

INTRODUCTION AND METHODS

BACKGROUND

► Infantile Spasms (IS) is a rare and devastating form of epilepsy, with an incidence of 1.6-4.5 per 10,000 live births and typical onset in the first year of life.¹
 ► Children who develop IS are at great risk for seizures, autism spectrum disorders, and developmental delays.² Earlier diagnosis and treatment are generally associated with improved outcomes.³
 ► Currently, only 2 drugs are FDA-approved and recommended⁴ for treatment of IS: repository corticotropin injection (RCI; H.P. Acthar® Gel)⁵ and vigabatrin (VGB; Sabril).⁶
 ► IS is often difficult to recognize, having a subtle appearance which may be similar to common disorders. Most pediatricians only see 1-2 cases in practice.²
 ► According to the United States (US) Consensus Report and a recent survey of members of the Child Neurology Society,⁷ most neurologists prefer first-line treatment with RCI for IS not caused by tuberous sclerosis (TSC) and VGB for IS caused by TSC.
 ► Treatment of IS may be more variable in practice, as suggested by prior study.⁸ This may adversely impact time to receipt of proven therapy and health outcomes.

PURPOSE

► To characterize treatment patterns and all-cause healthcare resource utilization (HCRU) in patients with IS in the 90 days prior to initiating RCI.

METHODS

- Truven MarketScan® Commercial Claims and Encounters data, reflecting employee-sponsored health insurance plan data (medical and pharmacy claims, and enrollment information), from 1/1/07-12/31/15 were used.
- Patients with a diagnosis code for IS (International Classification of Diseases, 9th / 10th Revision, Clinical Modification, i.e. ICD-9-CM 345.60 or ICD-10-CM G40.821, G40.822), less than 2 years of age at the time of initiating RCI ("index date"), with health plan coverage 90 days prior ("pre-index") were included.
- Age, gender and health plan type (e.g. Preferred Provider Organization or PPO) were evaluated on the index date.
- Pharmacy claims were used to identify treatments of interest, by drug class (each drug class could reflect >1 drug):
 - Corticosteroids Only – CS Only
 - Vigabatrin Only – VGB Only
 - Non-vigabatrin anti-epileptic drugs Only – AEDs Only
 - Multiple classes (>1 listed above) – Multiple Classes
 - No IS treatments listed above, i.e. initiated on RCI first - No IS Meds
- Unique dates of claims indicating HCRU per person per month during months 3, 2, and 1, were counted:
 - Outpatient visits by location (OP: office, hospital, other)
 - OP visits to specialist and non-specialist care providers (SHCP, NSHCP)
 - Hospital admissions (i.e. Inpatient stays, or IP)
 - Emergency room use (ER)
- All medications dispensed via the pharmacy were counted (Rx)
- Differences between treatment groups were evaluated descriptively.

RESULTS (prior to use of RCI)

