square test was performed for categorical variables; if counts were ≤5, Fisher's exact test was performed. To minimize study selection bias, patients categorized into the Auvi-Q and Other EAIs cohorts were subjected to propensity score matching in a 1:3 ratio, where all baseline differences observed between non-matched treatment cohorts were eliminated and the patients were "quasi-randomized" to one or another treatment using the "nearest neighbor" matching algorithm. Propensity score matching was performed in the cohort of patients with mild-to-moderate anaphylaxis and in the cohort of patients with severe anaphylaxis. All statistical analyses were performed using the IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

Results

Overall, 18,791 subjects were identified in the retrospective claims database as patients experiencing anaphylaxis with an EAI prescribed within the year preceding the anaphylactic event. Based on the symptoms observed in the retrospective database, patients were separated into subgroups with mild-to-moderate or severe anaphylaxis according to a previously established grading system.[2]

A total of 119 (28.6%) patients in the Auvi-Q cohort and 5,480 (29.8%) patients in the Other EAIs cohort were excluded from further analysis as we were not able to quantify the severity of anaphylaxis based on the claimed diagnoses (Table 1).

Table 1. Patients stratified in the subgroups based on the severity of anaphylaxis

Severity grade, n (%)	Auvi-Q (N=416)	Other EAIs (N=18,375)	*P*-value*
Severity undetermined	119 (28.6%)	5,480 (29.8%)	0.591
Mild-to-moderate anaphylaxis			
Grade I	59 (14.2%)	1,645 (9.0%)	<0.001
Grade IIA	42 (10.1%)	1,637 (8.9%)	0.401
Grade IIB	2 (0.5%)	151 (0.8%)	0.778
Severe anaphylaxis			
Grade IIIA	169 (40.6%)	7,908 (43.0%)	0.326
Grade IIIB	25 (6.0%)	1,551 (8.4%)	0.077
Grade IIIC	0 (0.0%)	3 (0.0%)	1.000

*Chi-square test of independence was applied to assess the difference

The mildest grade of anaphylaxis was more common in patients prescribed Auvi-Q than in those prescribed a different EAI (14.2% vs. 9.0%; *P*<0.001). Severe anaphylaxis involving multiple organ systems was observed with the same frequency among patients in both cohorts.

A total of 3,536 patients were classified as having mild-to-moderate anaphylaxis, and 9,656 were classified as having severe anaphylaxis. In the mild-to-moderate anaphylaxis subgroup, 103 patients were prescribed Auvi-Q, while 3,433 patients were prescribed other EAIs. In the severe anaphylaxis subgroup, 194 patients were prescribed Auvi-Q and 9,462 patients were prescribed other EAIs (Table 1).

The mean age of Auvi-Q patients was significantly lower than that of Other EAI patients in both the mild-to-moderate (8.5 vs. 16.0 years, P<0.001) and severe anaphylaxis (14.8 vs. 19.4 years, P<0.001) cohorts, while other demographic characteristics were similarly distributed in both groups.

