FRAGILE X SYNDROME
Q-FXS: QUALITY IMPROVEMENT PROJECT TO INCREASE OPPORTUNITIES TO DIAGNOSE FRAGILE X SYNDROME AND OTHER GENETIC ASSOCIATED DEVELOPMENTAL DELAYS

FINAL QUALITY IMPROVEMENT PROJECT REPORT

INTRODUCTION AND OVERVIEW

The overarching goal of the project regarding the early identification, management and treatment of fragile X syndrome (FXS) is to link pediatric clinicians with information, resources and educational opportunities that enhance their ability to make appropriate diagnoses of FXS and young children as well as timely referrals for therapeutic services. This project is funded through a cooperative agreement between the American Academy of Pediatrics (AAP) and the Centers for Disease Control and Prevention’s National Center on Birth Defects and Developmental Disabilities (NCBDDD); grant number 5 U38 OT000167.

The goal for this initiative is to gain a better understanding of challenges encountered by pediatricians when assessing and diagnosing global developmental delay and intellectual disability (GDD/ID) in children. The quality improvement initiative within the overall program activities is focused on increasing awareness of clinical guidance and educational resources to inform the medical home. Additionally, the initiative focused on enhancing clinician and family knowledge about the purpose and processes of genetic evaluation.

BACKGROUND

Fragile X syndrome (FXS) is an identifiable genetic disorder that is one of the more common heritable forms of intellectual disability. FXS and other fragile X-associated disorders are caused by mutations in the Fragile X Mental Retardation 1 gene (FMR1). Both males and females can have FXS; however, females can have milder symptoms.

People who have FXS show a range of intellectual disability and may also experience emotional, behavioral, sensory, and/or social difficulties. Any child with unexplained developmental delay, intellectual disability and/or autism spectrum disorder should receive genetic testing for FXS. The typical age of diagnosis for FXS is around 36 months despite evidence that symptoms are present as early as the first year of life. A delayed diagnosis could potentially reduce access to early intervention, family support programs, and medical treatments or create emotional stress and financial burden for families.

Pediatric clinicians can support early identification and evaluation, which empowers families to make informed decisions about FXS-specific services for their child, as well as family planning. A diagnosis also helps healthcare providers assess comorbidities and associated conditions.

In the American Academy of Pediatrics (AAP) clinical report Health Supervision for Children with Fragile X Syndrome (Pediatrics, 2011) the authors establish guidelines for molecular testing for FXS and discuss the benefits of diagnosis for the family. These guidelines were further reinforced through the publication of Comprehensive Evaluation of the Child With Intellectual Disability or Global Developmental Delays (Pediatrics, 2014). Establishing a diagnosis of FXS also will allow parents and/or caregivers to gain an understanding of the disorder and how it affects the child’s development and behavior. Early identification allows the family to focus on the appropriate management strategies that will maximize their child’s potential.
EXPERT GROUP

An expert group was convened to provide oversight and strategic direction to various quality improvement project components including, but not limited to, the design and implementation of the project and related materials development. Specifically, expert group members were expected to attend monthly conference calls, travel to participate in one in-person meeting, serve as faculty for webinars and other educational efforts throughout the project and coach/mentor project participants. A roster of the expert group is available as Appendix 1.

QUALITY IMPROVEMENT PROJECT METHODS

The Q-FXS: Quality Improvement Project to Increase Opportunities to Diagnose Fragile X Syndrome and other Genetic Associated Developmental Delays, was conducted by the Practice Improvement Network (PIN), part of the Quality Improvement Innovation Networks (QuIIN). The Q-FXS project was intended to improve primary care in the outpatient clinic setting regarding genetic evaluation and testing with young children who have identified global developmental delay and older children who have intellectual disability. In the process continuum that ranges from suspecting developmental delay to diagnosis and treatment, Q-FXS focused on assessing and improving the ordering of genetic tests (when warranted due to current evidence and clinical opinion) and steps toward diagnosis and treatment (see process diagram below).

Long-term, outcomes from this project were expected to address a systematic approach to ensure appropriate referrals and follow up occur, enhanced communication with families, and the development of a coordinated plan of care for children with special healthcare needs such as those who might have fragile X syndrome.

