Healthcare Resource Utilization Patterns in US Patients with Rett Syndrome

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INTRODUCTION

- Rett syndrome (RTT) is a severe neurodevelopmental disorder that almost exclusively affects females and is associated with substantial disease burden[1-4]
- To date, there are no approved therapies that target the underlying cause of RTT; such therapies may help reduce the reliance on healthcare resources. Moreover, literature on the economic burden associated with RTT in the United States is limited, representing a much-needed area of study
- To fill the gap in the literature on RTT, this study aimed to provide an overview of healthcare resource utilization (HRU) and costs among female individuals with RTT in the United States

METHODS

Data Source

- Pre-adjudicated and adjudicated administrative healthcare claims data from the IQVIA™ Medical Claims Data (Dx) and Longitudinal Prescription Data (LRx) databases, respectively, were used to address the study objectives

Study Design

- A longitudinal, retrospective, cohort study was used to address the study objectives (November 1, 2016–October 31, 2019)
- The index date was defined as the date of the first observed diagnosis of RTT in any position
- The baseline period was defined as 6 months prior to the index date for patients ≥1 years of age or from the start of clinical activity to the index date for patients <1 year of age and was used to describe demographic and clinical characteristics
- The observation period was defined as the period from the index date to the earliest of end of clinical activity or end of data availability, during which HRU and associated costs were described

Study Population

- Females with ≥1 medical claim with a diagnosis code of RTT in any position were included. Those with medical claims for cerebrovascular disease or brain trauma during the baseline period were excluded
- Individuals were further stratified into pediatric (<18 years of age on index) and adult (≥18 years of age on index) subgroups

Statistical Analysis

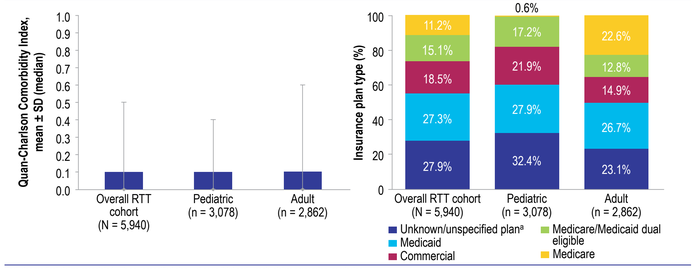
- Annual incidence rates of HRU were reported per person-year (PPY) for each type of healthcare encounter and calculated as the number of healthcare encounters divided by the total person-years of observation
- Healthcare costs, including medical and pharmacy costs, were reported per-person-per-year (PPPY) and calculated as the total costs incurred over the observation period divided by the length of observation per person
- All costs were inflation-adjusted to 2021 US dollars and summarized using mean, standard deviation, and median values
- Extreme values were truncated at the 95th percentile to reduce sensitivity to outliers

RESULTS

Study Population

- A total of 5,940 females met the eligibility criteria and were included in the study population, of whom 3,078 (51.8%) comprised the pediatric cohort and 2,862 (48.2%) comprised the adult cohort
- Median age of the overall RTT cohort was 17.0 years (interquartile range: 9–28 years), most individuals were from the southern region (34.5%), and Medicaid was the most common non-missing insurance plan type (27.3%; Figure 1)

Figure 1. Baseline characteristics of patients with RTT, overall and by pediatric and adult patients



[a]Includes medical claims associated with an unspecified plan, unknown third party, cash, claims processing, or missing

RTT, Rett syndrome; SD, standard deviation

Treatment Patterns of Pharmacological Agents

- High persistence in the use of pharmacological agents was observed, with the longest mean durations of therapy in the overall cohort being for antiepileptic drugs (683.50 days), sedatives/hypnotics (365.47 days), and prokinetic agents (321.19 days; Table 1)

