Psychiatric disorders in children and adolescents with 22q11DS and their correlations with role/social function

Marco Armando$^{1,2}$

$^1$Office Médico-Pédagogique, Department of Psychiatry, University of Geneva School of Medicine, Geneva, Switzerland.
$^2$Child and Adolescents Psychiatric Unit, Department of Neuroscience, Children Hospital Bambino Gesu’, Rome, Italy.

Bruxelles, 10-11 October 2015
Contents of the talk

✓ Psychiatric disorders in CAD general population and impact on Role and Social functioning.

✓ Psychiatric disorders in CAD with 22q11DS.

✓ Preliminary results from an ongoing study on CAD with 22q11DS.

✓ Overview of possible interventions aimed at improving Role and Social Functioning.
Psychiatric disorders in children and adolescents

50% of psychiatric disorders start by age 14 years.

---

**Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication**

Ronald C. Kessler, PhD; Patricia Berglund, MBA; Olga Demler, MA, MS; Robert Jin, MA; Kathleen R. Merikangas, PhD; Ellen E. Walters, MS

**Context:** Little is known about lifetime prevalence or age of onset of DSM-IV disorders.

**Objective:** To estimate lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the recently completed National Comorbidity Survey Replication.

**Design and Setting:** Nationally representative face-to-face household survey conducted between February 2001 and April 2003 using the fully structured World Health Organization World Mental Health Survey version of the Composite International Diagnostic Interview.

**Participants:** Nine thousand two hundred eighty-two English-speaking respondents aged 18 years and older.

**Main Outcome Measures:** Lifetime DSM-IV anxiety, mood, impulse-control, and substance use disorders.

**Results:** Lifetime prevalence estimates are as follows: anxiety disorders, 28.8%; mood disorders, 20.8%; impulse-control disorders, 24.8%; substance use disorders, 14.6%; any disorder, 46.4%. Median age of onset is much earlier for anxiety (11 years) and impulse-control (11 years) disorders than for substance use (20 years) and mood (30 years) disorders. Half of all lifetime cases start by age 14 years and three fourths by age 24 years. Later onsets are mostly of comorbid conditions, with estimated lifetime risk of any disorder at age 75 years (50.8%) only slightly higher than observed lifetime prevalence (46.4%). Lifetime prevalence estimates are higher in recent cohorts than in earlier cohorts and have fairly stable intercohort differences across the life course that vary in substantively plausible ways among sociodemographic subgroups.

**Conclusions:** About half of Americans will meet the criteria for a DSM-IV disorder sometime in their life, with first onset usually in childhood or adolescence. Interventions aimed at prevention or early treatment need to focus on youth.

*Arch Gen Psychiatry. 2005;62:593-602*
Influence of psychiatric disorders on functioning in children and adolescents

Worldwide, the first main cause of functioning impairment (YLDs) under the age of 24 are psychiatric disorders.

Global burden of disease in young people aged 10–24 years: a systematic analysis

Fiona M Gore, Paul J N Bloem, George C Patton, Jane Ferguson, Véronique Joseph, Carolyn Coffey, Susan M Sawyer, Colin D Mathers

Summary
Background Young people aged 10–24 years represent 27% of the world’s population. Although important health problems and risk factors for disease in later life emerge in these years, the contribution to the global burden of disease is unknown. We describe the global burden of disease arising in young people and the contribution of risk factors to that burden.

Findings The total number of incident DALYs in those aged 10–24 years was about 236 million, representing 15·5% of total DALYs for all age groups. Africa had the highest rate of DALYs for this age group, which was 2·5 times greater than in high-income countries (208 vs 82 DALYs per 1000 population). Across regions, DALY rates were 12% higher in girls than in boys between 15 and 19 years (137 vs 153). Worldwide, the three main causes of YLDs for 10–24-year-olds were neuropsychiatric disorders (45%), unintentional injuries (12%), and infectious and parasitic diseases (10%). The main risk factors for incident DALYs in 10–24-year-olds were alcohol (7% of DALYs), unsafe sex (4%), iron deficiency (3%), lack of contraception (2%), and illicit drug use (2%).
Genetic syndromes and psychiatric disorders

✓ Psychiatric disorders are more frequent in genetic syndromes compared to general population (Morgan et al., 2008; Stinton et al., 2010).

✓ Prevalence around 30-40% of psychiatric disorders in genetic syndromes with intellectual disability (Einfeld and Tonge, 1996; Coe et al., 1999).
N= 802; Age 6-18; recruitment across 15 sites (Schneider et al, Am J Psy 2014)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Children (6–12 Years)</th>
<th>Adolescents (13–17 Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Any schizophrenia spectrum disorder</td>
<td>9/456</td>
<td>1.97</td>
</tr>
<tr>
<td>Any anxiety disorder</td>
<td>155/435</td>
<td>35.63</td>
</tr>
<tr>
<td>Any mood disorder</td>
<td>15/456</td>
<td>3.29</td>
</tr>
<tr>
<td>ADHD</td>
<td>161/434</td>
<td>37.10</td>
</tr>
<tr>
<td>Autism spectrum disorders</td>
<td>12/94</td>
<td>12.77</td>
</tr>
<tr>
<td>Any disruptive disorder</td>
<td>57/400</td>
<td>14.25</td>
</tr>
</tbody>
</table>
Psychiatric disorders and correlation with role/social functioning in 22q11DS