THE MODEL FOR IMPROVEMENT

The quality improvement project utilized a collaborative methodology that included virtual learning sessions (eg, webinars/videoconferences) with three practices over the course of a nine-month period. Each practice identified a quality improvement team that included two to three members. Similar to other quality improvement projects, it was anticipated that the involvement of interdisciplinary teams would support sustainability of project improvements over time.
PROJECT AIMS AND MEASURES

The Q-FXS quality improvement project hinged on the hypothesis that providing pediatricians with education, tools and resources related to genetic testing and follow-up along with support through a quality improvement modified learning collaborative would increase the number of children with GDD/ID who receive genetic testing and improve both the time between when a GDD/ID is suspected and the tests are ordered and the time between when the tests are ordered and completed. Ultimately, these activities were expected to increase the number of patients who are diagnosed with a genetic condition such as fragile X syndrome.

Global Aim: By June 2016, improve the outpatient clinic process regarding genetic evaluation and testing of all children who have an identified global developmental delay so that:

- At least 90% of children age 18 months to 18 years who are identified to have a global developmental delay/intellectual disability, and no clinical diagnosis is documented, will have genetic testing ordered.

- 100% of the ordered tests will include a DNA test for fragile X syndrome.

The project aim and measures were developed by the expert group; they are available as Appendix 2.

DATA COLLECTION

Qualitative interviews (Appendix 3) were conducted at the outset of the project to learn more about each practice’s challenges and barriers related to facilitating genetic testing for children and youth with GDD/ID. Five months of baseline and four monthly data cycles were entered into the AAP Quality Improvement Data Aggregator (QIDA) in order to measure improvement. After patient charts were reviewed by the practice team and if inclusion/exclusion criteria (below) were met, resource utilization (eg, labs ordered, next steps taken) and time sequences (eg, time between identification and testing) for the patient encounter were recorded based on the outcomes described above. A standard chart review tool (Appendix 4) was utilized.

Over a three-month period, practice teams performed plan, do, study, act (PDSA) cycles of improvement where subsequent plans for improvement were based on the small tests of process change previously tried and shown with displays of data (e.g., run charts). Additionally, practices were required to submit three qualitative reports (Appendix 5) regarding their project activities (one per month of the action period). A final qualitative interview was conducted at the close of the project to learn more about each practices’ experiences over the course of the project with regard to the identification and diagnosis of children with GDD/ID.

PATIENT CHART CRITERIA

For the purposes of this project patient chart criteria were developed by the expert group to support practices in their quality improvement efforts related to genetic evaluation and testing with young children. The criteria included the age ranges and diagnostic codes that were considered as a child with an identified global developmental delay.
Patient-specific inclusion criteria for this project were:

- Age(s) 18 months to 18 years
- One of more of the following ICD-9 and ICD-10 codes associated with the following categories of codes (a specific list was provided to the practices as an Excel spreadsheet)

<table>
<thead>
<tr>
<th>ICD-9</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>783</td>
<td>R62</td>
</tr>
<tr>
<td>315</td>
<td>F82, F88, R48.2</td>
</tr>
<tr>
<td>299</td>
<td>F84</td>
</tr>
</tbody>
</table>
- Family history or other clinical indication that would warrant genetic evaluation and testing

Patient-specific exclusions for this project were:

1. Speech delay only
2. Infants and children under 18 months completed months of age or youth over 18 completed years of age
3. Children age(s) 18 months to 18 years old with GDD/ID and a clinical diagnosis is known or strongly suspected

**SUPPORT TO PRACTICES:**

Practices received coaching via AAP staff, expert group members and the project quality improvement advisor/consultant. Practices were able to communicate with the expert group and the other practices via a listserv (qfxs@listserv.aap.org). In addition, and as needed, AAP project staff and the project quality improvement consultant contacted individual practices by email and phone. As topics of interest and areas of challenge arose on the listserv from practices, the Expert Group members distributed ideas, resources and strategies to the practice teams.

The minimum requirement for participating physicians to obtain American Board of Pediatrics Maintenance of Certification Part 4 (ABP MOC Part 4) credit illustrates the activities of the project as well as the support provided to practices.

