

# Gastrointestinal manifestations in pediatric and adult patients with Rett syndrome – an analysis of US claims data

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## INTRODUCTION & OBJECTIVE

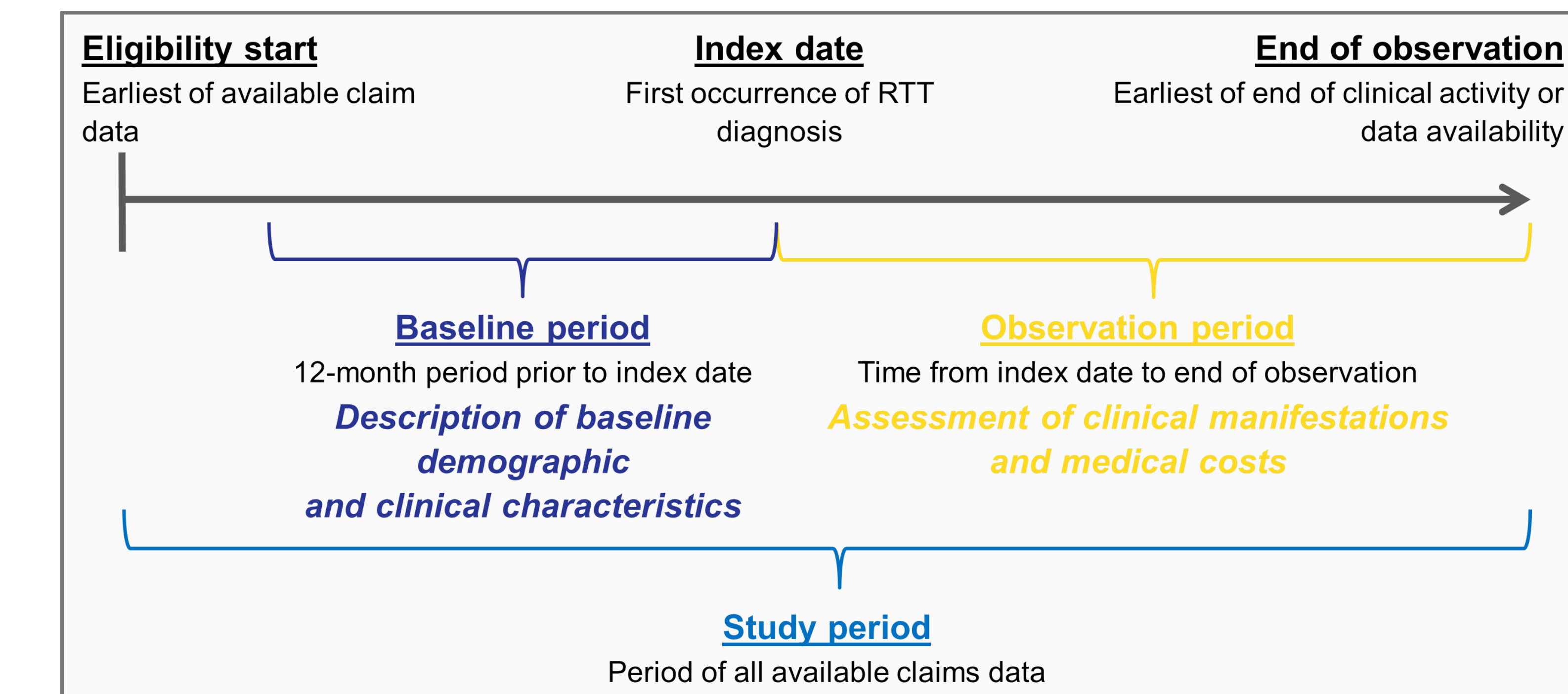
- Rett syndrome (RTT) is a rare and severe neurodevelopmental disorder that almost exclusively affects girls.<sup>1</sup> The estimated incidence of RTT is 1 per every 10,000–15,000 live female births worldwide.<sup>1</sup> Patients with RTT develop debilitating symptoms that evolve throughout the patient's lifespan, rendering them severely disabled.<sup>1,2</sup>
- Gastrointestinal (GI) symptoms related to reduced GI motility and autonomic dysfunction are common in patients with RTT and add to patient burden and caregiver concerns.<sup>3,4</sup>
- The aim of the present study was to describe the prevalence of GI manifestations of RTT and the associated medical costs in pediatric and adult RTT patients.