Table 1. Treatment patterns during follow-up

Treatment patterns: pharmacologic agents	Overall RTT cohort N = 5,940	Stratification by age: Pediatric (<18 years of age) n = 3,078	Stratification by age: Adult (≥18 years of age) n = 2,862
Duration of therapy (days, all episodes), mean ± SD [median]			
Antiepileptic drugs	683.50 ± 379.43 [806]	655.07 ± 395.64 [763]	714.64 ± 358.38 [838]
Sedatives/hypnotics	365.47 ± 402.00 [115]	240.03 ± 344.25 [56]	443.44 ± 415.99 [312]
Prokinetic agents	321.19 ± 390.15 [112]	314.12 ± 379.30 [129]	323.30 ± 396.61 [111]
Nutritional supplements	273.69 ± 297.67 [141]	254.25 ± 336.70 [49]	285.35 ± 280.28 [194]
Antiarrhythmic drugs	312.75 ± 309.14 [282]	190.33 ± 231.15 [114]	680.00[a] [680]
Duration of therapy (days, first episode), mean ± SD [median]			
Antiepileptic drugs	631.45 ± 406.94 [721]	595.10 ± 425.12 [653]	671.27 ± 382.24 [774]
Sedatives/hypnotics	321.57 ± 394.86 [74]	198.13 ± 333.06 [24]	398.29 ± 411.11 [251]
Prokinetic agents	266.19 ± 367.79 [76]	261.47 ± 368.31 [65]	267.60 ± 370.90 [77]
Nutritional supplements	249.72 ± 295.27 [93]	251.58 ± 338.46 [33]	248.60 ± 275.55 [125]
Antiarrhythmic drugs	149.00 ± 203.99 [71]	189.33 ± 229.47 [114]	28.00[a] [28]

[a]SD could not be calculated because there was only one participant in this group

RTT, Rett syndrome; SD, standard deviation

All-Cause and RTT-Related HRU

- Over a mean observation period of 2.04 years, the incidence rate of any all-cause HRU was 44.43 visits PPY in the overall population, 52.43 visits PPY in the pediatric subgroup, and 35.86 visits PPY in the adult subgroup (Table 2)
- The all-cause HRU was driven primarily by home and hospice care visits (16.31), outpatient visits (9.58), and therapeutic services visits (7.26), and similar trends were observed across the pediatric and adult subgroups (Table 2)
- The overall incidence rate of any RTT-related HRU was 20.98 visits PPY (pediatric, 25.14; adult, 16.52), comprising nearly 50% of all-cause HRU across all cohorts (Table 2)
- As with all-cause HRU, key drivers of RTT-related HRU in the overall population included home and hospice care visits (7.57), outpatient visits (4.39), and therapeutic services visits (3.83), and similar trends were observed across the pediatric and adult subgroups (Table 2)

Table 2. HRU among patients with RTT, overall and by pediatric and adult patients

Incidence rate, PPY[a–c]	Overall RTT cohort N = 5,940	Stratification by age: Pediatric (<18 years of age) n = 3,078	Stratification by age: Adult (≥18 years of age) n = 2,862
All-cause HRU	44.43	52.43	35.86
Inpatient stay	0.37	0.36	0.38
ED visit	0.56	0.56	0.57
OP visit	9.58	13.22	5.69
Long-term care/skilled nursing facilities	0.17	0.02	0.32
Other place of service	2.30	2.29	2.30
Unknown place of service[d]	31.46	35.97	26.61
Home/hospice care	16.31	18.50	13.96
Therapeutic services visit[e]	7.26	9.57	4.78
Medical supplies	5.41	5.25	5.59
Durable medical equipment use	2.47	2.99	1.91
Other	2.81	4.11	1.41
RTT-related HRU[f]	20.98	25.14	16.52
Inpatient stay	0.21	0.24	0.17
ED visit	0.12	0.13	0.11
OP visit	4.39	6.53	2.10
Long-term care/skilled nursing facilities	0.07	0.02	0.14
Other place of service	1.04	1.14	0.93
Unknown place of service[d]	15.14	17.09	13.07
Home/hospice care	7.57	7.95	7.16
Therapeutic services visit[e]	3.83	5.16	2.41
Medical supplies	2.43	2.54	2.30
Durable medical equipment use	1.21	1.48	0.93
Other	1.39	2.10	0.62

[a]Among patients with multiple types of visits on the same day, inpatient stays were prioritized over all other types of visits, followed by ED visits, OP visits, long-term care/skilled nursing facilities, other places of service, and unknown place of service; [b]Consecutive days of inpatient stays, ED visits, or long-term care visits were considered 1 visit; [c]Evaluated on each distinct day during the follow-up period, including the index date; [d]Unknown places of service included medical claims that described the place of service as "other" or "unassigned." Procedure codes associated with each medical claim were used to define the type of visit; [e]Therapeutic services visits included physical therapy, hydrotherapy, occupational therapy, speech therapy, and feeding assistance; [f]RTT-related was defined as a medical service claim with a diagnosis of RTT in the primary or secondary position. RTT was identified using the following *ICD-10-CM* diagnosis code: F84.2

