# **Economic Burden of Care and Treatment Options** for Patients With Rett Syndrome: Two Systematic Literature Reviews

POSTER 96

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### OBJECTIVE

### To identify clinical trials in Rett syndrome and assess the economic burden of care for patients with this condition

### INTRODUCTION

• Rett syndrome is a rare, non-inherited, genetic, post-natal, neurological disorder that occurs almost exclusively in girls and leads to e impairments in a child's development.<sup>1</sup> It is characterized by apparently normal development for the first 6 to 18 months of llowed by the loss of acquired fine and gross motor skills and the ability to engage in social interaction, and the development life follow of stereotypic hand move

Rett syndrome affects approximately 1 in 9,000 girls under 12 years of age<sup>3</sup> and almost all cases of Rett syndrome are caused by a mutation in MeCP2, found on the X chromosome<sup>4</sup>

Limited treatment options target symptoms and not the genetic cause of the disease, leaving a significant unmet need<sup>6</sup>

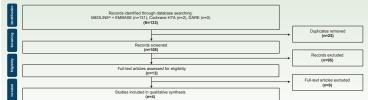
### METHODS

### Two systematic literature reviews related to Rett syndrome were performed on 25 June 2018

eXis, Inc., Bann

### 1) ECONOMIC BURDEN

Outcomes of interest were costs (direct and indirect medical costs), medical resource use (hospital admissions, length of stay, physician and specialist visit, medications) and non-medical resource use (lost productivity and homecare or caregiver's time)



## 2) TREATMENT OPTIONS

Outcomes of interest were studies assessing the efficacy and safety of treatments for Rett syndrome



### RESULTS

### ECONOMIC BURDEN

Four studies were included in the qualitative synthesis out of 133 articles identified through database searching The 4 includes where included in the quantative synthesis out or 100 and/es deriving undogs reactive section mg The 4 included studies were conducted in the US, UK, Canada, China, Australia, Switzerland, Ireland, and Italy and provided data on resource use and costs of Rett syndrome

STUDY DESIGN AND POPULATION CHARACTERISTICS										
Study	Country	Population Overview	Study Design	Intervention(s)	Follow-up (Years)	Sample Size	Mean Age (Years)			
Urion et al. (2016) <sup>6</sup>	US	Rett syndrome	Retrospective cohort	Care integration	1	-	-			
Hammett et al. (2014) <sup>7</sup>	υκ	Rett syndrome	Retrospective cohort	Surgical correction of scoliosis	2	11	12.6			
MacKay et al. (2018) <sup>8</sup>	US, UK, Canada, Australia, China, Ireland, Switzerland	Rett syndrome	Cross- sectional	-	-	399	-			
Labianca et al. (2013) <sup>9</sup>	Italy	Patients with Rett syndrome and neuromuscular scoliosis	Prospective cohort	Surgery (posterior spinal fusion and Luque or hybrid instrumentation)	Mean: 12.9 (2–24)	21	12.4			

### DIRECT MEDICAL RESOURCE USE RESULTS - LENGTH OF STAY

Likainac et al. 2013<sup>6</sup>, reported a mean length of stay of 12.3 days (range: 2–61) for patients with Rett syndrome and neuromuscular scoliosis treated by surgery According to Hammett et al., 2014<sup>7</sup> – A mean length of inpatient stay of 18.2 days (range: 8–42) was seen for 11 patients with Rett syndrome who underwent a surgical correction of socilosis (posterior instrumented fusion of the curves) – Complications had considerable implications on the length of hospital stay, patients without complications were discharged on aurone 0<sup>7</sup> of due necheoreticity is whose these with exercision and engineed as inscribed for an exercise of 2.4.8 days

average 8.7 days postoperatively, whereas those with complications remained as inpatients for an average of 21.8 days • MacKay et al., 2018<sup>a</sup>, studied patients with confirmed *MeCP2* mutation and reported the shortest mean cumulative length of respiratory-related hospital stay was for patients younger than 7 years old and the greatest rate was in those 20 years or older over the 5-year exposure period