## METHODS

### Study Design

- The study combined an insurance claims database analysis and a physician survey.
- Administrative claims data from IQVIA™ Medical Claims Data and Longitudinal Prescription Data from 11/1/2016–10/31/2019 were used to identify the demographic and clinical characteristics of girls and women diagnosed with RTT, the frequency of common GI manifestations, and the associated management costs per patient per year (PPPY) inflation-adjusted to 2021 USD.
  - The date of the first observed diagnosis was defined as the index date. Baseline demographics were collected on index date and clinical characteristics were collected during the 12-month baseline period (Figure 1). The observation period spanned the time from the index date until the end of clinical activity or the end of data availability (whichever occurred first). Clinical outcomes and costs of interest were assessed during the observation period (Figure 1).
- The claims data analysis was supplemented with information on prevalence of GI manifestations and treatment goals obtained from a cross-sectional, web-based survey of 100 US physicians (pediatricians and pediatric neurologists) experienced in RTT management. The survey was designed to capture a broad range of data on RTT burden and management, including that pertaining to GI manifestations. Only data related to GI manifestations are presented here.
- All analyses were descriptive and no statistical comparisons between adult and pediatric groups were performed.

Figure 1. Design of the IQVIA databases study



### Eligibility criteria

- For the claims data analysis, female patients with ≥1 medical claim with a primary or secondary diagnosis code for RTT (ICD-10-CM: F84.2) were included. Patients aged ≥1 year were required to have ≥12 months of continuous enrollment prior to the index date. Patients with ≥1 medical claim for cerebrovascular disease (ICD-10-CM: I60–I69) or brain trauma (ICD-10-CM: S06) were excluded.
- The clinician survey enrolled neurologists or pediatricians practicing in the US, who had treated ≥2 patients with RTT (male or female) at any time, including ≥1 patient in the past 2 years. Physicians who had seen an unexpectedly high number (≥2 patients or ≥20% of RTT cases) of male RTT patients were excluded. The participant sample was derived from a large panel of registered physicians practicing in a wide range of geographic locations in the US.

## RESULTS

### Participant characteristics

- Data on 5,940 female RTT patients including 3,078 pediatric patients and 2,862 adult patients were analyzed.
- Median age at index date was 17.0 years (interquartile range [IQR]: 9–28 years). All four mainland US regions were well represented. Medicaid (27.3%) was the most common pre-specified insurance plan type (Table 1).
- The frequency of MECP2 genetic testing prior to RTT diagnosis was low (1.2%) (Table 1).

