Discordance in diagnoses and treatment of psychiatric disorders in children and adolescents with 22q11.2 deletion syndrome

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Abstract:
This study examines the rate of utilization of mental health services in children and adolescents with 22q11.2DS relative to their remarkably high rate of psychiatric disorders and behavior problems. Seventy-two children and adolescents with 22q11.2DS were participants; their parents completed the Diagnostic Interview Schedule for Children (DISC) and the Child Behavior Checklist (CBCL). The results indicated that 22q11.2DS children and adolescents have higher rates of psychopathology than the general pediatric population, with ADHD and anxiety disorders being the most common. However, among youth with 22q11.2DS, those with psychopathology are often no more likely to receive either pharmacological or non-pharmacological mental health care than those without a given psychiatric diagnosis. Thus, although psychopathology is fairly common in this sample, many children with 22q11.2DS may not be receiving needed psychiatric care. These results have significant implications for these children and their families, as well as for the health care providers who treat them. In particular, the results may suggest a need for careful screening of psychiatric disorders that are likely to affect this population, as well as making appropriate treatment recommendations to remedy childhood mental health problems. Since these children face an extraordinarily high risk of psychoses in late adolescence/adulthood, treatment of childhood psychopathology could be crucial in mitigating the risk/consequences of major psychiatric illnesses in later life.

Keywords: 22q11.2DS | velocardiofacial syndrome | digeorge syndrome | children/adolescents | psychopathology | service utilization | psychology

Articles:
1. Introduction
Perhaps as evidenced by its many names, 22q11.2 Deletion Syndrome (22q11.2DS; also known as velo-cardio-facial syndrome or DiGeorge syndrome) is a complex condition with multiple phenotypic features. As the most common microdeletion syndrome in humans, it affects 1 in 1600–4000 live births ([Driscoll et al., 1992], [Wilson et al., 1994], [Tezenas Du Montcel et al., 1996], [Shprintzen, 2000] and [Kobrynski and Sullivan, 2007]). Common manifestations include heart malformations, palatal abnormalities and typical facial features ([Shprintzen et al., 1981] and [Shprintzen, 2000]).

1.1. Cognitive impairments in 22q11.2DS
Cognitive impairments are almost universal in individuals with 22q11.2DS, with a mean IQ of 75 ([Swillen et al., 1997], [Moss et al., 1999] and [Woodin et al., 2001]). A complex pattern of impairments occurs, with deficits in sustained attention, working memory, executive function, verbal learning, and visual–spatial processing ([Bearden et al., 2001], [Niklasson et al., 2001], [Campbell et al., 2006], [Kiley-Brabeck and Sobin, 2006] and [Lewandowski et al., 2007]).

1.2. Psychiatric/behavior problems in 22q11.2DS
In addition to cognitive deficits, children with 22q11.2DS are highly susceptible to psychiatric problems and disorders such as attention-deficit/hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), depression, generalized anxiety disorder, separation anxiety, and specific and social phobia ([Niklasson et al., 2001], [Gothelf et al., 2004], [Baker and Skuse, 2005], [Antshel et al., 2006], [Shashi et al., 2010a] and [Shashi et al., 2010b]). High rates of overall behavior problems, elevated internalizing symptoms, and poor social skills are also common ([Heineman-de Boer et al., 1999] and [Kiley-Brabeck and Sobin, 2006]). Most remarkably, children with 22q11.2DS are 25 times more likely to experience serious mental illness during late adolescence/early adulthood than the general population (reviewed in Shprintzen, 2008), with up to one-third eventually developing schizophrenia spectrum disorders; also evident with increasing age are bipolar disorder and major depression ([Shprintzen et al., 1992], [Pulver et al., 1994], [Papolos et al., 1996], [Antshel et al., 2007] and [Gothelf et al., 2008]). The exact cause of the high rate of psychotic disorders is unclear, although the hemizygous deletion undoubtedly plays a role. It is widely believed that the childhood psychiatric problems may be associated with the later risk of psychosis; thus, early treatment of these may have an effect upon the psychosis risk later in life ([Gothelf, 2007] and [Shprintzen, 2008]), underscoring the importance of diagnosing and treating childhood psychopathology.