ED, emergency department; HRU, healthcare resource utilization; *ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification*; OP, outpatient; PPY, per person-year; RTT, Rett syndrome

All-Cause and RTT-Related Healthcare Costs

- Over a mean observation period of 2.04 years, the mean all-cause total healthcare cost PPPY was $40,326.08 (pediatric, $45,717.69; adult, $34,547.79), comprising $34,772.36 in medical costs (pediatric, $40,258.45; adult, $28,892.81) and $5,553.73 in pharmacy costs (pediatric, $5,459.25; adult, $5,654.98; Table 3)
- All-cause medical costs were primarily driven by home and hospice care visits ($12,054.33), followed by therapeutic services ($7,070.61), outpatient visits ($6,790.76), and inpatient visits ($6,087.85) among the overall cohort, and similar trends were observed across the pediatric and adult subgroups (Table 3)
- Mean RTT-related total healthcare costs PPPY were $18,070.17 (pediatric, $20,775.66; adult, $15,170.65), accounting for nearly 50% of all-cause healthcare costs across both pediatric and adult subgroups (Table 3)
- As with all-cause medical costs, key drivers of RTT-related medical costs among the overall cohort included home and hospice care visits ($5,026.20), therapeutic services ($3,973.31), outpatient visits ($2,692.22), and inpatient visits ($2,235.28), and similar trends were observed across the pediatric and adult subgroups (Table 3)

Table 3. Healthcare costs among patients with RTT, overall and by pediatric and adult patients

PPPY healthcare costs,[a,b] USD 2021	Overall RTT cohort N = 5,940	Stratification by age: Pediatric (<18 years of age) n = 3,078	Stratification by age: Adult (≥18 years of age) n = 2,862
All-cause total healthcare costs, PPPY, mean ± SD [median]	40,326.08 ± 45,816.41 [22,161]	45,717.69 ± 48,177.75 [28,306]	34,547.79 ± 42,387.85 [17,327]
Medical costs	34,772.36 ± 42,746.72 [16,605]	40,258.45 ± 45,022.67 [22,397]	28,892.81 ± 39,323.94 [11,705]
Inpatient	6,087.85 ± 15,776.45 [0]	6,718.32 ± 16,482.26 [0]	5,412.17 ± 14,953.67 [0]
ED	960.97 ± 1,911.36 [0]	950.67 ± 1,883.12 [0]	972.01 ± 1,941.11 [0]
OP	6,790.76 ± 10,012.37 [2,269]	8,379.33 ± 10,971.80 [3,611]	5,088.25 ± 8,547.96 [1,387]
Long-term care/skilled nursing facilities[c]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]
Other place of service	1,063.21 ± 2,040.66 [61]	1,140.77 ± 2,134.07 [26]	980.08 ± 1,932.10 [84]
Unknown place of service[d]	19,869.57 ± 31,660.39 [5,929]	23,069.35 ± 33,274.28 [8,105]	16,440.29 ± 29,450.54 [3,922]
Home/hospice care	12,054.33 ± 58,526.51 [0]	15,161.01 ± 66,024.12 [0]	8,724.84 ± 49,021.61 [0]
Therapeutic services[e]	7,070.61 ± 19,386.18 [0]	7,801.62 ± 17,537.50 [193]	6,287.16 ± 21,161.11 [0]
Medical supplies	1,712.45 ± 4,431.68 [595]	1,738.07 ± 3,601.65 [596]	1,684.99 ± 5,175.37 [595]
Durable medical equipment	2,941.85 ± 12,095.75 [93]	3,924.70 ± 13,320.73 [631]	1,888.51 ± 10,525.90 [0]
Other/missing	3,491.05 ± 24,611.75 [259]	3,653.69 ± 24,535.43 [624]	3,316.74 ± 24,692.09 [68]
Pharmacy costs	5,553.73 ± 8,958.07 [1,146]	5,459.25 ± 8,940.76 [1,046]	5,654.98 ± 8,975.49 [1,253]
RTT-related total healthcare costs,[f] PPPY, mean ± SD [median]	18,070.17 ± 22,131.18 [9,214]	20,775.66 ± 22,978.75 [12,489]	15,170.65 ± 20,798.11 [6,221]
Medical costs	14,642.50 ± 20,159.61 [5,908]	17,342.97 ± 21,044.67 [8,969]	11,748.36 ± 18,738.57 [3,463]
Inpatient	2,235.28 ± 6,294.44 [0]	2,656.46 ± 6,804.42 [0]	1,783.90 ± 5,662.76 [0]
ED	51.56 ± 169.43 [0]	57.77 ± 176.57 [0]	44.90 ± 161.17 [0]
OP	2,692.22 ± 4,778.25 [475]	3,512.81 ± 5,357.78 [857]	1,812.78 ± 3,878.31 [279]
Long-term care/skilled nursing facilities[c]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]	0.00 ± 0.00 [0]
Other place of service	425.41 ± 964.81 [0]	497.70 ± 1,054.95 [0]	347.93 ± 850.97 [0]
Unknown place of service[d]	9,238.03 ± 16,345.78 [2,148]	10,618.23 ± 16,946.74 [3,334]	7,758.85 ± 15,540.67 [1,144]
Home/hospice care	5,026.20 ± 30,727.50 [0]	5,463.78 ± 28,617.45 [0]	4,557.24 ± 32,832.24 [0]
Therapeutic services[e]	3,973.31 ± 16,395.43 [0]	4,054.24 ± 13,872.62 [0]	3,886.58 ± 18,725.19 [0]
Medical supplies	770.11 ± 1,998.00 [0]	832.84 ± 2,136.24 [0]	702.88 ± 1,835.95 [0]
Durable medical equipment	1,948.83 ± 11,047.98 [0]	2,623.53 ± 12,130.40 [0]	1,225.74 ± 9,703.57 [0]
Other/missing	1,578.36 ± 12,212.14 [0]	1,581.49 ± 11,105.48 [92]	1,575.01 ± 13,296.31 [0]
Pharmacy costs	3,427.67 ± 6,761.45 [223]	3,432.70 ± 6,769.67 [216]	3,422.29 ± 6,752.62 [230]