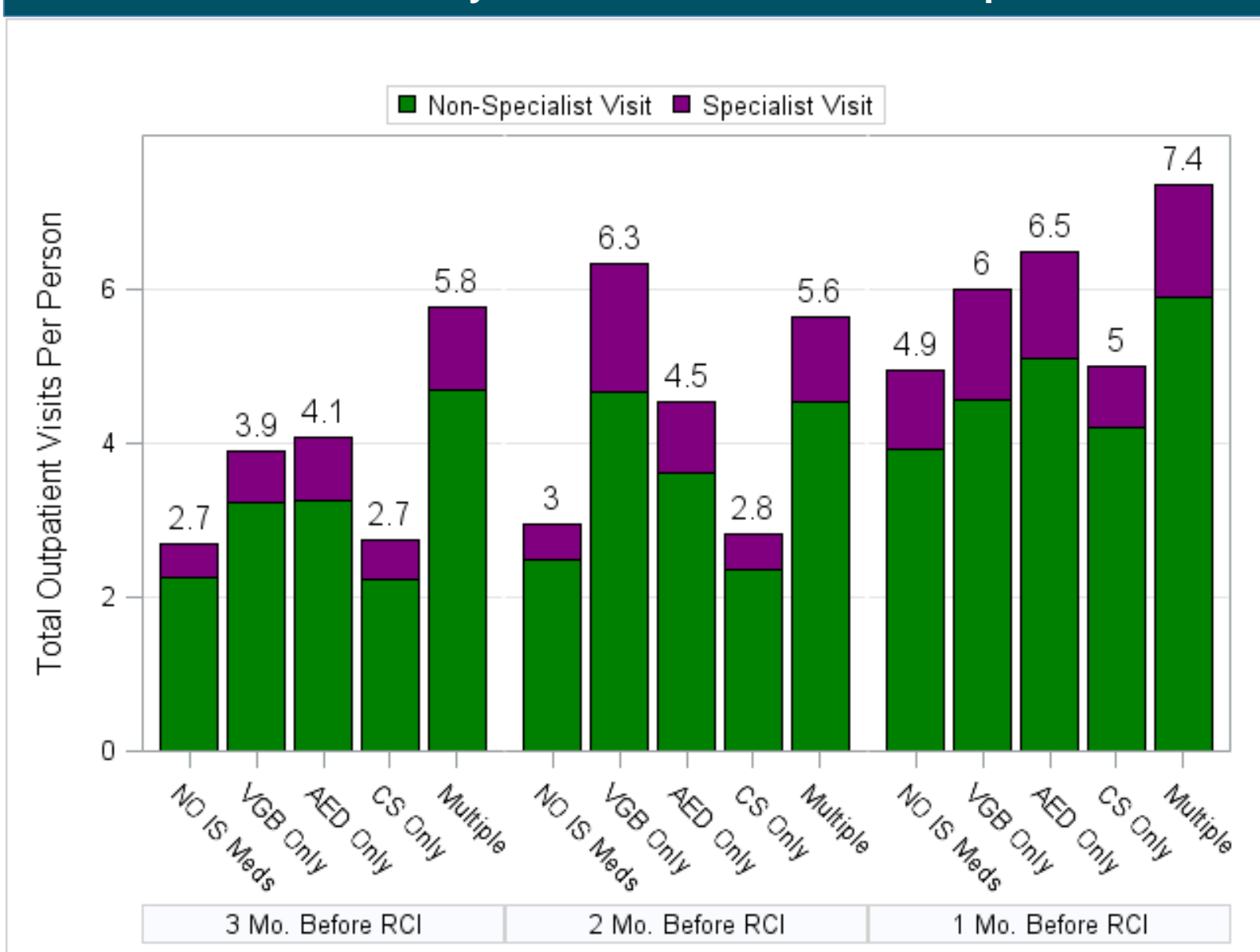
- During the study period, 462 patients initiated RCI [Table 1]. The majority of patients were male (57%), <1 year of age (84%), and enrolled in a PPO (60%).
- The most common diagnosis other than IS was Other Convulsions (49%).
- RCI was the first treatment dispensed to 54% of patients. AEDs Only and Multiple Classes were dispensed prior to RCI in 30% and 9% of patients, respectively.
- Among all patients, mean all-cause HCRU was: OP [11.4], SHCP [2.5] and NSHCP [10.0], ER [0.4], IP [1.0], and Rx [4.2].
- Patients receiving Multiple Classes tended to have more pre-index HCRU (i.e. OP, IP, Rx; not ER), vs. patients receiving 0 or 1 drug class. The next largest HCRU was in the VGB Only and AEDs Only groups.
- HCRU was lowest in No IS Meds and CS Only.

Table 1. Demographic Characteristics, Clinical Characteristics, and Healthcare Resource Use, Stratified by Treatment Group