1.3. The present study
Despite the fact that the condition clearly has an impact upon psychological function and behavior, little effort has been made to design and implement interventions for children with 22q11.2DS (Hatton, 2007). The effectiveness of psychosocial interventions in this group is
completely unknown, but there is preliminary evidence that particular pharmacological interventions are effective at treating psychiatric problems in 22q11.2DS. Specifically, metyrosine and clozapine for psychosis resistant to other treatments ([Carandang and Scholten, 2007] and [Gladston and Clarke, 2005]), methylphenidate for ADHD (Gothelf et al., 2003), and flouxetine for OCD (Gothelf et al., 2004) may be promising treatment options. It is important to note that these efficacy studies are few and have small sample sizes (ranging from 1 to 12 participants). Furthermore, to date, there are no known studies examining differential utilization of existing interventions or whether service utilization may differ by co-morbid conditions. Based on our clinical observations, we hypothesized that, despite relatively high rates of psychiatric disorders/behavior problems in this population, the reported rate of services being provided would indicate underutilization of mental health services (i.e., the difference in utilization rates between the 22q11.2DS cases with and without a co-morbid psychiatric disorder would not be significant).

2. Methods

2.1. Participants

Participants included 72 children and adolescents with a 22q11.2 deletion, confirmed by fluorescence in situ hybridization or microarray analyses, recruited from genetics clinics at two medical centers located in southeastern United States. The institutional review boards of both medical centers approved the study. Control subjects ($n = 58$) consisted of typically developing healthy children, matched to the 22q11.2DS group by age (within 9 months) and gender. The control subjects were recruited from the local public schools and pediatric practices in the community. For controls, exclusion criteria included having a neurodevelopmental disorder or a genetic disorder; however, control children with ADHD were permitted to enroll in the study. It is to be noted that the control group in this study was utilized only to compare treatment rates for ADHD between that group and the 22q11.2DS children who had ADHD, since the incidence of this disorder was similar in both groups. Since the focus of the study is on children with 22q11.2DS, no other comparisons between the control and 22q11.2DS groups were made.

The 22q11.2DS study participants ranged in age from 6 to 16 years, with an average age at study enrollment of 10.49 years (SD = 2.6). The sample was 54.8% male and largely white (84.7%), with African-Americans (6.9%), Hispanics (6.9%), and Native Americans (1.3%) also being represented in the sample. The Hollingshead Index placed the sample within the middle socioeconomic stratum (SES) ($M = 32.29, SD = 13.69$).

2.2. Procedures

For this study we employed two major data collection tools along with a semi-structured interview. In every instance, the child's primary caregiver was the informant for each of the measures employed. Of the 72 study participants, four had a primary caregiver that was not a parent (i.e., an aunt or grandmother), but in each case, the primary caregiver had raised the child and was thus a reliable informant. To obtain psychiatric diagnoses we utilized the Computerized Diagnostic Interview Schedule for Children (C-DISC), a comprehensive, structured interview
that covers 36 mental health disorders for children and adolescents using DSM-IV criteria (NIMH-CDISC, 2004). The C-DISC is the most widely used and studied mental health interview that has been tested in both clinical and community populations. From the C-DISC, we extracted the specific diagnoses, the number of diagnoses, and whether a child received any diagnosis. The C-DISC was administered by trained research personnel (graduate students in psychology or a doctoral level clinician).

In addition, we employed the Child Behavior Checklist (CBCL), a highly reliable (test–retest reliability: $r = 0.95$; inter-interviewer reliability: $r = 0.93$), widely used parent-rating scale for child social–behavioral problems ([Achenbach, 1991] and [Achenbach and Ruffle, 2000]). The CBCL generated standardized scores for Internalizing, Externalizing, and Total Behavior Problems, with subgroups being designated based on summary scores falling at or below the tenth percentile ($t$-score $\geq 62$).

Finally, to obtain data on the type of pharmacological and non-pharmacological treatments the children were receiving, we employed a semi-structured interview that was developed by the researchers. The interview, conducted by the trained researchers mentioned above, provided parent-reported information related to medication use and any type of mental health intervention (e.g., counseling, behavioral therapy). For this study we focused on the response to these questions: (1) has your child ever been diagnosed with an emotional, behavioral, or mental health disorder? (2) Seen a doctor or therapist for emotional, behavioral, or mental health issues? (3) Ever been prescribed medications for these problems?