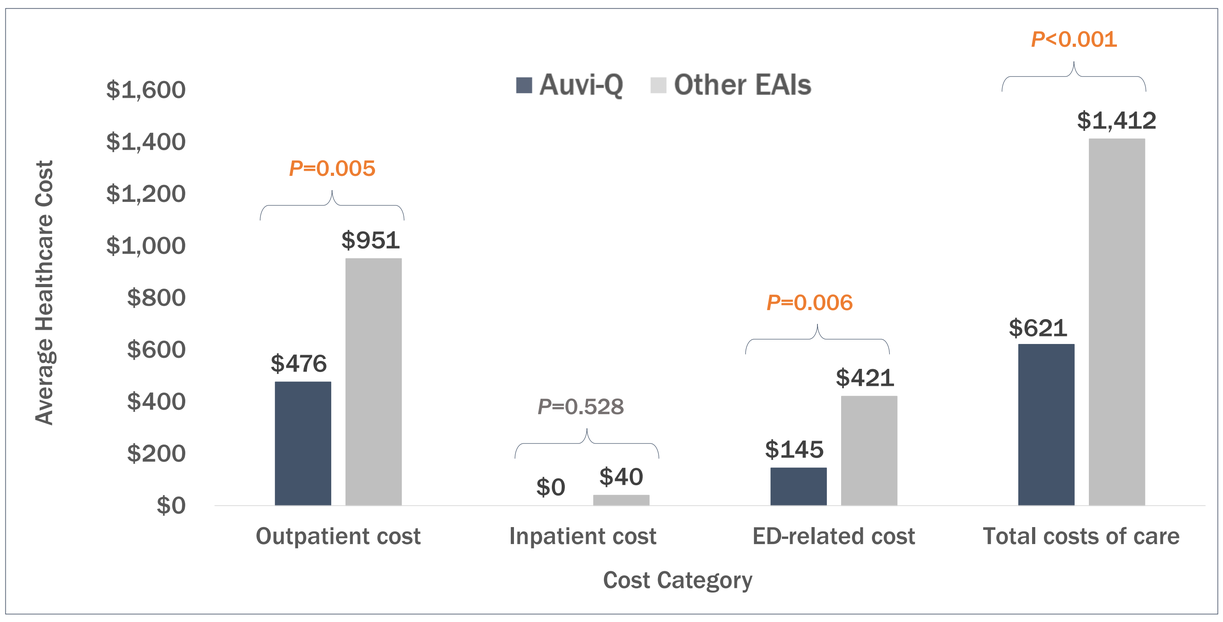
Matched Study Population

In the mild-to-moderate anaphylaxis subgroup, 83 Auvi-Q patients were matched to 207 Other EAI patients. In the severe anaphylaxis subgroup, 166 Auvi-Q patients were matched to 406 patients prescribed other EAIs. No demographic or clinical differences were observed among matched patients.

In patients with mild-to-moderate anaphylaxis, the Auvi-Q cohort had significantly lower total costs of care excluding prescription costs over the 3-month, post-anaphylaxis period ($621 vs. $1412, *P*<0.001). Auvi-Q patients had lower healthcare costs in all cost categories (Figure 2).

Similar results were observed in terms of resource consumption. A lower proportion of Auvi-Q patients had at least one ED visit during the anaphylactic episode (12.0% vs. 27.5%, *P*=0.005), with a lower number of mean ED visits among those patients (1.1 vs. 1.4 visits, *P*=0.032).

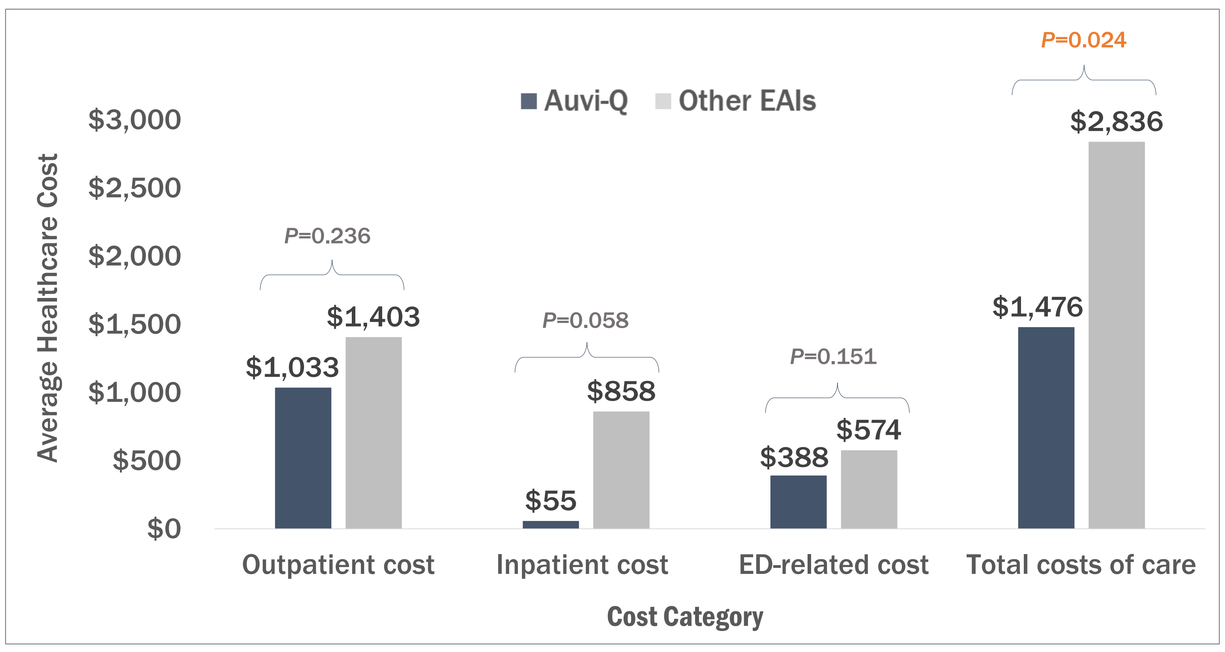
Figure 2. Healthcare cost breakdown for matched study population of mild-to-moderate anaphylaxis