In order to receive MOC Part 4 points, participants were required to:

- Participate in the project over a 5-month period (March 2016 – July 2016)
- Plan and test three PDSA related to the project aims
- Test and implement change concepts from the projects’ key drivers
- Submit baseline data for five months (100% of eligible charts up to 10 charts per month) of eligible patients using a web-based data collection tool
- Submit 3 months of data during the Action Period (up to 10 charts per month) using a web-based data collection tool
- Review reports provided about their data on a monthly basis; utilize data to guide future improvements
- Participate in four live videoconferences/webinars where data is presented, QI principles are discussed, and education on topics relevant to the project are presented by experts in the field during the project period (these can be local meetings for participating physicians)
- Submit findings and progress through three brief surveys
PROJECT DESIGN

RECRUITMENT

Primary care clinical teams were recruited from the membership of the QuIN as well as through the Expert Group and other AAP email lists. The goal was to obtain a diverse sample of practices, based on practice geographic location, practice setting (urban, rural, and suburban), practice size, insurance population/socioeconomic status, practice type (federally qualified health center, continuity clinic, private practice etc), and patient population served. The recruitment information that was disseminated is included as attachment 6.

In order to gather the amount of data to support that a change is an improvement, practices were advised that the would need to have over 7,500 well child visits annually with patient ages 18 months-18 years per calendar year. Priority for selection to participate in the project was be given to applying practice applicant teams (1) that currently record patients’ family history, (2) that had the ability to order genetic testing at an internal practice or practice affiliated lab, and (3) used an electronic health record.

PROJECT INTERVENTION RESOURCES

Project resources (also called change package resources) for the participants were collated based on the driver diagram that was developed by the expert group. Project intervention resources were prioritized based on their utility to support the change interventions of the participating practices.

Primary drivers were identified to be:

1. All children with identified global developmental delay receive genetic testing including a DNA test for Fragile X Syndrome
2. Practice based patient management systems support providers to appropriately manage patients with identified developmental delay
3. Improved family/provider communication in identifying delay and planning care

The secondary drivers and related resources are included as Attachment 7. These materials were available to the practices through the QIDA website Workspace [http://qidata.aap.org/qfxs](http://qidata.aap.org/qfxs).

PRE-WORK AND ACTION PERIODS

Over the project period, each practice completed the following:

Pre-application

- Assembled a core improvement team (up to three individuals including physicians, clinic staff, nurses, NPs) committed to supporting the Q-FXS project.
- Achieved buy-in from practice leadership and administration to support the Q-FXS project (practice manager, administration, Information Technology, etc)
- Investigated whether local IRB approval will be necessary at their institution for participation in this project.
- Viewed a 45-minute informational video (optional recorded webinar); practices had the option to watch the video any time prior to the initial orientation webinar.
Pre-work activities

- Participated in two Learning Session webinars/videoconferences on the orientation of core improvement teams to fragile X syndrome and the Q-FXS Project as well as an introduction to the data collection mechanism (Quality Improvement Data Aggregator) quality improvement and the Q-FXS change package.
- Assigned a Group Administrator (person on the core team who was to be responsible for data entry into QIDA)
- Participated in a 60-minute qualitative phone interview with the Q-FXS Quality Improvement Advisor/Consultant.
- Collect baseline data: 100% of eligible charts (minimum 5 charts up to a maximum of 20 charts per month) over a five-month period (October 2015-February 2016)

Action period

- Devoted necessary resources and time to testing and implementing changes related to the identification of eligible charts, genetic testing and follow-up over a specified three-month action period and work to obtain buy-in from all members of the practice.
- Attended three 60-minute virtual learning sessions (webinar/videoconference) to discuss run chart data, successes, barriers and strategies for improvement.
- Attended a final virtual session (webinar/videoconference) that summarized the project data and give practices the opportunity to elaborate on opportunities for sustainability within their practice. This session included a qualitative focus group with the practices regarding the project outcomes and sustainability over time.
- Collected action period data: Three months of the charts (10 charts per month for 30 charts total) during the action periods.
- Made the appropriate changes in the structure of how genetic testing is referred/ordered for patients with a GDD/ID.

CONCLUSIONS AND RECOMMENDATIONS

GENETIC TESTING ORDERED:

- In reviewing data for the percent of charts reviewed where a genetic test was ordered it is clear that this data did not move in the direction of improvement. It is also recognized that fewer children were being identified for genetic testing. When these results are reviewed with the teams during the post-project focus group, the following qualitative findings were identified:

  1. In the first few months of the project it was much easier to identify individuals with the ICD-10 codes necessary for chart review. As time progressed teams felt like they were hitting a saturation point, where they had already reviewed charts for many of the children who met the inclusion criteria and were therefore struggling to find new patients.