Characteristics (n (%) or mean ± SD)	Total n=462	No IS Meds n=249 (54%)	Vigabatrin Only n=9 (2%)	AEDs Only n=138 (30%)	CS Only n=26 (6%)	Multiple Classes n=40 (9%)
Age 0	390 (84%)	227 (91%)	8 (89%)	108 (78%)	21 (81%)	26 (65%)
Age 1	72 (16%)	22 (9%)	1 (11%)	30 (22%)	5 (19%)	14 (35%)
Female	198 (42.8%)	104 (42%)	3 (33%)	62 (45%)	10 (38%)	19 (47%)
Top non-IS diagnoses during 90 days prior						
Other convulsions	225 (49%)	84 (34%)	4 (44%)	96 (70%)	13 (50%)	28 (70%)
Acute upper respiratory infections (unspecified site)	148 (32%)	79 (32%)	1 (11%)	44 (32%)	10 (38%)	14 (35%)
Esophageal reflux	141 (31%)	68 (27%)	1 (11%)	43 (31%)	10 (38%)	19 (48%)
Epilepsy, unspecified	107 (23%)	18 (7%)	1 (11%)	59 (43%)	5 (19%)	24 (60%)
Abnormal involuntary muscle movements	101 (22%)	49 (20%)	1 (11%)	31 (22%)	5 (19%)	15 (38%)
All-cause HCRU pre-index						
-Outpatient (OP) visits*	11.4 ± 10.0	9.5 ± 9.6	14.2 ± 10.9	13.4 ± 10.3	9.5 ± 6.4	16.6 ± 10.1
OP specialists visits	2.5 ± 3.4	1.9 ± 2.8	3.8 ± 3.7	3.1 ± 3.9	1.8 ± 1.9	3.9 ± 4.0
OP non-specialists visits	10.0 ± 9.5	8.4 ± 9.2	12.3 ± 10.5	11.6 ± 9.8	8.6 ± 6.2	14.8 ± 9.8
OP office visits	6.4 ± 5.7	5.4 ± 5.3	8.0 ± 8.3	7.5 ± 6.0	5.3 ± 3.2	9.1 ± 6.6
OP visits at hospital	3.3 ± 3.8	2.6 ± 3.3	4.6 ± 7.1	3.8 ± 4.0	4.6 ± 4.8	5.1 ± 4.2
OP visits (other location)	3.5 ± 7.2	3.0 ± 7.3	3.6 ± 3.8	4.0 ± 7.7	1.2 ± 1.4	5.8 ± 7.1
-ER use	0.4 ± 0.7	0.3 ± 0.7	0.4 ± 1.0	0.4 ± 0.8	0.4 ± 0.7	0.4 ± 0.7
-IP use	1.0 ± 0.8	0.8 ± 0.6	1.3 ± 1.3	1.0 ± 0.8	1.0 ± 0.8	1.4 ± 1.4
-Rx dispensed	4.2 ± 4.9	1.9 ± 2.7	4.3 ± 3.3	6.3 ± 4.9	4.7 ± 3.0	11.0 ± 7.1