In the severe anaphylaxis subgroup, total costs of care excluding prescription costs were substantially lower in the Auvi-Q cohort compared to the Other EAI cohort ($1,476 vs. $2,836, *P*=0.024). Although the Auvi-Q patient cohort experienced somewhat lower costs in all healthcare settings, the observed differences were not significant (Figure 3).

In terms of healthcare resource consumption, a significantly lower number of hospitalizations was observed in the Auvi-Q cohort vs. Other EAIs cohort (0.006 vs. 0.035, *P*=0.023); this difference may explain the higher healthcare costs in the cohort of patients prescribed other EAIs.

Figure 3. Healthcare cost breakdown for matched study population of severe anaphylaxis



Conclusions

- Regardless of anaphylaxis severity and independent of prescription costs, patients prescribed Auvi-Q had lower healthcare resource use and healthcare costs associated with the episode of care than patients prescribed other EAIs.
- Sample stratification and propensity score matching were successfully combined in this analysis to allow for the fair comparison of outcomes between similar patient populations.

References

1. Harduar-Morano L, Simon MR, Watkins S, Blackmore C. Algorithm for the diagnosis of anaphylaxis and its validation using population-based data on emergency department visits for anaphylaxis in Florida. *J Allergy Clin Immunol.* 2010;126(1):98-104.e4.
2. Niggemann B, Beyer K. Time for a new grading system for allergic reactions? *Allergy.* 2016;71(2):135-6.

Conflict of Interest

The study was funded by kaleo, Inc. This funding source had no role in study execution or data analysis.

A U.S. COMMERCIAL CLAIMS ANALYSIS OF CHARACTERISTICS AND HEALTHCARE COSTS OF PATIENTS WITH ANAPHYLAXIS PRESCRIBED AUVI-Q VS. OTHER EPINEPHRINE AUTO-INJECTORS

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Introduction

Anaphylaxis is a potentially life-threatening allergic reaction characterized by acute onset and rapid progression. The incidence of anaphylaxis has been on the rise, with an increasing number of related emergency department (ED) visits and hospitalizations. Epinephrine is considered first-line treatment for anaphylaxis and should be administered immediately after symptom occurrence. Auvi-Q® (epinephrine injection, USP) is an epinephrine auto-injector (EAI) available in the U.S. market for anaphylaxis treatment, designed with audible and visible cues for use, a compact size, and an auto-retractable needle. There is limited real-world evidence on the health-economic consequences of patients with anaphylaxis who were prescribed Auvi-Q vs. a different EAI; this study was conducted to bridge that gap.