Although some participants were receiving both types of interventions, these categories were mutually exclusive for this study in an effort to determine if specific diagnoses were aligning with specific types of treatment. Operationally, medication use was defined as a child taking any psychotropic medication for a psychiatric or behavioral problem, whereas the mental health intervention was operationally defined as individual or group counseling, parent-training, behavioral therapy, or participation in family therapy.

2.3. Data analyses

We employed chi-square statistics and Fisher's exact test to examine differences in the rates of mental health services and pharmacology utilization in the 22q11.2DS sample with and without a specific diagnosis. This would allow us to determine whether 22q11.2DS children with co-morbid psychiatric diagnoses were using mental health services at a rate lower than would be expected. All statistical analyses were performed with the use of SPSS version 18.0.

3. Results

3.1. Rates of psychiatric diagnoses in 22q11.2DS

The rates of psychiatric disorders in the sample ranged from 1% (Panic Disorder, Agoraphobia, and Post-Traumatic Stress Disorder) to over 43% (ADHD). When compared to estimated rates in the general pediatric population, several discrepancies are noteworthy. As can be seen in Table 1, the presence of a specific phobia, OCD, and ADHD was over 7 times, 4 times, and 6 times
more common than in the general pediatric population. Additionally, approximately two-thirds received at least one clinical diagnosis, while about 29% had two or more.

Table 1. Rate of psychiatric disorders in our cohort of children with 22q11.2DS ($N=72$), compared to the rate in the general pediatric population, illustrating the high rate of psychopathology in these children.

<table>
<thead>
<tr>
<th>DSM-IV diagnosis</th>
<th>Number</th>
<th>Percentage</th>
<th>Estimated percentage in pediatric population$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social phobia</td>
<td>4</td>
<td>5.6</td>
<td>1</td>
</tr>
<tr>
<td>Separation anxiety</td>
<td>5</td>
<td>6.9</td>
<td>5</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>27</td>
<td>37.5</td>
<td>5</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>1</td>
<td>1.4</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>1</td>
<td>1.4</td>
<td>1</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>4</td>
<td>5.6</td>
<td>4–7</td>
</tr>
<tr>
<td>Obsessive compulsive disorder</td>
<td>7</td>
<td>9.7</td>
<td>1–2</td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
<td>1</td>
<td>1.4</td>
<td>2</td>
</tr>
<tr>
<td>Any anxiety disorder</td>
<td>33</td>
<td>45.8</td>
<td>13</td>
</tr>
<tr>
<td>Attention-deficit hyperactivity disorder</td>
<td>31</td>
<td>43.1</td>
<td>5–7</td>
</tr>
<tr>
<td>Oppositional defiant disorder</td>
<td>10</td>
<td>13.9</td>
<td>10</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>2</td>
<td>2.8</td>
<td>2–8</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Schizophrenia spectrum disorder$^b$</td>
<td>1</td>
<td>1.4</td>
<td>1</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>Any DSM-IV diagnosis</td>
<td>48</td>
<td>66.7</td>
<td>11–21</td>
</tr>
<tr>
<td>No DSM-IV diagnosis</td>
<td>23</td>
<td>31.9</td>
<td>79–89</td>
</tr>
<tr>
<td>One DSM-IV diagnosis</td>
<td>28</td>
<td>38.9</td>
<td>–</td>
</tr>
<tr>
<td>Two or more DSM-IV diagnoses</td>
<td>21</td>
<td>29.2</td>
<td>–</td>
</tr>
</tbody>
</table>

$^a$ National Institutes of Mental Health Statistics and National Health and Nutrition Examination Survey ([Merikangas et al., 2010] and [Costello et al., 1996]).