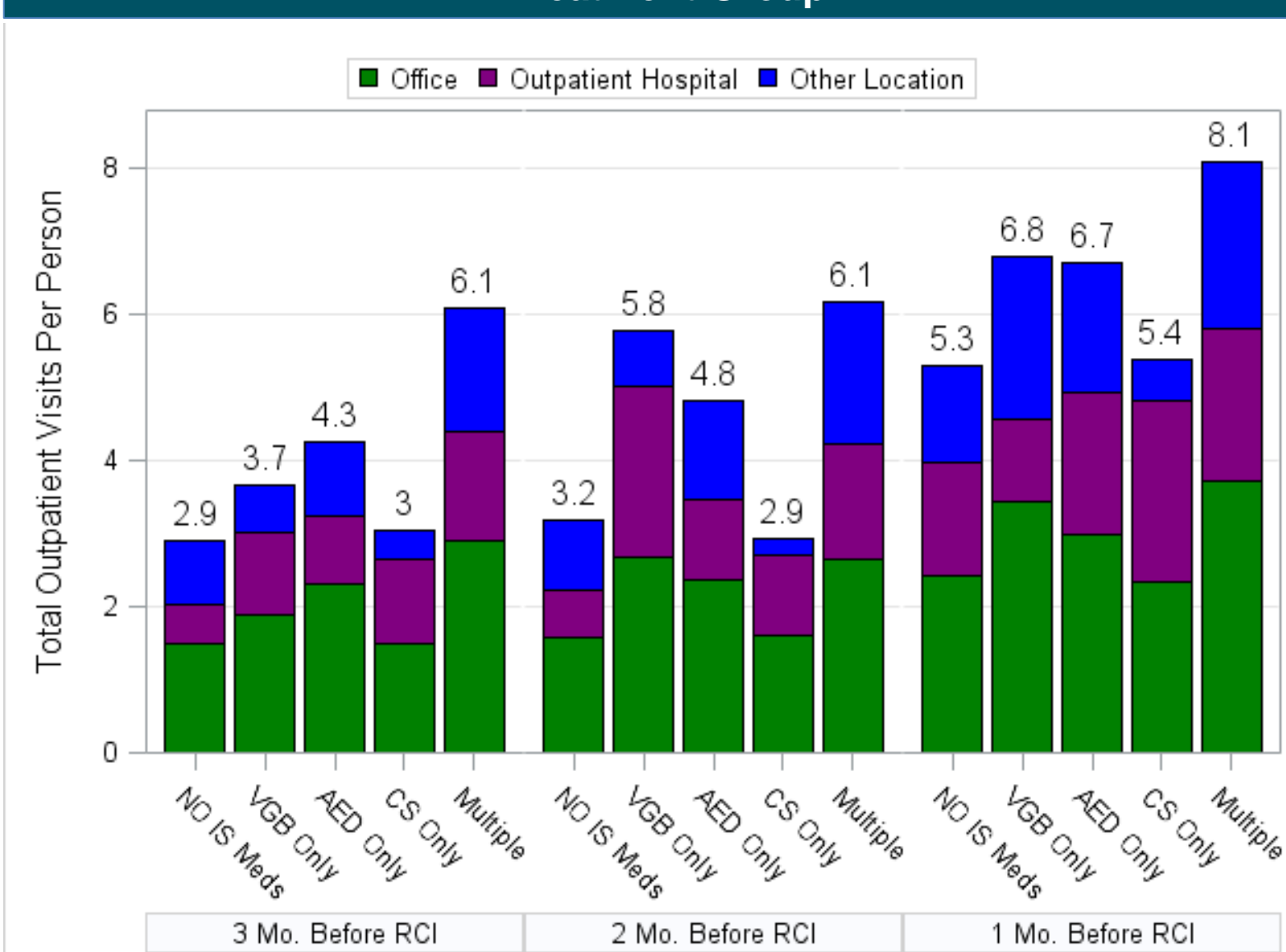
*Although OP categories are mutually exclusive, patients could have had >1 type of visit on the same day. Therefore, categories sum to more than the total.

Figure 1. Outpatient Visits to Specialists and Non-Specialists, Stratified by Month and Treatment Group



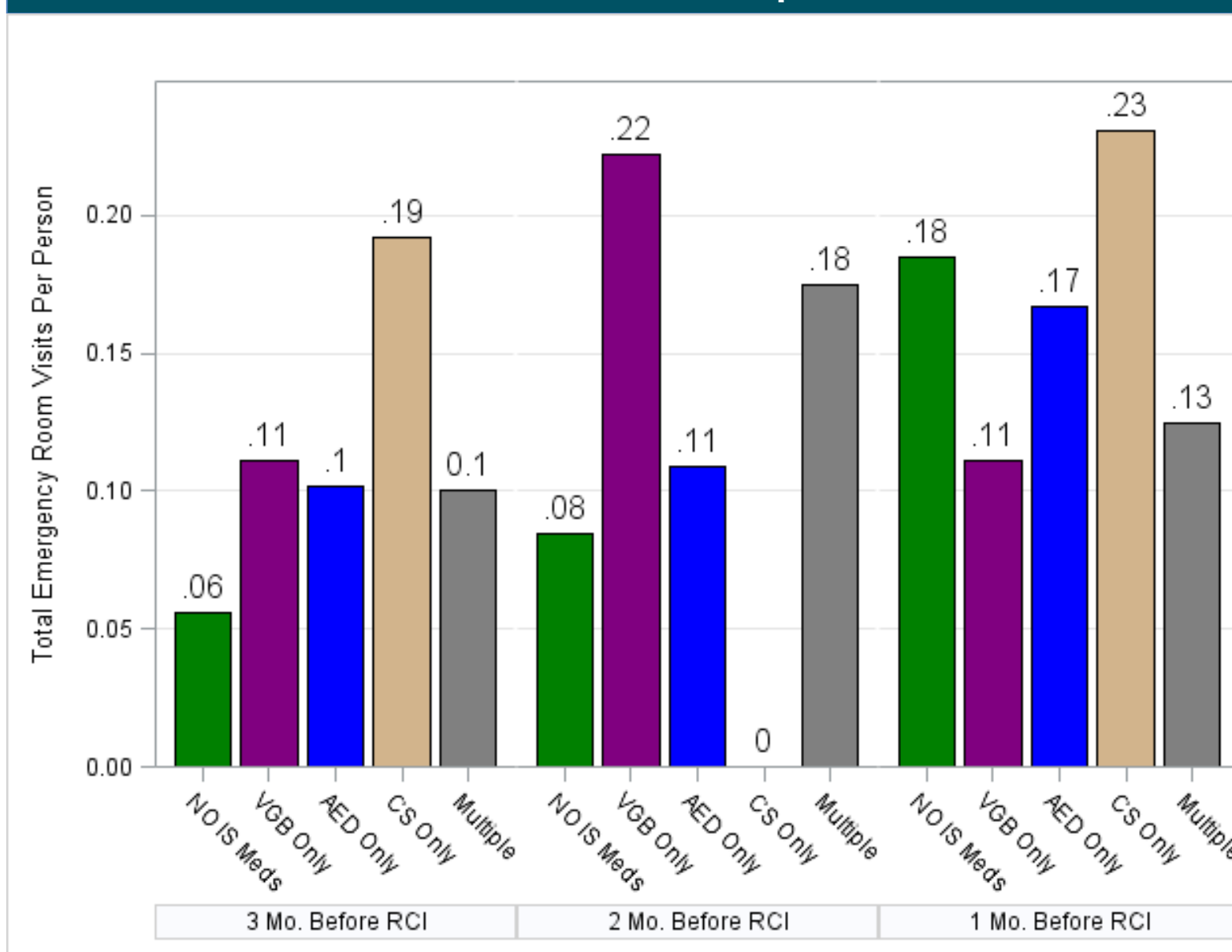
- Overall, OP visits to SHCPs and NSHCPs generally increased across all treatment groups during the period leading up to RCI use.
- Patients receiving Multiple Classes, VGB Only and AEDs Only had higher proportions of OP visits to SHCPs and NSHCPs. Patients receiving No IS Meds and CS Only had the lowest proportions of OP visits.