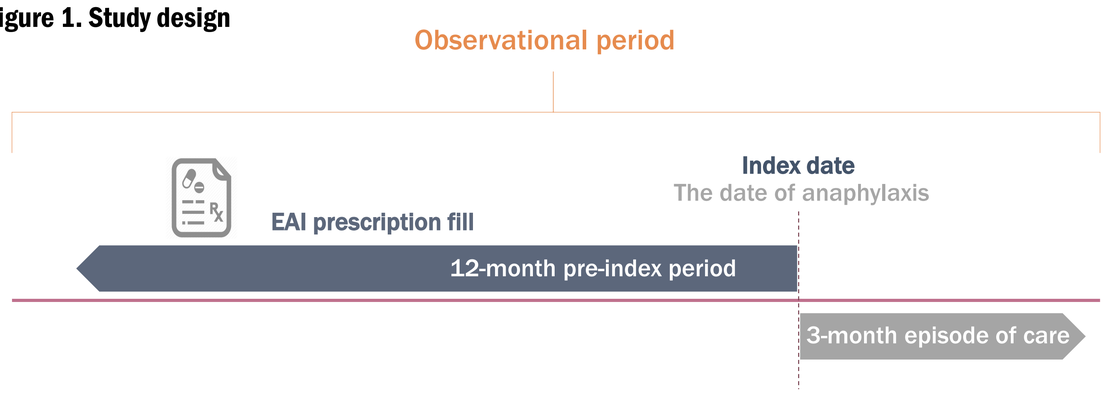
Objective

To analyze healthcare resource use and costs of care in non-matched and matched patient populations who experienced anaphylaxis and were previously prescribed Auvi-Q vs. other EAIs.

Materials and Methods

The IBM MarketScan® Commercial Claims and Encounters Database (January 01, 2016–October 31, 2019) was used to identify patients who experienced anaphylaxis based on a previously validated algorithm of Harduar-Morano.[1] To identify the events of anaphylaxis in the database, ICD-9 and ICD-10 codes were used. The date of initial anaphylactic episode was set as the index date. Continuous medical and pharmacy coverage were required 12 months pre-index and 3-months post-index, and a filled EAI prescription was required in the pre-index period. Patients were assigned to a treatment cohort (Auvi-Q vs. Other EAIs) based on the last prescribed EAI before the index date. The study design is shown in Figure 1.

Figure 1. Study design



Patients' demographics and clinical characteristics were summarized and reported as mean and standard deviation (SD) for continuous variables, while counts and percentages were reported for categorical variables. The independent t-test was performed to determine the difference between the cohorts for continuous variables, while the chi-square test was performed for categorical variables; if counts were ≤5, Fisher's exact test was performed. To minimize study selection bias, patients categorized into the Auvi-Q and other EAIs cohorts were subjected to propensity score matching in a 1:3 ratio, where all baseline differences observed between non-matched treatment cohorts were eliminated and the patients were "quasi-randomized" to one or another treatment using the "nearest neighbor" matching algorithm. All statistical analyses were performed using the IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

Results

Non-Matched Study Population Data

The final sample consisted of 416 patients who were prescribed Auvi-Q prior to the index anaphylaxis event and 18,375 patients who were prescribed other EAIs. Patients experiencing anaphylaxis were on average 18 years old, and both genders were equally affected. Patients prescribed Auvi-Q were substantially younger, 12 years old on average. Differences between cohorts were also observed in region of patients' residence, insurance types, Charlson comorbidity index, and certain conditions commonly seen in patients with anaphylaxis (Table 1).