[a]Among patients with multiple types of visits on the same day, inpatient stays were prioritized over all other types of visits, followed by ED visits, OP visits, long-term care/skilled nursing facilities, other places of service, and unknown place of service; [b]All costs were truncated at the 95th percentile. For patients with no utilization of medical or pharmaceutical services, costs were set to zero dollars; [c]Medical claims with non-zero costs for long-term care/skilled nursing facilities fell above the 95th percentile of costs among patients with RTT; [d]Unknown places of service included medical claims that described the place of service as "other" or "unassigned." Procedure codes associated with each medical claim were used to define the type of visit; [e]Therapeutic services visits included physical therapy, hydrotherapy, occupational therapy, speech therapy, and feeding assistance; [f]RTT-related medical costs were defined as all costs for a medical service claim with a diagnosis of RTT in the primary or secondary position. RTT was identified using the following *ICD-10-CM* diagnosis code: F84.2. RTT-related pharmacy costs were defined as all costs for a pharmacy claim for an RTT-related therapy (ie, antiepileptics, nutritional agents, sedatives, prokinetic agents, and antiarrhythmics)

ED, emergency department; *ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification*; OP, outpatient; PPPY, per-person-per-year; RTT, Rett syndrome; SD, standard deviation; USD, United States dollar

STUDY LIMITATIONS

- The IQVIA™ Medical Claims Data (Dx) comprises pre-adjudicated claims for which payment amounts have not yet been finalized and are often inflated compared with their adjudicated equivalent. Therefore, healthcare costs may be overestimated
- Miscoding of diagnoses or procedures in administrative claims data may result in misclassification of patients and endpoints of interest
- Study findings may not be generalizable to individuals who have no insurance

CONCLUSIONS

- Patients with RTT incur substantial HRU, with nearly 1 medical visit per week and nearly half of all visits attributed to RTT annually
- The corresponding cost burden is also substantial, with nearly half of all-cause healthcare costs associated with a diagnosis of RTT
- Both the HRU and cost burden are especially high among pediatric patients relative to adult patients
- These findings underscore the need for effective therapies to treat RTT, with the potential to reduce considerable economic burden and facilitate long-term clinical benefits

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ACKNOWLEDGMENTS

This analysis was sponsored by Acadia Pharmaceuticals Inc. Editorial support was provided by Evidence Scientific Solutions, Inc and funded by Acadia Pharmaceuticals Inc.

DISCLOSURES

DM is an employee of Acadia Pharmaceuticals Inc. **KK-S**, **MM**, **ND**, **KS**, **PL**, and **WYC** are employees of Analysis Group, Inc., a consultancy that received funding from Acadia Pharmaceuticals Inc. to conduct this study.

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