Table 1. Baseline demographics and clinical characteristics of RTT patients

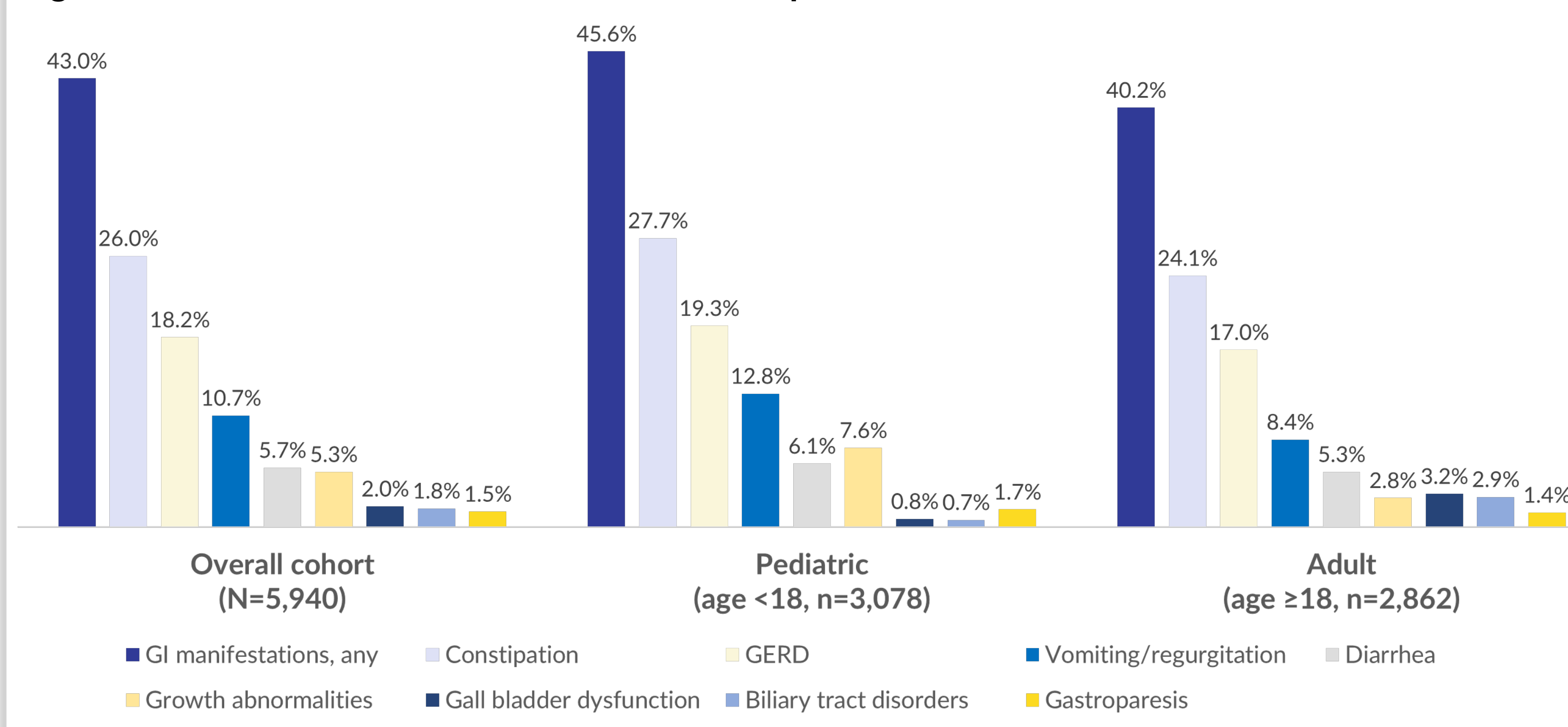
Characteristics	Overall cohort (N=5,940)	Pediatric (age <18, n=3,078)	Adult (age ≥18, n=2,862)
Age at index date, years, median (IQR)	17.0 (9–28)	9.0 (5–13)	29.0 (22–37)
Region, n (%)			
South	2,051 (34.5)	1,155 (37.5)	896 (31.3)
West	1,373 (23.1)	716 (23.3)	657 (23.0)
Midwest	1,328 (22.4)	648 (21.1)	680 (23.8)
Northeast	1,151 (19.4)	538 (17.5)	613 (21.4)
Other <sup>a</sup>	4 (0.1)	2 (0.1)	2 (0.1)
Unknown/unspecified	33 (0.6)	19 (0.6)	14 (0.5)
Insurance plan type, n (%)			
Medicaid	1,621 (27.3)	858 (27.9)	763 (26.7)
Commercial	1,101 (18.5)	675 (21.9)	426 (14.9)
Medicare/Medicaid Dual Eligible	895 (15.1)	528 (17.2)	367 (12.8)
Medicare	665 (11.2)	19 (0.6)	646 (22.6)
Unknown/unspecified plan <sup>b</sup>	1,658 (27.9)	998 (32.4)	660 (23.1)
Quan-CCI <sup>c</sup> , mean ± SD [median]	0.1 ± 0.4 [0.0]	0.1 ± 0.3 [0.0]	0.1 ± 0.5 [0.0]
MECP2 genetic testing <sup>d</sup> , n (%)	69 (1.2)	61 (2.0)	8 (0.3)

