A Literature Review of the Economic Burden of Fragile X Syndrome

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OBJECTIVE

- Published data were evaluated to understand the full economic burden and to identify cost drivers of fragile X syndrome (FXS) to the health care system, society, and families caring for individuals with FXS.

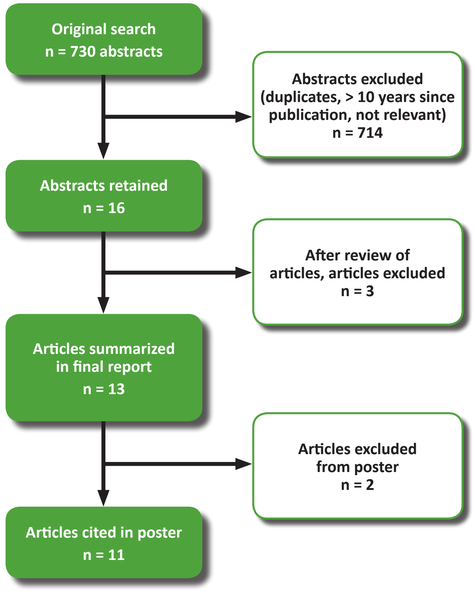
BACKGROUND

- Individuals with FXS experience intellectual disability and reduced functional abilities, including problems with attention, behavior, and anxiety.
- Evidence is beginning to converge on the use of medical specialists, allied health professionals, and prescription medication among individuals with FXS.
- Resource utilization and costs are critical to populate economic models to demonstrate the value of new health technologies for the treatment of FXS.
- Estimates of direct, indirect, and intangible costs by country are needed to evaluate cost-effectiveness and value of new therapies relevant to the local health care system.

DESIGN/METHODS

- PubMed served as the primary database for the electronic literature search.
- Abstracts were reviewed for relevance based on predefined criteria, focusing on the economic burden of FXS, resource utilization (e.g., medical services, medical tests, procedures, therapy, hospitalization), and direct and indirect costs (e.g., productivity, absenteeism, long-term care).
- As shown in Figure 1, the original search yielded 730 abstracts, and reduction of duplicates resulted in 695 abstracts. Limiting the search to 10 years since publication reduced abstract results to 488. After review of abstracts, 16 were retained. After review of articles, 13 were summarized in a full report, and 11 are cited in this poster.

Figure 1. Review and Selection Process for Cited Literature

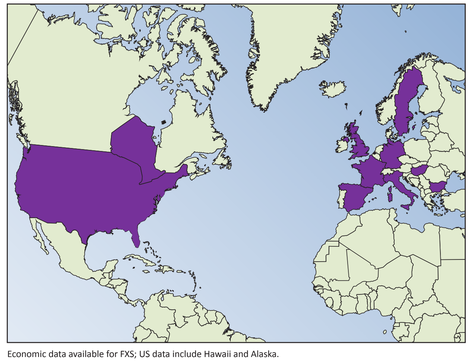


RESULTS

Study Geographies

- Eight articles report data from studies conducted in the United States (US).
  - Medicaid data 1997-2012 from Florida, New Jersey, Missouri, Iowa, Kansas[1]
  - Medicaid data 2000-2010 from South Carolina[2,3]
  - Administrative health care claims data 2004-2009 for commercial/ Medicare and Medicaid patients. These data represented inpatient and outpatient prescription drug claims and cost and utilization data for health care services of more than 33 million persons in the US.[4]
  - Administrative health care claims data 1999-2012 for Optum Health Reporting and Insights Employer database[5]
  - US caregiver survey data 2007.[6-8] Approximately 96% of families reported having insurance coverage.[7]
- Two articles report data from studies conducted in European Union countries (Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden, United Kingdom). Data were collected for 2011 through 2013.[9,10]
- One article reports data from a study conducted in Ontario, Canada.[11]

Figure 2. Study Geographies

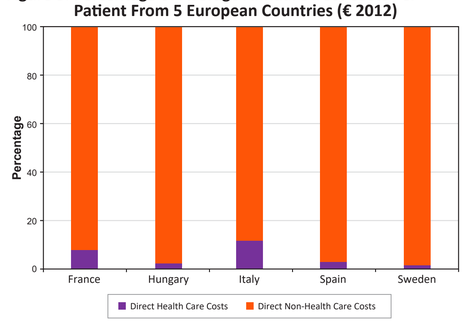


Economic data available for FXS; US data include Hawaii and Alaska.