Table 1. Demographic characteristics of non-matched patients

	Total Sample (N=18,791)	Auvi-Q (N=416)	Other EAI (N=18,375)	*P*-value*
Female gender, n (%)	9,347 (49.7%)	207 (49.8%)	9,140 (49.7%)	0.994
Age, mean years (SD)	17.7 (16.0)	12.3 (13.2)	17.9 (16.0)	<0.001
Geographic region, n (%)				
Northeast	5,151 (27.4%)	114 (27.4%)	5,037 (27.4%)	0.997
North Central	3,686 (19.6%)	123 (29.6%)	3,563 (19.4%)	<0.001
South	7,108 (37.8%)	101 (24.3%)	7,007 (38.1%)	<0.001
West	2,808 (14.9%)	78 (18.8%)	2,730 (14.9%)	0.028
Unknown region	38 (0.2%)	0 (0.0%)	38 (0.2%)	1.000
Health plan type, n (%)				
Comprehensive (COMP)	433 (2.3%)	19 (4.6%)	414 (2.3%)	0.002
Exclusive Provider Organization (EPO)	126 (0.7%)	5 (1.2%)	121 (0.7%)	0.207
Health Maintenance Organization (HMO)	2,087 (11.1%)	23 (5.5%)	2,064 (11.2%)	<0.001
Non-Capitated Point-of-Service (Non-Cap POS)	1,236 (6.6%)	31 (7.5%)	1,205 (6.6%)	0.467
Preferred Provider Organization (PPO)	9,784 (52.1%)	185 (44.5%)	9,599 (52.2%)	0.002
POS with capitation	99 (0.5%)	1 (0.2%)	98 (0.5%)	0.728
Consumer-Driven Health Plan (CDHP)	2,295 (12.2%)	51 (12.3%)	2,244 (12.2%)	0.977
High Deductible Health Plan (HDHP)	2,296 (12.2%)	86 (20.7%)	2,210 (12.0%)	<0.001
Unknown	435 (2.3%)	15 (3.6%)	420 (2.3%)	0.077
Charlson Comorbidity Index (CCI), mean (SD)	0.5 (0.6)	0.4 (0.6)	0.5 (0.6)	<0.001
Anaphylaxis-related disorders, n (%)				
Anxiety	2,444 (13.0%)	31 (7.5%)	2,413 (13.1%)	<0.001
Asthma	7,076 (37.7%)	136 (32.7%)	6,940 (37.8%)	0.035
Chronic obstructive pulmonary disease (COPD)	587 (3.1%)	7 (1.7%)	580 (3.2%)	0.088
Allergic rhinitis	8,286 (44.1%)	217 (52.2%)	8,069 (43.9%)	0.001
Angioedema	951 (5.1%)	11 (2.6%)	940 (5.1%)	0.023
Mastocytosis	40 (0.2%)	0 (0.0%)	40 (0.2%)	1.000
Dermatitis	5,063 (26.9%)	173 (41.6%)	4,890 (26.6%)	<0.001
Atopic dermatitis	3,036 (16.2%)	123 (29.6%)	2,913 (15.9%)	<0.001
Contact dermatitis	2,361 (12.6%)	66 (15.9%)	2,295 (12.5%)	0.040
Dermatitis due to other substances	840 (4.5%)	35 (8.4%)	805 (4.4%)	<0.001
History of allergy	5,718 (30.4%)	176 (42.3%)	5,542 (30.2%)	<0.001

*Independent t-test was applied for continuous variables and chi-square test of independence for categorical variables

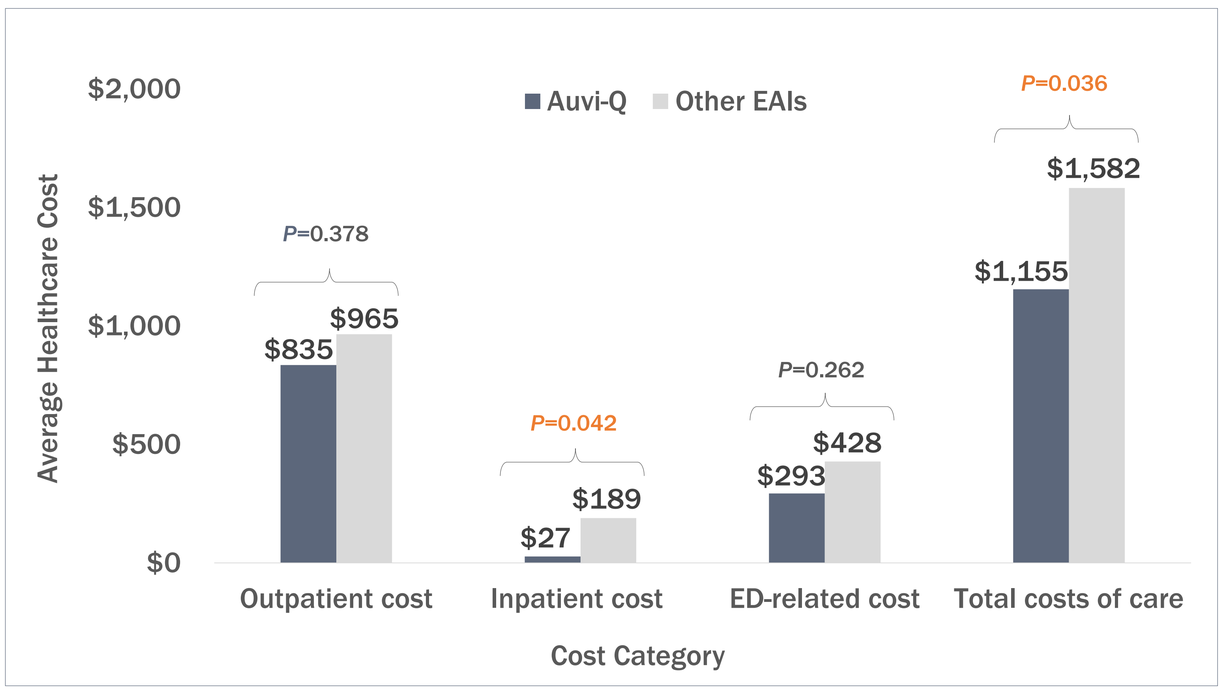
In the non-matched cohort, Auvi-Q patients had significantly lower all-cause total cost of care excluding prescription costs ($1,155 vs. $1,918, *P*<0.001) due to lower costs of outpatient visits, hospitalizations, and emergency care.