  2. Many of the charts reviewed may have met the criteria for coding but the providers did not feel genetic testing was warranted, or they identified that the child only had delay in one domain. The inclusion of children with global developmental delay (where children have developmental delay in at least 2 domains) seemed to limit the amount of children who actually qualified for genetic testing.
3. Finally, teams found it very difficult to identify these children. Many practices were not regularly utilizing the ICD-10 codes we identified in the inclusion criteria. Coding was not done as a method of population management, rather this was used purely for billing. Many hours were spent by teams seeking out charts of children who should have genetic testing completed.

**GENETIC TESTING INCLUDING FRAGILE X TESTING**

- In reviewing data that identifies the percentage of genetic tests ordered during this collaborative which also included an order for Fragile X, it is clear that pediatricians participating in this collaborative made their most remarkable improvement here.

- During the baseline period of this work teams only included a Fragile X test 63% of the time. For the collaborative this was completed 100% of the time, representing a 59% improvement in three short months.
**FAMILIES COMPLETING BLOOD DRAW FOR GENETIC TESTING**

- In reviewing data for the percent of families who completed the blood draw for genetic testing, a concerning trend is identified.
- While pediatricians improved the rate at which they were identifying children in need of testing, and following through with issuing this order, it seems fewer and few families were actually completing this testing.
- Teams often reported this as a key concern to their work, indicating that many families refused testing or simply did not follow through on the order.

![% Families Having Blood Drawn for Genetic Testing](image)

**FAMILIES RECEIVING GENETIC TESTING RESULTS**

- While very few families actually completed the genetic testing (only 11 families across all three practices during the collaborative) 100% of families received contact from the pediatrician regarding these results.
- This result highlights the willingness of the practices to close the loop with parents, and to have the crucial conversation about the genetic tests.

**UNDERSTANDING POINTS OF DELAY**

- A key effort of this work was to understand the different points in the system that might delay the diagnosis of Fragile X and other associated genetic conditions. To learn more about the delay points, measures were established to understand the delay at three different points in the system (1) the point when developmental delay was first a concern to the point where the provider felt genetic testing was warranted, (2) the point from when genetic testing was warranted to when it was ordered, (3) the point from when the order was placed to when the blood was drawn for the test. While there is still interest in learning more about what contributes to delayed testing and identification of Fragile X, overall we had limited learnings from these three measures. The findings by measure are reviewed below.
1. The expert group was interested in learning more about if pediatricians were delaying ordering genetic testing. For the group this was especially interesting for children under five years of age. The theory was that perhaps as pediatric offices are assessing developmental delay more frequently in younger children they might be taking the “wait and see” approach before ordering genetic testing. Overall we did not find anything to support this hypothesis.

   - In general the time between when developmental delay was first identified to the point that genetic testing was ordered was quite close together. Qualitatively there is some information to support the fact that this could be due to a lack of utilization of the appropriate ICD-10 codes. This project sparked pediatricians to begin coding these delays and then immediately also order testing. Essential they had not been “thinking about it” and therefore, after raised awareness with Q-FXS, were nowmore apt to immediately order testing. This is something future projects could continue to examine.

2. The expert group also felt perhaps a major source of delayed diagnosis would be from the point delay required testing to the point that the testing was actually ordered. The main reasoning behind this concern was that genetic testing including Fragile X is costly and often not covered by insurers without prior authorization. This theory was also not supported in our data.

   - Practices reported many of the patients whom they ordered genetic testing for were covered under Medicaid programs, which eased the prior authorizations burden. This data was also reported rather infrequently by teams as they reported this data is both difficult to ascertain in the medical record and often not recorded at all.

3. Finally, the expert group was interested if there would be delay from the point the pediatrician orders the genetic testing to the point the family completed the blood draw. As noted previously, a sizable amount of families did not complete genetic testing, therefore these data points were not often available. For those families who did complete testing, having approval to complete the blood draw did not seem to be a key source of delay. Practices also reported difficulty with extracting this data from their electronic health record.

**LIST OF APPENDIX**

1. Expert Group roster
2. Aim and measures
3. Qualitative interview guide
4. Chart review tool
5. Periodic progress report
6. Recruitment package
7. QIDA web interface with change package

Appendices available by request from Rachel Daskalov, rdaskalov@aap.org