

# US Caregiver Burden in Fragile X Syndrome as a Function of a Health-State Utility Index

Melissa Raspa,<sup>1</sup> Ellen Bishop,<sup>1</sup> Sean D Candrilli,<sup>2</sup> Debanjali Mitra,<sup>2\*</sup> Patricia Sacco,<sup>3</sup> Jennifer Petrillo,<sup>4</sup> Don Bailey<sup>1</sup>  
<sup>1</sup>RTI International, Research Triangle Park, NC, United States; <sup>2</sup>RTI Health Solutions, Research Triangle Park, NC, United States;  
<sup>3</sup>Novartis Pharmaceuticals, East Hanover, NJ, United States; <sup>4</sup>Novartis AG, Basel, Switzerland

\* Ms. Mitra was an employee of RTI Health Solutions at the time that this study was conducted. She is currently an employee of Becton, Dickinson and Company.

## Background

- Fragile X syndrome (FXS), the most common inherited form of intellectual disability, causes moderate to severe intellectual delays in males and milder, yet significant, limitations for females
- The incidence of FXS in the United States (US) is approximately 1:4,000 males and 1:4,000-6,000 females<sup>1</sup>
- Previous research suggests that parenting a child with FXS confers risk in such domains as stress,<sup>2,3</sup> depression and anxiety,<sup>4</sup> quality of life,<sup>5</sup> parenting,<sup>6</sup> and self-concept<sup>7</sup>
- Although research has shown that caregivers of patients with special health care needs experience elevated burden,<sup>8</sup> few data focus specifically on the burden of caregiving for children and adults with FXS
- The Aberrant Behavior Checklist-Community version (ABC-C) is a parent-completed measure of a child's behavior across a number of maladaptive domains.<sup>9</sup> Recently, a utility index, the ABC-UI, was derived from the ABC-C to reflect health-related quality-of-life (HRQOL) changes in patients<sup>10</sup>

## Objective

- To assess the relationship between health care resource utilization by patients with FXS, as well as burden experienced by their caregivers, with the ABC-UI

## Methods

### Study Design

- A retrospective analysis of results from a 2011 survey of US caregivers of children and adults with FXS<sup>11,12</sup>
  - Invitations to participate in this survey were sent to 508 families of children (> 5 years of age) and adults with FXS enrolled in a research registry<sup>12</sup>
- Survey questions collected information on standardized measures of FXS-related behavior, attention, and anxiety problems, as well as resource use parameters

### Study Measures

- Demographic characteristics of individuals with FXS (i.e., age, sex, family income)
- Overall cognitive ability of individuals with FXS (i.e., poor, fair, good/very good)
- Resource use by individuals with FXS (visits to medical specialists and medical tests or procedures performed in the past year, and prescription medications currently used)
- Caregiving requirements (number of hours of care they or other family members provided during a typical day for FXS-related needs; number of hours of paid caregiving provided)
- Economic and employment impact (extent to which FXS caused a financial burden or family member to quit working)
- Caregiver injuries (injuries caused by individual with FXS) in the past year
- Caregiver mental health (whether caregiver had been treated by a professional for depression, stress, or anxiety in the past year)
- The ABC-UI (7 items with 3 response options each, reporting utilities from 0 = dead to 1 = full health); five utility score categories were created to group into HRQOL ranges: very low (0.00–0.33), low (0.34–0.66), moderate (0.67–0.77), high (0.78–0.89), and very high (0.90–1.00)

### Analytic Approach

- Descriptive analyses summarized characteristics of the study population
- Multivariable logistic regression models formally assessed the association between ABC-UI score and 9 FXS burden-related outcomes controlling for sex, age, overall cognitive ability level, and family income:
  - The likelihood of  $\geq 5$  (versus < 5) specialist visits in the past year
  - The likelihood of 0 (versus  $\geq 1$ ) medical tests or procedures in the past year
  - The likelihood of  $\geq 2$  (versus < 2) prescription medications currently used
  - The likelihood of  $\geq 8$  (versus < 8) hours, on average, of daily unpaid caregiving
  - The likelihood of use of any (versus no) daily paid caregiving
  - The likelihood of  $\geq 1$  (versus 0) caregiver injuries related to FXS-related caregiving in the past year
  - The likelihood of  $\geq 1$  (versus 0) caregiver mental health provider visits related to FXS-related caregiving in the past year
  - The likelihood of high (versus low) financial burden
  - The likelihood that a family member did (versus did not) ever quit working due to FXS-related caregiving
- Separate models were estimated for each outcome which included continuous ABC-UI score as the main independent variable of interest
- Additional models were estimated replacing the continuous utility index score with the 5 ABC-UI score categories that were developed
- The study was approved by the RTI International Institutional Review Board