$^b$ It is to be noted that the rate of schizophrenia spectrum disorders is lower in our cohort than expected, since all of our subjects are in an age range where high rates of schizophrenia are not anticipated.
3.2. Rates of non-pharmacological treatment in 22q11.2DS

As can be seen in Table 2, children with 22q11.2DS and co-morbid ADHD did receive non-pharmacological mental health services at a significantly higher rate than children with 22q11.2DS who did not have ADHD; however, it is important to note that still only 27.6% of the children with ADHD were being treated. In the control group, the rate of ADHD (41%) is similar to that in the 22q11.2DS group, but 74.6% of the control group is receiving some type of behavioral intervention, compared to the 22q11.2DS group, $p < .001$. For any type of anxiety disorder, only 12.9% were receiving non-pharmacological mental health services for their anxiety symptoms, which was not significantly different from their 22q11.2DS peers who did not have anxiety disorders (Fig. 1).

Table 2. Rates of non-pharmacological and pharmacological treatments for children with 22q11.2DS with and without clinical diagnosis/behaviors on the C-DISC and CBCL.

<table>
<thead>
<tr>
<th>Diagnosis/behavior</th>
<th>Number of subjects/non-pharmacological Rx</th>
<th>$p$-Value</th>
<th>Number of subjects/pharmacological treatment</th>
<th>$p$-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>29/8, Absent/Yet Rx 38/2</td>
<td>&lt;.01</td>
<td>29/11, Absent/Yet Rx 38/2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Any anxiety disorder</td>
<td>31/4, Absent/Yet Rx 36/6</td>
<td>NS</td>
<td>31/6, Absent/Yet Rx 36/11</td>
<td>NS</td>
</tr>
<tr>
<td>Any psychiatric diagnosis</td>
<td>44/14, Absent/Yet Rx 23/3</td>
<td>NS</td>
<td>44/8, Absent/Yet Rx 23/2</td>
<td>NS</td>
</tr>
<tr>
<td>Two or more diagnoses vs. none/one diagnosis</td>
<td>21/5, Absent/Yet Rx 46/12</td>
<td>NS</td>
<td>21/5, Absent/Yet Rx 46/12</td>
<td>NS</td>
</tr>
<tr>
<td>Int. symptoms &gt; 62</td>
<td>29/4, Absent/Yet Rx 26/2</td>
<td>NS</td>
<td>29/7, Absent/Yet Rx 26/3</td>
<td>NS</td>
</tr>
<tr>
<td>Ext. symptoms &gt; 62</td>
<td>8/0, Absent/Yet Rx 47/6</td>
<td>NS</td>
<td>8/1, Absent/Yet Rx 47/9</td>
<td>NS</td>
</tr>
<tr>
<td>Total problem score &gt; 62</td>
<td>33/6, Absent/Yet Rx 22/0</td>
<td>&lt;.05</td>
<td>33/10, Absent/Yet Rx 22/0</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>
Fig. 1. Illustration of poor non-pharmacological treatment rates for children with 22q11.2DS who have anxiety disorders, compared to those that did not have an anxiety disorder. 1 = diagnosis of anxiety disorder 0 = no anxiety disorder.

Similarly, when compared to children with 22q11.2DS with no co-morbid diagnosis, children with 22q11.2DS and any co-morbid diagnosis (approximately two-thirds of the sample; see Table 1) did not have a significantly different rate of non-pharmacological treatment utilization. Finally, when those with two or more diagnoses were compared to those with one, or no psychiatric diagnoses, there were no significant differences in rates of treatment between the three groups, \( \chi^2 (2) = 3.23, p = \text{NS} \); consequently, even those with multiple psychiatric diagnoses were not receiving non-pharmacological mental health services at the rate that might be expected.

When rates of behavior problems were examined, a similar pattern was observed. Specifically, children with 22q11.2DS who had a high rate of internalizing or externalizing symptoms (<10th percentile) did not have a significantly different rate of non-pharmacological mental health services utilization when compared to children with 22q11.2DS whose ratings were not at clinical levels. When the Total Behavior Problems were examined, those falling below the 10th percentile did receive mental health services at a significantly higher rate than their non-affected 22q11.2DS peers; however, as with the observations for non-pharmacological treatment for ADHD, only 18.2% of those with behavior problems below the 10th percentile were receiving services, a rate that is indicative of the remarkably low rates of treatment of psychiatric/behavior problems in these children.