## DIRECT COSTS - IMPACT OF CARE INTEGRATION

 Urion et al., 2016<sup>6</sup>, reported a decrease in inpatient charges from 48% total spend to 41% over the first year of care integration, suggesting that this intervention reduces costs in a population with Rett syndrome

DIRECT MEDICAL RESOURCE USE – HOSPITAL ADMISSION • Two studies (Urion et al. 2016<sup>th</sup> and MacKay et al. 2018<sup>th</sup>) reported hospital admissions for patients with Rett syndrome

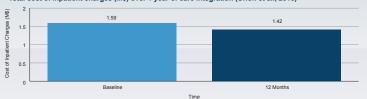
## Hospital admissions

Urion et al. (2016)6	MacKay et al. (2018) <sup>8</sup>
Unanticipated hospital admissions decreased an average of 2.06 per person/year to 1.32 per person/year over the first year of care integration	<ul> <li>Hospital admission over a 5-year exposure period due to LRTI was reported for slightly more than one-fifth (21.4%) of individuals, with a total of 230 admissions</li> <li>Mean rate of hospital admissions for LRTI was 0.12 (95% CI: 0.11–0.13) per person/year over 5 years</li> <li>Enteral feeding increased the risk of hospital admissions for LRTI (adjusted relative risk<sup>a</sup> 1.79, 95% CI: 1.21–2.65)</li> <li>Compared with independent walking, being unable to walk was associated with a 6-fold increased risk of respiratory-related hospital admissions (adjusted relative risk<sup>a</sup> 6.73, 95% CI: 3.42–13.25)</li> </ul>
*Adjusted for age group and r	nutation type. <sup>b</sup> Adjusted for age group and impacts of breath holding and hyperventilation.
Mean cumulative lengt (MacKay et al., 2018) <sup>8</sup>	h of stay (days per person/year) over the 5-year exposure period according to age

1.5 Length of Stay ber Person/Year) 1.09 0.59 0.41 Mean (Days r 0.5 <7 Years 7-12 Years 13-19 Years >20 Years

Age

### Total cost of inpatient charges (M\$) over 1 year of care integration (Urion et al., 2016)6



### TREATMENT OPTIONS

A total of 652 articles were identified, out of which 28 publications (20 studies) were included in the qualitative synthesis

A total of 652 articles were identified, out of which 25 publications (20 studies) were including the dualitative synt.
 Out of 20 studies including from 8 to 82 identified patients, 19 focused on pharmacological treatments of Rett syndrome symptoms and 1 study examined the effects of environmental enrichment.
 Overall, 5 (26%) were single-arm studies, <sup>10-14</sup> 15 (74%) were randomized controlled trials,<sup>15-29</sup> and 18 studies reported follow-up duration of 1 to 26 months.