Economic Burden on the Health Care System

- Patients with FXS incur greater health care costs compared with patients without FXS.
- US administrative claims data found that patients with FXS had median all-cause direct costs ranging from $2,222 to $2,955 (commercial/ Medicare), $4,548 to $9,702 (Medicaid),[4] and annualized total all-cause mean direct costs of $14,677 (privately insured).[5] (Commercial health insurance can be sold individually or as part of a group plan; private health insurance is often offered through employers or other organizations.)
- Direct health care cost drivers in the US across all payer types were outpatient visits, home care and long-term care services, medical procedures, hospitalizations, and medications. Data from three US studies are reported in Table 2.
- In an analysis of privately insured US patients with FXS and their caregivers, employed patients with FXS and employed caregivers of patients with FXS had higher costs associated with short- and long-term disability compared with matched controls.[5]
- In a cross-sectional survey study of 5 European countries, direct health care costs (drugs, medical tests, medical visits, hospitalizations, medical devices, health care transport) were the smaller proportion of total direct costs.[10] See Figure 3.
  - Direct non-health care costs (formal costs include professional caregivers, social services and non-health care transport; informal costs include informal care provided by the patient's relatives) represented the larger proportion of total direct costs, but there were differences in the share incurred by formal and informal care among those costs.[10]
  - The distribution of direct non-health care costs varied by country. The main costs in Italy and Spain were attributable to informal care and may be explained by stronger family ties in Southern European countries.[10]

Figure 3. Percentage of Average Annual Direct Costs Per Patient From 5 European Countries (€ 2012)



Direct health care costs = all goods and services directly linked to the diagnosis and treatment of the disease. Direct non-health care costs = formal costs (professional caregivers, social services and non-health care transport) and informal costs (informal care provided by the patient's relatives).

Economic Burden on the Family

- Many patients with FXS have difficulty with basic functional skills and need specialized therapy, such as speech and language therapy, occupational therapy, and physical therapy.[4] Within FXS, the utilization of these services is high across payer types (Figure 3).
- In a survey of 1,019 families in the US reporting out-of-pocket (OOP) expenditures in 2007, most OOP expenses were for therapy (31%), transportation (31%), medication (19%), supervision (6%), and other medical costs (6%).[7]
- More than 60% of families in the US survey report an employment impact (i.e., quit working, turned down a job, changed work hours) because of FXS.[7]
- Higher percentages of US parents of children with FXS (64%) reported reducing work hours when compared with parents of children with autism spectrum disorder and intellectual disability (48%), parents of children with intellectual disability (36%), or parents of children with autism spectrum disorder only (36%).[8]
- Limits in reasoning or learning ability, irritability, and co-occurring seizures or anxiety were significantly associated with more financial and employment impacts for caregivers.[8]

Table 1. Select Studies Reporting Direct and Indirect Costs of FXS

Article	Data Source Year(s) of Data Collection	FXS Sample (n)	Age (yrs)	Males (%)	Cost Drivers	Key Results on Costs[b]
Bailey et al., 2012[6]	US: Survey of FXS caregivers 2007	350	Mean (male) 20	83.4	• Specialist visits • Medication • Anesthesia for dental care • Medical aids (e.g., orthotics, glasses)	46% of caregivers of males reported OOP costs for prescription medications, with an average monthly cost of $89.44
Ouyang et al., 2010[7]	US: Survey of FXS families	1,019 families	NA	NA	• Therapy • Transportation • Medication	47% of families reported FXS caused an excessive financial burden; 60% of families had to change work or stop work; median annual OOP expenses were $1,900
Nazareth et al., 2016[1]	US: Medicaid (5 states) 1997-2012	697	Median 12	82	• Outpatient visits • Long-term care services • Home services • Inpatient visits	Patients with FXS had incremental annual total health care costs of $33,409 per person vs. a non-FXS comparison group
Sacco et al., 2013[4]	US: Truven MarketScan Commercial/Medicare supplemental, Medicaid 2004-2009	Com/Med: 784 Medicaid: 721	Mean 18	Com/ Med: 71.2 Medicaid: 80.7	• Medical procedures • Hospitalizations • Medications	All FXS: Median annual all-cause direct costs[a] range: $2,222-$2,955 (Com/Med), $4,548-$9702 (Medicaid)
Vekeman et al., 2015[5]	US: Optum, privately insured, 1999-2012	590	Median 26.5	45.9	• Hospitalizations • Outpatient visits • Home care • Outpatient therapy	Annualized health care costs: FXS $14,677 vs. non-FXS $6,103
Chevreul et al., 2015[9]	EU: BURQOL-RD survey (France) 2012-2013	95	Mean 19.4	87	• Hospitalizations • Medical visits • Medications • Devices • Medical Tests	Mean Annual total direct cost of FXS: €25,800 per patient
Chevreul et al., 2016[10]	EU: BURQOL-RD survey (France, Hungary, Italy, Spain, Sweden) 2011-2013	241	Mean 18.1	88	• Hospitalizations • Medical visits • Medications	Mean annual total direct cost range €4,951 per person (Hungary) to €58,862 per person (Sweden) Mean annual direct health care costs range €110 per person (Hungary) to €2,675 per person (France)