We also examined the impact of social position upon treatment rates in our cohort. There were no differences in non-pharmacological treatment rates for ADHD and anxiety disorders, when parental SES was above or below the 25th percentile.
3.3. Rates of pharmacological treatment

As can be seen in Table 2, children with co-morbid ADHD did receive pharmacological treatment at a significantly higher rate than their peers with 22q11.2DS without ADHD; however, as with those receiving non-pharmacological treatments, it is important to note that only 38% of the affected children were receiving medication for their ADHD symptoms. In contrast, 72.7% of the ADHD typical comparison children were receiving pharmacological treatment, p < 0.01. For any type of anxiety disorder, only 19.3% were receiving pharmacological intervention for their anxiety symptoms, which was not significantly different from their non-affected 22q11.2DS peers.

When children with 22q11.2DS and any psychiatric diagnosis were compared to children with 22q11.2DS and no co-morbid diagnoses, there was no significant difference in the rate of medication use. Finally, when those with none, one, and two or more diagnoses were compared, there was a significant difference; those with one diagnosis having higher treatment rates than those with two diagnoses or none (X² = 10.37, p < .006). However, when those with none or one diagnosis were grouped together, there were no significant rates in treatment between them and those with two or more diagnoses (Table 2).

When rates of behavior problems were examined, children with 22q11.2DS who also had a high rate of internalizing or externalizing symptoms (<10th percentile) did not have a significantly different rate of receiving pharmacological treatment than children with 22q11.2DS whose ratings were not at clinical levels. The pharmacological treatment rate for those with total problem scores above 62 was higher than for those without, but again, it is to be noted that this is still an overall low treatment rate of 30%.

There was no significant difference in pharmacological treatment rates for ADHD and anxiety disorders, when parental SES was examined; children whose parental SES was above the 75th percentile were no more likely to be treated with medications for these two highly prevalent disorders, compared to those that were more socioeconomically disadvantaged.

4. Discussion

Our study is the first to examine treatment utilization for mental health problems in children with 22q11.2DS; consistent with our hypothesis, it provides evidence that these children are being inadequately treated for the range of psychiatric/behavior problems that they face in childhood, despite their poor functionality and the resultant stress on the families ([Heineman-de Boer et al., 1999] and [Hercher and Bruenner, 2008]).

Psychopathology is significantly elevated in children and adolescents with 22q11.2DS, with about 67% of this sample having at least one DSM-IV diagnosis and ADHD and anxiety disorders being the most common. However, relatively few children with 22q11.2DS are receiving either pharmacological or non-pharmacological care for even the most common disorders. In fact, none of the children with significant externalizing problems (as identified by the CBCL) were receiving non-pharmacological services and only one had received pharmacological services. Although a total problem score of ≥62 was associated with significant non-pharmacological and pharmacological treatment rates, these are still very low rates of
treatment overall (18% and 30% respectively). Even when two or more psychiatric co-morbidities occurred, the treatment rates did not increase; paradoxically, children with one diagnosis received pharmacological treatment at a higher rate than those with two diagnoses. Altogether, these results suggest an inconsistency of treatment and underutilization of mental health services in children with 22q11.2DS; such services could significantly improve the quality of life for a group of youth with a demonstrated need for mental health care.

It is important to note that the rates we ascertained for non-pharmacological mental health services for 22q11.2DS children with ADHD stand in striking comparison to findings from our typical control group. In that comparison sample, the rate of ADHD is comparable to that in the 22q11.2DS group, but a significantly higher percentage of the control children receive treatment for ADHD compared to the 22q11.2DS group. Thus, it is clear that with other factors such as age and gender being equal, our cohort of 22q11.2DS children are strikingly undertreated for even common and well-recognized problems such as ADHD, despite preliminary evidence for effective pharmacological treatments for ADHD in these children (Gothelf et al., 2003).

We considered the possibility that, within the 22q11.2DS group, the social position of the family could have an impact upon treatment rates. We found that parental SES did not influence treatment rates in a significant fashion. We have previously shown that in children with 22q11.2DS, behavior problems are more prevalent with a lower SES background ([Shashi et al., 2010a] and [Shashi et al., 2010b]), but it is apparent from this study that all children with 22q11.2DS, no matter their social circumstances, have unusually low rates of treatment for psychiatric/behavior problems.