## STATISTICALLY SIGNIFICANT RESULTS FROM CLINICAL STUDIES

Outcome Measure	Author, year	Intervention	Results (P-value)
RSBQ	Percy, et al. (2017)18	TFT 200 mg/kg vs PLC	Clinical benefit was observed for patients treated by TFT (0.042 <sup><math>T</math></sup> )
CGI	Percy, et al. (2017)18	TFT 200 mg/kg vs PLC	Clinical benefit was observed for patients treated by TFT $(0.029^{T})$
VAS	Percy, et al. (2017)18	TFT 200 mg/kg vs PLC	Clinical benefit was observed for patients treated by TFT (0.025 <sup>T</sup> )
VAS	O'Leary, et al. (2018)22	PLC-MCS vs MCS-PLC	Worsening of symptoms for patients treated by PLC-MCS (0.0211 <sup>T</sup> ; 0.0111 <sup>W</sup> )
ADAMS	O'Leary, et al. (2018) <sup>22</sup>	PLC-MCS vs MCS-PLC	Worsening of symptoms for patients treated by PLC-MCS (0.5535 <sup>T</sup> ; 0.0272 <sup>W</sup> )
	O'Leary, et al. (2018) <sup>22</sup>	PLC-MCS vs MCS-PLC	Worsening of symptoms for patients treated by PLC-MCS (0.0208 <sup>T</sup> ; 0.0110 <sup>W</sup> )
EEG	Gorbachevskaya, et al. (2001) <sup>10</sup>	CL vs UT	Clinical benefit was observed for patients treated wit CL: lower value of LRP in alpha and beta bands (<0.00 <0.01 <sup>+</sup> ), higher levels of LRP in the theta band (<0.001
	Gorbachevskaya, et al. (2001) <sup>10</sup>	Before CL vs after CL	Improvement of the brain functional stage after treatment with CL: decrease of theta LRP in centra and frontal regions ( $<0.05^{+}$ , $<0.01^{+}$ ), increase of bet activity LRP in the parietal region ( $<0.05^{-}$ ), restoration of occipital alpha rhythm ( $<0.05^{+}$ )
ECG	Guideri, et al. (2005)25	ALC at BS vs ALC after 6 mo	Clinical benefit was observed in patients treated with ALC: increase of total power (0.01 <sup>T</sup> ), VLF (0.01 <sup>T</sup> ), and LF (0.009 <sup>T</sup> )
ECG	Guideri, et al. (2005) <sup>25</sup>	UT at BS vs UT after 6 mo	<b>Decrease in heart rate variability</b> was observed in UT: decrease of total power $(0.04^{T})$ and LF $(0.05^{T})$ , and increase of QTcD $(0.01^{T})$
	Percy, et al. (1994) <sup>19</sup>	NLT vs PLC	Positive effect of NLT was observed: higher awa min. $\Omega_2$ saturation value (0.03 <sup>+</sup> ), less % time spent with disorganized breathing (0.02 <sup>+</sup> ), higher end tida carbon dioxide value (0.02 <sup>+</sup> )
Respiratory function	Djukic, et al. (2016) <sup>12</sup>	Before glatiramer acetate 20 mg vs after	Improvement of respiratory function: decrease of breath hold index (0.004 $^{\rm T}\!\!;0.03^{\rm W})$ and breath hold time (0.007 $^{\rm T}\!\!;0.004^{\rm W})$
	Khwaja, et al. (2014)13	Pre MAD MCS vs post OLE	Improvement of respiratory function: improvement of apnea $(0.012^{T})$
CSS	Maffei, et al. (2014)26	ω-3 PUFAs at BS vs ω-3 PUFAs after 6 mo	Significant improvements were observed: decreas in score for CSS (<0.005 <sup>A</sup> ), ambulation (0.02 <sup>A</sup> ), hand use (0.002 <sup>A</sup> ), motor (0.009 <sup>A</sup> ), non-verbal communicati (0.002 <sup>A</sup> ), and respiratory dysfunction (<0.0001 <sup>A</sup> )

## LIMITATIONS OF THE STUDIES

In the economic burden analysis, studies by Urion et al., 2016<sup>9</sup>, and Labianca et al., 2013<sup>9</sup>, were published as conference abstracts. Findings should be interpreted cautiously as detailed information on these studies is lacking
 Almost half of the treatment options studies followed a crossover design and almost half had small sample sizes of 12 participants or fewer. Outcome data are limited, and evidence for PedsQL<sup>TM</sup>, HAS, PEDI-m, and PEG use are lacking

### CONCLUSIONS

- Data on the costs of Rett syndrome management are sparse. Economic burden data were available only for direct medical resource use and direct medical costs;
- data on non-medical and indirect resource use and costs within the last 5 years were not identified
- There is an unmet need for safe and effective treatments for Rett syndrome
- Available treatment options address symptoms but do not improve disease progression
- Treatments that target the underlying cause of disease (e.g., gene-replacement therapy) could improve quality of life and overall prognosis for patients with Rett syndrome
- Further research is needed to better understand the impact of medical interventions for patients with Rett syndrome and their potential to reduce costs and/or increase utility

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