Matched Study Population Data

After propensity score matching, 340 patients remained in the Auvi-Q cohort and 934 patients in the Other EAIs cohort, with no significant demographic or clinical differences observed between the samples.

Auvi-Q patients had significantly lower total cost of care excluding prescription costs over the 3-month, post-anaphylaxis period (mean, $1,155 vs. $1,582, *P*=0.036). Significant savings in inpatient costs were observed for Auvi-Q patients ($27 vs. $189, *P*=0.042), which is in line with the fewer hospitalizations observed among Auvi-Q patients. Patients prescribed Auvi-Q appeared to have lower costs of care in other settings as well; however, these differences were not statistically significant (Figure 2).

Figure 2. Total cost of care breakdown in the matched population



In terms of healthcare resource consumption, patients prescribed Auvi-Q prior to the anaphylaxis event had lower ED visits (17.9% vs. 22.3%, *P*=0.094) and hospitalizations (0.3% vs. 1.6%, *P*=0.085) (Table 2). However, these differences were not significant. Thus, we subcategorized healthcare resource utilization based on specific services (visit to an Allergist/Immunologist, laboratory referrals, allergy-related test referrals, and allergy-related therapy). Patients prescribed Auvi-Q received significantly less laboratory referrals (0.6 vs. 0.8, *P*=0.001) and laboratory-related immunology referrals (0.2 vs. 0.3, *P*=0.004) than those prescribed other EAIs.

Table 2. Healthcare utilization for matched study population

	Auvi-Q (N=340)	Other EAIs (N=934)	*P*-value*
Outpatient visits			
Outpatient visits per total sample, mean (SD)	4.6 (5.4)	4.9 (6.0)	0.443
Patients with ≥1 outpatient visit, n (%)	337 (99.1%)	921 (98.6%)	0.470
Outpatient visits in patients with ≥1 outpatient visit, mean (SD)	4.7 (5.4)	5.0 (6.0)	0.402
Emergency department (ED) visits			
ED visits per total sample, mean (SD)	0.3 (0.6)	0.3 (0.7)	0.097
Patients with ≥1 ED visit, n (%)	61 (17.9%)	208 (22.3%)	0.094
ED visits in patients with ≥1 ED visit, mean (SD)	1.4 (0.6)	1.4 (0.9)	0.817
Hospitalizations			
Hospitalizations per total sample, mean (SD)	0.003 (0.054)	0.018 (0.156)	0.010
Total hospitalization length (days), mean (SD)	0.023 (0.434)	0.065 (0.849)	0.386
Patients with ≥1 hospitalization, n (%)	1 (0.3%)	15 (1.6%)	0.085
Hospitalization length (days), in patients with ≥1 hospitalization, mean (SD)	8.0 (0.0)	4.1 (5.5)	-

*Chi-square test was applied for categorical and independent t-test for continuous variables to test the difference between cohorts. A missing p-value indicates a lack of sample size to perform statistical testing

Conclusions

- Significantly lower total costs of care were observed for patients with anaphylaxis who were prescribed Auvi-Q compared to other EAIs, independent of prescription costs.
- Auvi-Q patients had less resource consumption with significantly less laboratory-related and immunology referrals.
- Auvi-Q was the less costly option in comparison to other EAIs in terms of total cost of care due to lower cost of hospitalizations. Prescription costs were not assessed in this analysis.

References

1. Harduar-Morano L, Simon MR, Watkins S, Blackmore C. Algorithm for the diagnosis of anaphylaxis and its validation using population-based data on emergency department visits for anaphylaxis in Florida. *J Allergy Clin Immunol.* 2010; 126(1):98-104.e4.

Conflict of Interest

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