Figure 2. Outpatient Visit Setting, Stratified by Month and Treatment Group



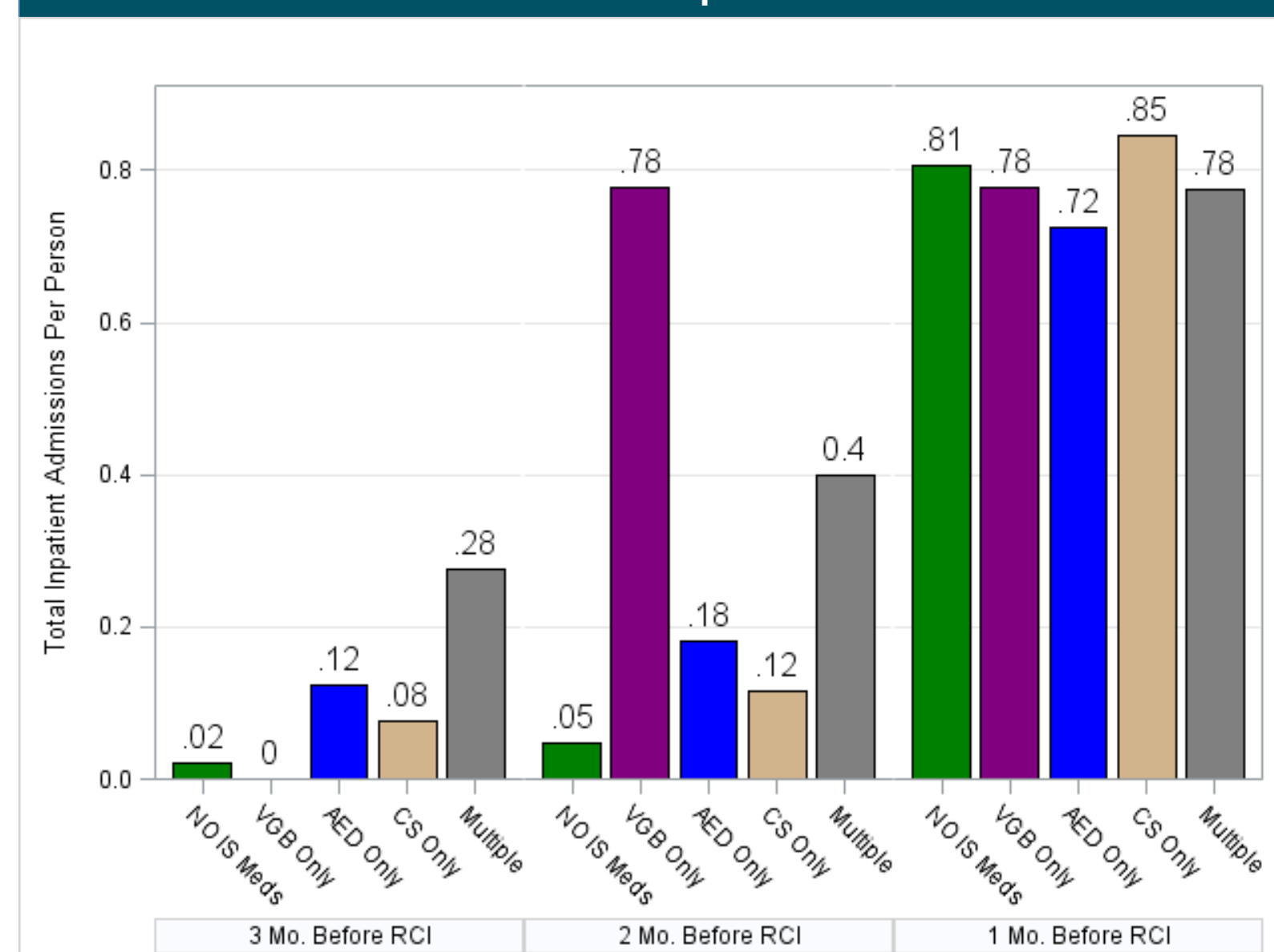
- Across all treatment groups, OP visits increased with time. The most OP visits were seen in the 1-month prior to initiation of RCI.
- Patients receiving Multiple Classes, VGB Only and AEDs Only had higher proportions of OP visits; those receiving No IS Meds and CS Only prior had the lowest.