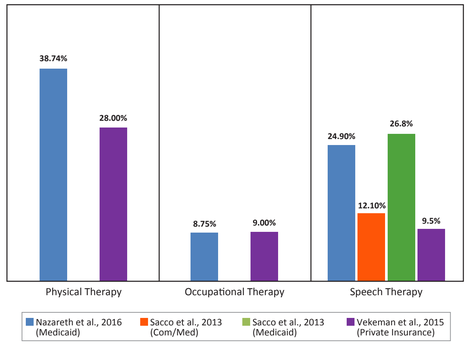
BURQOL-RD = Social Economic Burden and Health-Related Quality of Life In Patients With Rare Diseases in Europe; Com/Med = Commercial/Medicare; NA = Not available; OOP = out-of-pocket.
[a]All-cause health care utilization during the 1-year post-index date included costs resulting from emergency department visits, hospitalizations, outpatient visits, and medical procedures.
[b]The inclusion of individuals with disproportionately high costs and differences in sample sizes may explain differences in estimates of per-patient per-year costs.

Table 2. Annual All-Cause Direct Health Care Cost Drivers From 3 US Studies[a]

Costs Per Patient ($)	Vekeman FXS[b] Mean (2012 USD)	Vekeman Non-FXS[b] Mean (2012 USD)	Nazareth FXS[c] Mean (2012 USD)	Nazareth Non-FXS[c] Mean (2012 USD)	Sacco FXS[d] Mean NA	Sacco FXS[e] Mean NA
Hospitalization or inpatient	$4,509	$1,659	$2,396	$768	$21,677	$25,847
Outpatient visits	$4,730	$2,346	$13,675	$2,189	$4,643	$12,608
Home care	$1,370	$158	$7,171	$2,196	NA	NA
Pharmacy or medication	$2,331	$1,597	$2,358	$1,672	$665	$1,418

NA = not available.
[a]The inclusion of individuals with disproportionately high costs and differences in sample sizes may explain differences in estimates of per-patient per-year costs.
[b]Optum, privately insured, 1999-2012.
[c]Medicaid (Florida, New Jersey, Missouri, Iowa, Kansas) 1997-2012.
[d]MarketScan Commercial, Medicare Supplemental, 2004-2009.
[e]MarketScan Medicaid 2004-2009.

Figure 4. Percentages of US Patients Who Received Therapy Services



DISCUSSION

- While there is no current treatment for FXS, evidence is beginning to emerge on direct and indirect costs associated with FXS.
- In the US, across payer types, annual direct health care costs are a greater proportion of annual costs associated with FXS, in contrast with European countries, where the annual direct non-health care costs (i.e., informal caregivers) are the larger proportion of annual costs.
- In the US and Europe, the most frequently identified direct cost drivers are hospitalizations, medications, outpatient visits, and home care.
- The economic burden on the family is driven by lost productivity, inadequate medical insurance, and OOP expenditures.
- Longitudinal studies can elucidate health care resource utilization and cost drivers across the life span to provide evidence to health care providers, policy makers, and payers on more cost-effective delivery of care. Contemporary cost estimates for pediatric and adolescent patients will be helpful to understand the value of future targeted treatment soon after diagnosis.

CONCLUSIONS

- This review highlights the considerable economic burden experienced by caregivers and families across geographies caring for an individual with FXS. Beyond direct health care costs, economic burden includes direct non-health care costs, OOP expenses not covered by health care insurance, lost work productivity, and other societal costs.
- The cost of care varies across payer types, geographies, and symptom severity.
- New research is warranted to provide contemporary cost estimates that can be used in economic models and to better characterize symptom-related cost drivers and the impact of economic burden for all stakeholders.

REFERENCES

See handout for references.

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