It is also notable that some children with 22q11.2DS who had no co-morbid diagnoses (none diagnosed by our measures) were nonetheless receiving treatment of some kind. We suspect this is because some children may be undergoing treatment for subclinical symptoms or problems reported by the parents without an evaluation to substantiate a specific diagnosis (symptom treatment). This type of treatment may often be initiated by their primary care physicians. It is also possible that some children who did not meet diagnostic criteria for a particular disorder in our research assessments may have been diagnosed in the community. Despite their documented validity, our research measures may not reveal diagnoses that are concordant with a clinical diagnosis given by a physician or mental health care provider in the community. In typical children, utilization of mental health services is known to be dependent on race, SES, cultural influences, stigma associated with a psychiatric illness, ethnicity/country of origin, perceived severity of psychiatric problems, knowledge about mental health, and even provider biases (e.g., a provider's tendency to refer one group of people to needed services over another group despite the groups having comparable needs) ([Heflinger and Hinshaw, 2010], [Merrick et al., 2006], [Bradby et al., 2007], [Wilcox et al., 2007], [Ghanizadeh et al., 2008], [Tan et al., 2008], [Bussing et al., 2007], [Lau and Takeuchi, 2001] and [Muroff et al., 2008]). Although we have no explicit information on why children with 22q11.2DS underutilize mental health services, it is likely that many of the above-mentioned factors have contributed to service underutilization in this population.

However, there may be unique barriers to accessing mental health care for children with 22q11.2DS; these may include: (a) lack of awareness of 22q11.2DS among health care...
professionals leading to inadequate screening for mental health symptoms (although there are no published data on this, our clinical experience is that many are not familiar with the condition): (b) the numerous medical problems that these children face, such as heart disease, take precedence over mental health problems in the attention they necessitate (Hopkin et al., 2000); (c) the cognitive deficits and poor social and communication skills of these children may preclude them from verbalizing their symptoms related to disorders, such as anxiety or phobias, as well as a typical child may be able to; (d) relatively fewer externalizing problems, compared to internalizing problems may result in few overt behavior problems, thus escaping medical attention; (e) the relatively better treatment rates for ADHD compared to anxiety disorders may be a function of ADHD contributing to disproportionately lower academic performance and pediatric health care providers being more conversant with the evaluation and treatment of ADHD; (f) poor academic performance and functionality may be attributed to their cognitive deficits rather than co-existing psychiatric problems; (g) parents may view any psychiatric or behavioral problems as simply another feature of the disorder, and therefore do not seek specialized psychiatric care; and (h) the stressful process of finding a pharmacological intervention that works with minimal side effects is a deterrent for many parents.

Furthermore, the treatment rates in developing countries are likely to be even lower for children with 22q11.2DS; no data exists at this time regarding the incidence of 22q11.2DS in developing countries, although based on the incidence in the USA and European countries (Kobrynski and Sullivan, 2007), we expect it to be similar, since 22q11.2DS occurs in all ethnic groups. Studies on the incidence and prevalence of the condition and the utilization of mental health services by these children in developing countries would be an important avenue of investigation.

4.1. Limitations

One limitation of our study is that, while there is a clear pattern of underutilization of mental health services in general, we do not have information regarding the specific types of behavioral or pharmacological treatments that the children in this study received. As such, we are unable to assess whether one particular therapy or pharmacological treatment is more commonly used than another. Another limitation is that we do not have a sufficient number of minority participants to determine if there were racial/ethnic differences in treatment rates. Additionally, most of the children in this study are at an age wherein we do not expect to see high rates of psychotic disorders. There were no other hospitalizations of children in the study, and thus we could not effectively evaluate inpatient mental health care utilization in our cohort. A study incorporating adults with 22q11.2DS would provide data on this subject. This study is also limited by its reliance on a single informant; we had no means of controlling for response or recall biases. Lastly, we did not directly assess barriers to families of 22q11.2DS obtaining mental health services, information which would be important to know to help improve utilization; this would be an important topic for future research.

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