Figure 3. Emergency Room Visits, Stratified by Month and Treatment Group



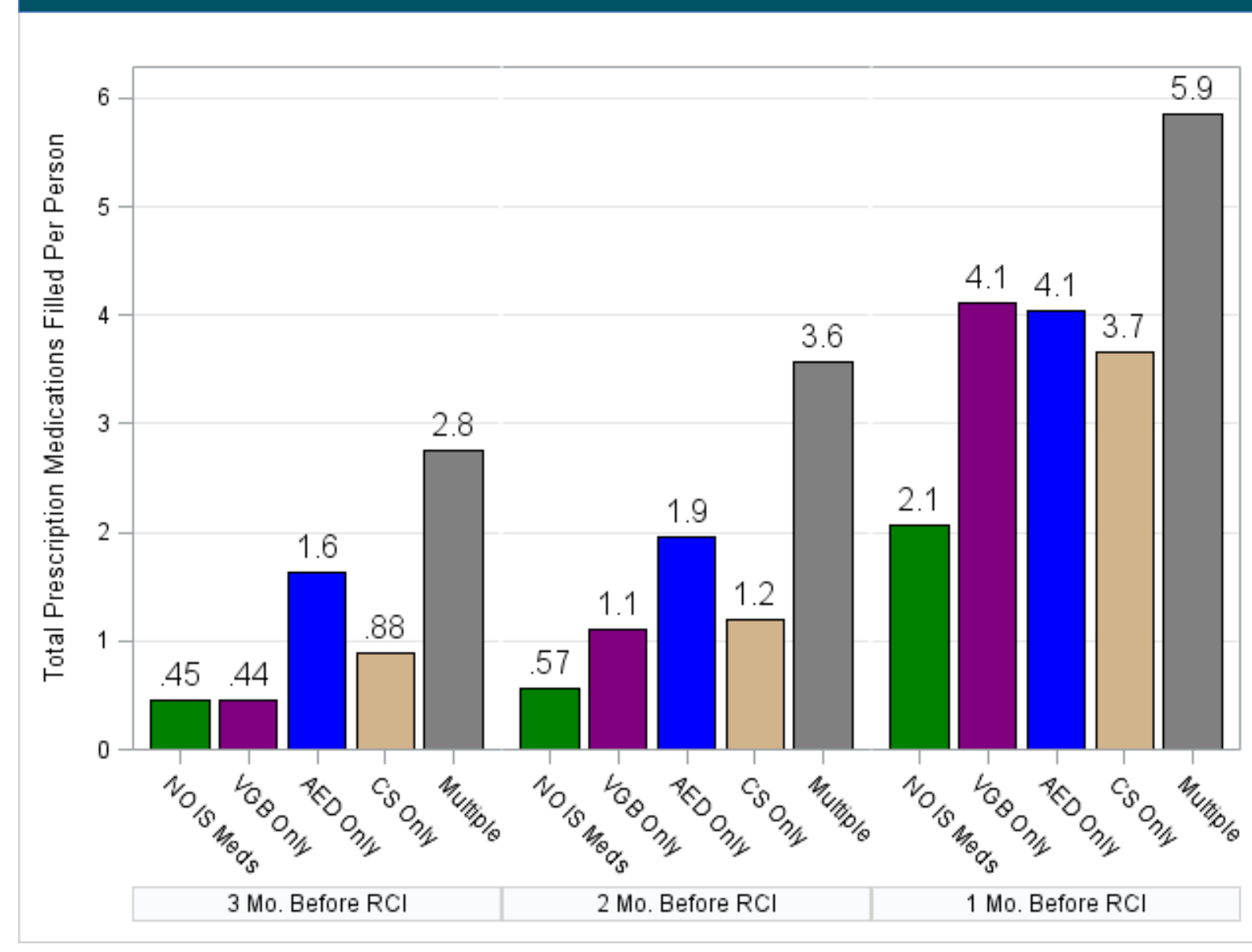
- Very low ER use per person was observed in all treatment groups pre-index.
- Across all treatment groups, ER use per person increased with time, and was highest in the 1-month prior to initiation of RCI.