a: Includes Puerto Rico, Virgin Islands, and Guam; b: Includes medical claims associated with an unspecified plan, unknown third party, cash, claims processing, or missing; c: Evaluated during the baseline period, including the index date; d: Identified using CPT codes: 81302–81304, 0234U, 81470, 81471, 81479. Abbreviations: CPT, Current Procedural Terminology; IQR, interquartile range; Quan-CCI, Quan-Charlson comorbidity index; SD, standard deviation

### Prevalence of GI manifestations of RTT

- GI manifestations affected 43.0% of all patients with a slightly higher prevalence in pediatric patients relative to adult patients (45.6% and 40.2%, respectively).
- The most common GI manifestations in the overall cohort of patients were constipation (26.0%), gastro-esophageal reflux disease (GERD, 18.2%), vomiting/regurgitation (10.7%), and diarrhea (5.7%) (Figure 2).
- All GI manifestations except for gall bladder dysfunction and biliary tract disorders were slightly more prevalent in pediatric RTT patients relative to adult RTT patients (Figure 2).

Figure 2. Prevalence of GI manifestations in RTT patients



Abbreviations: GERD, gastro-esophageal reflux disease

### Medical costs associated with management of GI manifestations of RTT

- The mean medical cost of managing GI manifestations was \$4,473 PPPY and numerically higher in pediatric patients relative to adult patients (\$5,530 and \$3,341 PPPY, respectively) (Table 2).

## RESULTS (Cont.)

- GERD was associated with the highest mean medical cost (\$2,630 PPPY) followed by constipation (\$923 PPPY).
- Mean medical costs were lower in adult patients than pediatric patients for all GI manifestations except for gall bladder dysfunction or biliary tract disorders (consistent with their lower prevalence in pediatric patients) and diarrhea (Table 2).

Table 2. Medical costs of managing GI manifestations of RTT (presented as mean cost PPPY ± SD)