## Results

### Respondent Characteristics

- 350 caregivers agreed to participate in the survey, and 340 provided complete information necessary to calculate the ABC-UI score
- Further details on respondent characteristics have been published<sup>11</sup>

### Patient Characteristics (Table 1)

- Individuals with FXS were approximately 19 years of age, 83% were male, > 90% were white, and > 50% were classified as having "fair" cognitive ability
- The mean (standard deviation [SD]) ABC-UI score was 0.7 (0.2), and ~2% of individuals with FXS were in the very low ABC-UI score category, 31% low, 27% moderate, 38% high, and 3% very high

### Burden of Illness (Table 2)

- In the past year:
  - The mean (SD) number of specialist visits for an individual with FXS was 5.3 (5.1), and 43.6% had  $\geq 5$  visits
  - The mean (SD) number of medical tests or procedures performed on an individual with FXS was 1.1 (1.3), and 54.7% had  $\geq 1$  medical test or procedure performed
  - 29.1% of caregivers reported being injured while providing care, and 35.6% reported seeking mental health-related care
- The mean (SD) number of prescription medications currently being used by an individual with FXS was 1.5 (1.5), and 41.4% used  $\geq 2$  prescription medications
- On average:
  - The mean (SD) number of hours of unpaid FXS caregiving was 8.4 (6.6), and 32.2% reported  $\geq 8$  hours of unpaid caregiving
  - The mean (SD) number of hours of paid FXS caregiving was 5.1 (4.8), and 29.4% reported use of any paid caregiving
- 57.1% of caregivers reported that FXS caregiving imposed a high financial burden on their family, and 37.7% reported that a family member quit working to provide FXS-related care

### Multivariable Regression Model Results: Continuous ABC-UI Score

- Caregivers whose children had higher ABC-UI scores were less likely to experience high financial burden ( $\beta = -2.972$ ;  $P = 0.0020$ )
- Individuals with lower ABC-UI scores had more visits to specialists ( $\beta = -4.583$ ;  $P < 0.0001$ ) and used more prescription medications ( $\beta = -4.517$ ;  $P < 0.0001$ )
- Caregivers of individuals with lower ABC-UI scores experienced greater burden, including more hours of unpaid FXS caregiving ( $\beta = -2.723$ ;  $P = 0.0030$ ), more frequent caregiver injuries ( $\beta = -7.540$ ;  $P < 0.0001$ ), and more caregiver visits to mental health providers ( $\beta = -2.613$ ;  $P = 0.0020$ )

### Multivariable Regression Model Results: ABC-UI Score Categories

- Due to small sample sizes, only four models were estimated with ABC-UI score categories:
  - Likelihood of  $\geq 5$  (versus < 5) specialist visits in the past year
  - Likelihood of 0 (versus  $\geq 1$ ) medical tests or procedures in the past year
  - Likelihood of high (versus low) financial burden
  - Likelihood that a family member did (versus did not) quit working as a result of FXS-related caregiving
- Results indicated that compared with those in the very high ABC-UI score group, those in the low ABC-UI score group were significantly more likely to have had  $\geq 5$  (versus < 5) specialist visits in the past year (odds ratio = 10.2;  $P = 0.0340$ ) and have high (versus low) financial burden related to FXS caregiving (odds ratio = 9.5;  $P = 0.0146$ )