Figure 4. Inpatient Admissions, Stratified by Month and Treatment Group



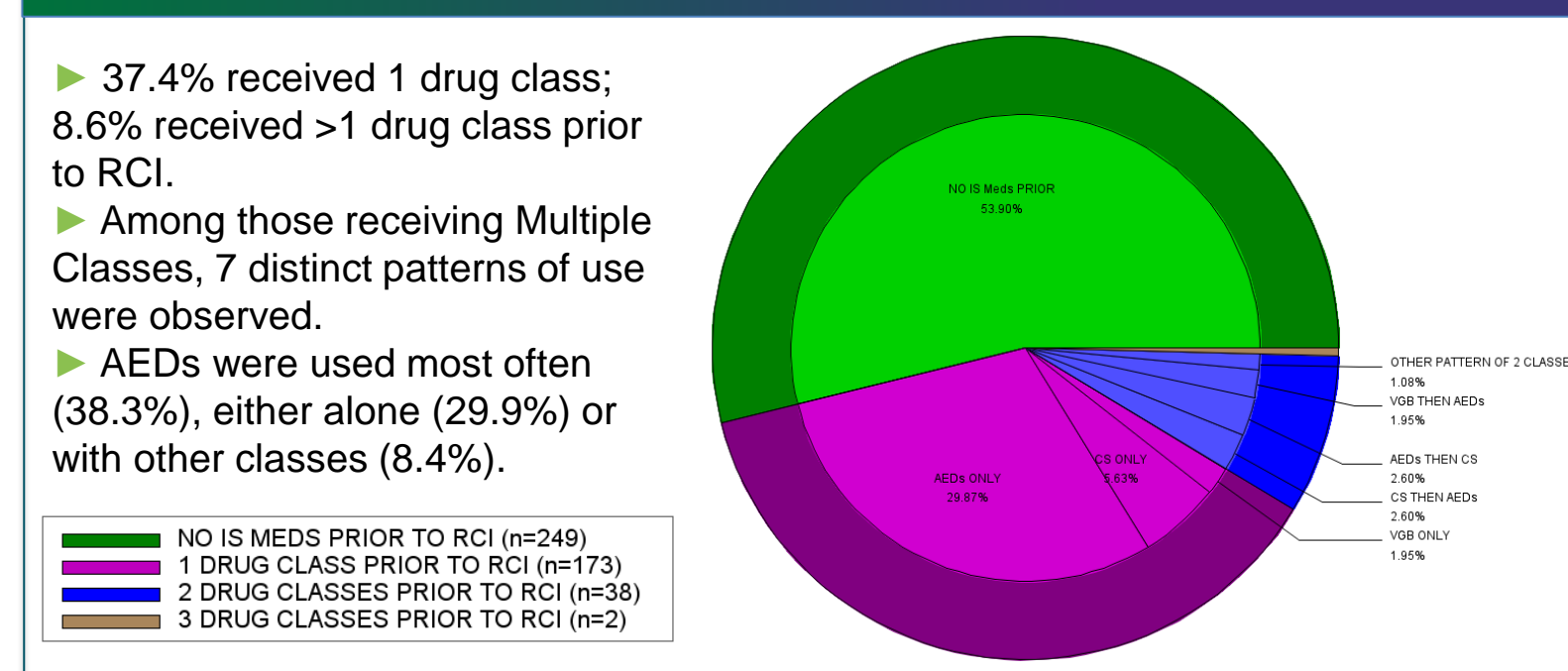
- Low pre-index IP use was observed in all treatment groups.
- IP use per person increased with time, occurring most 1 month prior to RCI.
- IP use with VGB Only was elevated and sustained in the 2 months prior to RCI compared to other treatment groups.