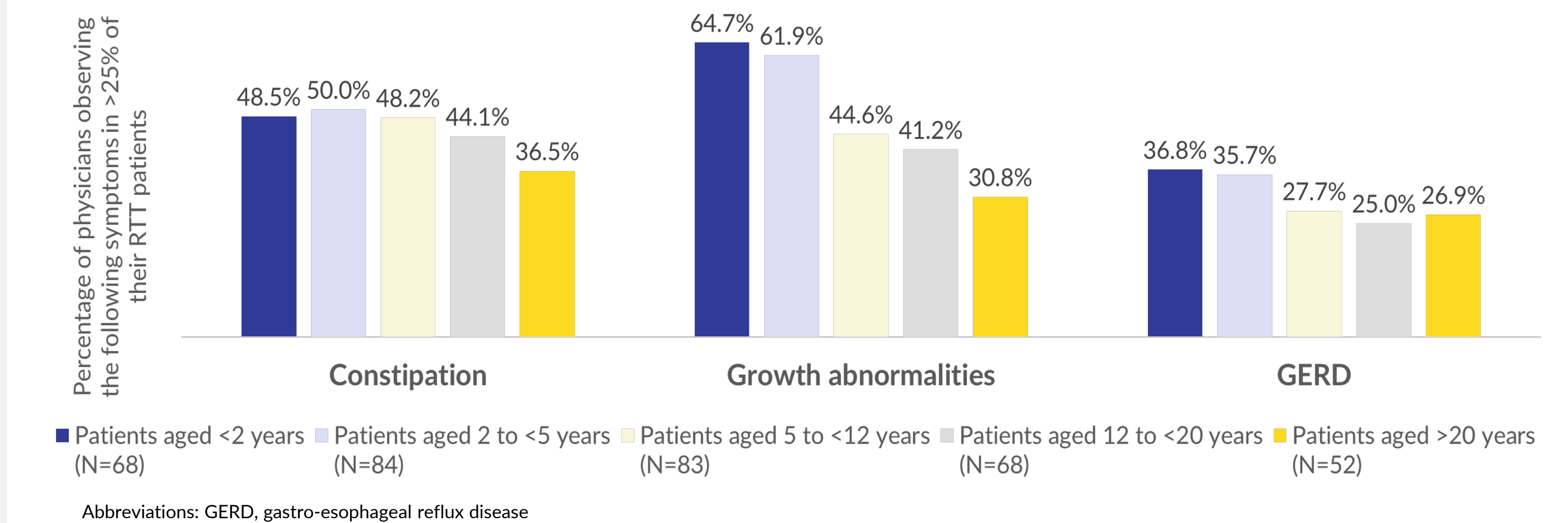
GI manifestation	Overall cohort (N=5,940)	Pediatric (age <18, n=3,078)	Adult (age ≥18, n=2,862)
GI manifestations, any	\$4,473 ± 27,286	\$5,530 ± 34,315	\$3,341 ± 16,679
Constipation	\$923 ± 7,552	\$1,010 ± 7,605	\$830 ± 7,495
GERD	\$2,630 ± 23,424	\$3,468 ± 30,202	\$1,732 ± 12,560
Vomiting/regurgitation	\$268 ± 3,993	\$342 ± 5,212	\$189 ± 1,977
Diarrhea	\$89 ± 1,614	\$70 ± 1,458	\$110 ± 1,765
Growth abnormalities	\$252 ± 3,014	\$368 ± 3,605	\$128 ± 2,206
Gall bladder dysfunction	\$158 ± 2,620	\$77 ± 1,774	\$245 ± 3,290
Biliary tract disorders	\$150 ± 2,582	\$76 ± 1,770	\$228 ± 3,232
Gastroparesis	\$415 ± 10,379	\$492 ± 12,970	\$332 ± 6,550

Abbreviations: GERD, gastro-esophageal reflux disease, GI, gastrointestinal, PPPY, per patient per year, SD, standard deviation.

### Prevalence of GI manifestations and treatment goals reported in the physician survey

- The survey respondents were predominantly pediatricians (47.0%), neurologists (31.0%), and pediatric neurologists (25.0%). None of the respondents were GI specialists. The mean number of RTT patients treated by survey respondents in the past 2 years was 6.7 (SD: 11.7, median: 3.0).
- Physician-reported prevalence of GI manifestations was generally higher in pediatric than adult RTT patients (Figure 3).
- Management of GI manifestations was ranked among the 5 most important treatment goals by 7 (7.0%) of respondents when considered from the physician perspective and by 15 (15%) respondents when considered from the patient and caregiver perspective.

Figure 3. Proportion of surveyed physicians observing selected GI manifestations in >25% of their patients (among physicians experienced in treating a given age group)



## CONCLUSIONS

- Gastrointestinal issues are a well-known, common manifestation of RTT. Insurance claims data and physician perspectives suggest that both pediatric and adult RTT patients experience a high burden of GI manifestations, which are also associated with substantial healthcare costs.
- Proactively addressing GI manifestations is achievable as a component of existing standard of care for RTT patients. However, despite the considerable clinical and financial burden of GI manifestations in RTT, management of GI symptoms remains under-represented as an RTT treatment goal among treating physicians.
- One notable limitation of the current study is that the prevalence of GI manifestations was likely underestimated, due to the reliance on coding of physician encounters with a GI symptom specifically, and the inability to capture over the counter medications.

## REFERENCES

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