Table 1. Patient Characteristics, Overall and by ABC-UI Score Category

Patient Characteristic	ABC-UI Score											
	All Children (N = 340)		Very Low (n = 7)		Low (n = 104)		Moderate (n = 92)		High (n = 128)		Very High (n = 9)	
	n	%	n	%	n	%	n	%	n	%	n	%
<b>Total</b>	340	100.0	7	2.1	104	30.6	92	27.1	128	37.6	9	2.6
<b>Sex</b>												
Male	283	83.2	6	85.7	98	94.2	77	83.7	98	76.6	4	44.4
Female	57	16.8	1	14.3	6	5.8	15	16.3	30	23.4	5	55.6
<b>Age, years</b>												
5-12	116	34.1	4	57.1	41	39.4	39	42.4	32	25.0	0	0.0
13-17	77	22.6	2	28.6	27	26.0	18	19.6	28	21.9	2	22.2
$\geq 18$	147	43.2	1	14.3	36	34.6	35	38.0	68	53.1	7	77.8
Mean (SD)	18.7 (10.8)		14.0 (0.3)		17.3 (11.4)		17.4 (10.0)		20.5 (10.5)		26.4 (12.2)	
<b>White</b>	306	90.0	6	2.0	92	30.0	82	26.8	118	38.6	8	2.6
<b>Mean (SD) utility index score</b>	0.7 (0.2)		0.3 (0.0)		0.5 (0.1)		0.7 (0.0)		0.9 (0.1)		0.9 (0.0)	
<b>Cognitive ability</b>												
Poor	82	24.5	5	71.4	34	33.3	26	28.9	16	12.6	1	11.1
Fair	173	51.6	1	14.3	55	53.9	45	50.0	69	54.3	3	33.3
Good/very good	80	23.9	1	14.3	13	12.8	19	21.1	42	33.1	5	55.6
<b>Income</b>												
< \$50,000	81	25.2	5	71.4	25	25.0	25	28.4	25	21.0	1	12.5
\$50,000-\$100,000	121	37.6	2	28.6	31	31.0	37	42.0	46	38.7	5	62.5
> \$100,000	120	37.3	0	0.0	44	44.0	26	29.6	48	40.3	2	25.0

Note: n's within each study measure may vary depending on missing responses

Table 2. Burden of Illness Summary, Overall and by ABC-UI Score Category

Study Measure	ABC-UI Score											
	All Children (N = 340)		Very Low (n = 7)		Low (n = 104)		Moderate (n = 92)		High (n = 128)		Very High (n = 9)	
	n	%	n	%	n	%	n	%	n	%	n	%
<b>Specialist visits in past 12 months</b>	337	100.0	6	1.8	103	30.6	92	27.3	128	38.0	8	2.4
Mean (SD)	5.3 (5.1)		9.3 (6.1)		7.4 (5.6)		4.9 (4.6)		4.0 (4.4)		1.6 (1.8)	
$\geq 5$	147	43.6	4	66.7	68	66.0	37	40.2	37	28.9	1	12.5
<b>Number of prescription medications currently used</b>	338	100.0	7	2.1	103	30.5	91	26.9	128	37.9	9	2.7
Mean (SD)	1.5 (1.5)		2.6 (1.1)		2.6 (1.5)		2.1 (1.1)		1.9 (1.1)		1.0 (0.0)	
$\geq 2$	140	41.4	4	57.1	63	61.2	40	44.0	33	25.8	0	0.0
<b>Medical tests or procedures received in past 12 months</b>	340	100.0	7	2.1	104	30.6	92	27.1	128	37.7	9	2.7
Mean (SD)	1.1 (1.3)		1.4 (1.4)		1.2 (1.5)		1.2 (1.4)		0.8 (0.9)		0.9 (0.9)	
$\geq 1$	186	54.7	5	71.4	60	57.7	51	55.4	64	50.0	6	66.7
<b>Caregiver injured in past 12 months while caregiving</b>												
Yes	99	29.1	5	71.4	61	58.7	25	27.2	8	6.3	0	0.0
No	238	70.0	2	28.6	41	39.7	67	72.8	119	93.4	9	100.0
Missing	3	0.9	0	0	2	0.6	0	0	1	0.3	0	0
<b>Caregiver sought mental health-related treatment as a result of FXS-related caregiving</b>												
Yes	121	35.6	6	85.7	42	40.4	38	41.3	35	27.3	0	0.0
No	216	63.5	1	14.3	61	59.3	53	58.1	92	72.4	9	100.0
Missing	3	0.9	0	0	1	0.3	1	0.3	1	0.3	0	0
<b>Average daily unpaid (family) caregiving hours</b>	335	98.5	6	1.8	102	30.0	91	27.2	127	37.9	9	2.7
Mean (SD)	8.4 (6.6)		11.5 (5.2)		11.3 (7.0)		8.0 (6.1)		6.3 (5.6)		5.0 (1.0)	
$> 8$	108	32.2	4	66.7	49	48.0	28	30.8	27	21.3	0	0.0
<b>Average daily paid caregiving hours</b>	333	97.9	6	1.8	100	30.0	91	27.3	127	38.1	9	2.7
Mean (SD)	5.1 (4.8)		0 (0)		4.1 (3.0)		5.9 (6.1)		5.2 (4.8)		0 (0)	
Any use, regardless of hours	98	29.4	0	0.0	34	34.0	33	36.3	31	24.4	0	0.0
<b>FXS-related caregiving imposes a high (compared with low) financial burden</b>												
High	193	57.1	4	57.1	77	74.8	47	51.1	63	49.6	2	22.2
Low	145	42.3	3	42.9	26	24.9	45	48.9	64	40.1	7	77.8
Missing	2	0.6	0	0.0	1	0.3	0	0.0	1	0.3	0	0.0
<b>Family member quit working to provide FXS-related care</b>												
Yes	121	37.7	4	57.1	42	42.4	32	37.2	40	33.3	3	33.3
No	200	56.7	3	42.9	57	56.1	54	61.0	80	64.3	6	66.7
Missing	19	5.6	0	0	5	1.5	6	1.8	8	2.4	0	0