Figure 5. Prescription Medications Dispensed, Stratified by Month and Treatment Group



- Rx per person increased with time, and was highest in 1 month prior to RCI.
- Patients receiving Multiple Classes filled the most prescriptions. In patients receiving 1 drug class, the highest prescription use per person was seen in patients using AEDs Only followed by those using CS Only and VGB Only; the latter were similar. Lowest use observed was in patients receiving No IS Meds prior.

Figure 6. Medication Utilization by Drug Classes of Interest



DISCUSSION

- 37.4% received 1 drug class; 8.6% received >1 drug class prior to RCI.
- Among those receiving Multiple Classes, 7 distinct patterns of use were observed.
- AEDs were used most often (38.3%), either alone (29.9%) or with other classes (8.4%).
- 54% of patients received RCI first for treatment of their IS. AEDs (ex-VGB) were most commonly dispensed (38.3%). Sparse evidence of efficacy supporting the use of AEDs exists in the treatment of IS. Results reflect utilization, not efficacy afforded.
- Patients with Multiple Classes generally had the highest HCRU [OP, ER, IP, Rx] of all groups. Of those receiving 1 drug class, VGB Only and AEDs (non-VGB) Only had the highest HCRU; No IS Meds and CS Only had the lowest HCRU, with similar HCRU between groups, albeit more IP [+0.2] and Rx [+2.8] use among the CS Only.
- Numerous healthcare encounters occurred in the 90 days before initiation of RCI. All measures of HCRU [OP, ER, IP, Rx] increased with time and across groups, with per person per month use peaking in the 1-month prior to RCI.
- Numerous non-specialist visits, frequent AED use, and diagnoses of Other convulsions, Epilepsy unspecified, and Abnormal involuntary muscle movement further suggest a delay in IS diagnosis and/or the possible presence of complex seizure types, as well as a delay in receipt of appropriate therapy.
- Even the lowest HCRU observed, in the No IS Meds group, imposes notable and potentially mitigable burden on patients, caregivers and the US healthcare system.
- Earlier diagnosis and initiation of approved therapy may streamline critical time and HCRU expenditures which may impact longer-term prognosis for IS patients.

LIMITATIONS

- The time interval between IS diagnosis and RCI initiation could vary. The specific chronology of diagnoses and outcomes pre-index were not evaluated.
- Sample size for some groups was small, complicating conclusions (e.g. VGB). Between group differences were evaluated descriptively only.
- By evaluating IS drug classes rather than IS medications, we likely underestimated the true heterogeneity in medication use.
- Administrative health insurance claims data is collected for reimbursement purposes; it does not typically contain robust clinical detail (e.g. seizure types) or test results.
- Marketscan results may not be generalizable to other populations, e.g. US health plans.
- Drug use outside of claims and reasons for use (e.g. diagnoses, events) could not be evaluated. Prescription claims reflect dispensation; utilization is assumed.

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