Note: n's within each study measure may vary depending on missing responses

## Limitations

- Respondents in this survey may not be representative of the entire universe of FXS caregivers in the US, and results may not be generalizable to FXS caregiver populations in countries with different health care systems
- Use of a survey format allows for data to be collected from a large sample but also necessitates a limited amount of response options and follow-up questions that can be included to further describe caregiver burden

## Conclusions

- The ABC-UI appears to function well as an indicator of health-related economic burden and quality of life in individuals with FXS and their caregivers
- Estimates of higher ABC-UI values appear to be associated with more favorable outcomes at the individual patient and caregiver level
- Health care providers, payers, and other key decision makers may find these results useful in the overall assessment of the value of new treatments for patients with FXS

## Disclosure

This study was sponsored by Novartis Pharmaceuticals Corporation

## Contact Information

Patricia Sacco, Novartis Pharmaceuticals Corporation

Telephone: +1.862.778.8668  
E mail: pat.sacco@novartis.com

Presented at: ISPOR 16th Annual European Congress  
November 2-6, 2013  
Dublin, Ireland

## References

- National Fragile X Foundation. Prevalence. Available at: <http://www.fragilex.org/fragile-x-associated-disorders/prevalence/>. Accessed 20 Aug 2013.
- McCarthy A, Cuskelly M, van Kraayenoord CE, Cohen J. Predictors of stress in mothers and fathers of children with fragile X syndrome. *Res Dev Disabil*. 2006;27(6):688-704.
- Seltzer MM, Barker ET, Greenberg JS, Hong J, Coe C, Almeida D. Differential sensitivity to life stress in FMR1 premutation carrier mothers of children with fragile X syndrome. *Health Psychol*. 2012 Sep;31(5):612-22.
- Roberts JE, Bailey DB, Jr., Mankowski J, et al. Mood and anxiety disorders in females with the FMR1 premutation. *Am J Med Genet B Neuropsychiatr Genet*. 2009;150B(1):130-9.
- Wheeler AC, Skinner DG, Bailey DB. Perceived quality of life in mothers of children with fragile X syndrome. *Am J Ment Retard*. 2008;113(3):159-177
- Warren SF, Brady N, Sterling A, Fleming K, Marquis J. Maternal responsivity predicts language development in young children with fragile X syndrome. *Am J Intellect Dev Disabil*. 2010;115(1):54-75.
- McConkie-Rosell A, Heise EM, Spiridigliozzi GA. Influence of genetic risk information on parental role identity in adolescent girls and young women from families with fragile X syndrome. *J Genet Couns*. 2012 Feb;21(1):59-71.
- Kuo DZ, Cohen E, Agrawal R, Berry JG, Casey PH. A national profile of caregiver challenges among more medically complex children with special health care needs. *Arch Pediatr Adolesc Med*. 2011;165(11):1020-6.
- Aman MG, Singh, NB. Aberrant Behavior Checklist—Community, Supplementary manual. East Aurora, NY: Slosson Educational Publications; 1994.
- Kerr C, Breheny K, Lloyd A, Brazier J, Bailey D. Developing a utility index for the Aberrant Behavior Checklist (ABC-C) for Fragile X Syndrome. Manuscript submitted to Qual Life Res.
- Bailey DB, Raspa M, Bishop E, Mitra D, Martin SA, Wheeler A, Sacco P. Health and economic consequences of fragile X syndrome for caregivers. *J Dev Behav Pediatr*. 2012;33:705-12.
- Our Fragile X World. Available at: <http://www.ourfragilexworld.org>. Accessed Sept 27, 2013.