<table>
<thead>
<tr>
<th>Variable</th>
<th>22q11DS + any psychiatric disorder (N=67) (M/SD)</th>
<th>22q11DS - any psychiatric disorder (N=60) (M/SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>14,3/4,6</td>
<td>13,6/4,7</td>
<td>0,07</td>
</tr>
<tr>
<td>IQ</td>
<td>84,5/11,7</td>
<td>91/8,6</td>
<td>0,06</td>
</tr>
<tr>
<td>Global F</td>
<td>56/5,7</td>
<td>60/6,7</td>
<td>0,006</td>
</tr>
<tr>
<td>Social F</td>
<td>4/0,7</td>
<td>4,6/1,2</td>
<td>0,03</td>
</tr>
<tr>
<td>Role F</td>
<td>4,1/0,8</td>
<td>4,7/0,4</td>
<td>0,03</td>
</tr>
</tbody>
</table>
Psychiatric disorders and correlation with role/social functioning in 22q11DS

<table>
<thead>
<tr>
<th></th>
<th>Depressive disorders (N=24; 36%)</th>
<th>Anxiety disorders (N=24; 36%)</th>
<th>Behavioural disorders (N=19; 28%)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role F</td>
<td>4.1</td>
<td>4.2</td>
<td>3.9</td>
<td>.107</td>
</tr>
<tr>
<td>Social F</td>
<td>4.0</td>
<td>4.3</td>
<td>4.3</td>
<td>.139</td>
</tr>
</tbody>
</table>

* After co-varying for IQ and age
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Psychosocial treatment</th>
<th>Pharmacological treatment</th>
<th>No treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressive disorders</td>
<td>5 (21%)</td>
<td>2 (8%)</td>
<td>17 (71%)</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>3 (12.5%)</td>
<td>3 (12.5%)</td>
<td>18 (75%)</td>
</tr>
<tr>
<td>Behavioural disorders</td>
<td>5 (26%)</td>
<td>0 (0%)</td>
<td>14 (74%)</td>
</tr>
</tbody>
</table>
22q11 patients with psychiatric disorders showed a significantly lower R/S functioning.

No significant differences in R/S functioning between different disorders (after co-variation for IQ and age).

Most of the patients are without any treatment addressed at:
1) the disorder in itself.
2) the improvement of R/S functioning.
Possible explanations

- Psychiatric disorders and functional impairment in genetic syndromes are in general under-treated.

- High exposure to medical context in early stages (cardiac and palatial surgical interventions, speech therapy, etc.).

- More concerns on possible side-effects.
Ideal intervention to improve R/S functioning

- Staging model providing interventions with progressive intensity.
- Outside a medical context.
- Low charge of side-effects if medications are needed.
## Clinical staging model framework for psychotic and severe mood disorders

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Target populations and referral sources</th>
<th>Potential interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Increased risk of psychotic or severe mood disorder</td>
<td>First-degree teenage relatives of probands</td>
<td>Improved mental health literacy, Family education, drug education, Brief cognitive skills training</td>
</tr>
<tr>
<td></td>
<td>No symptoms currently</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>Mild or non-specific symptoms (including neurocognitive deficits) of psychosis or severe mood disorder. Mild functional change or decline</td>
<td>Screening of teenage populations, Referral by: primary care physicians; school counsellors</td>
<td>Formal mental health literacy, Family psychoeducation, formal CBT, Active substance misuse reduction</td>
</tr>
<tr>
<td>1b</td>
<td>Ultra high risk: moderate but subthreshold symptoms, with moderate neurocognitive changes and functional decline (GAF, &lt; 70)</td>
<td>Referral by: educational agencies; primary care physicians; emergency departments; welfare agencies</td>
<td>Family psychoeducation, formal CBT, Active substance misuse reduction, Omega-3 fatty acids, Atypical antipsychotic agents, Antidepressant agents or mood stabilisers</td>
</tr>
<tr>
<td>2</td>
<td>First episode of psychotic or severe mood disorder</td>
<td>Referral by: primary care physicians; emergency departments; welfare agencies, specialist care agencies; drug and alcohol services</td>
<td>Family psychoeducation, formal CBT, Active substance misuse reduction, Atypical antipsychotic agents, Antidepressant agents or mood stabilisers, Vocational rehabilitation</td>
</tr>
<tr>
<td>3a</td>
<td>Incomplete remission from first episode of care</td>
<td>Primary and specialist care services</td>
<td>As for Stage 2, but with additional emphasis on medical and psychosocial strategies to achieve full remission</td>
</tr>
<tr>
<td>3b</td>
<td>Recurrence or relapse of psychotic or mood disorder, which stabilises with treatment at a GAF level, or with residual symptoms or neurocognition below the best level achieved after remission from the first episode</td>
<td>Primary and specialist care services</td>
<td>As for Stage 3a, but with additional emphasis on relapse prevention and strategies to detect “early warning signs”</td>
</tr>
<tr>
<td>3c</td>
<td>Multiple relapses, provided worsening in clinical extent and impact of illness is objectively present</td>
<td>Specialist care services</td>
<td>As for Stage 3b, but with emphasis on long-term stabilisation</td>
</tr>
<tr>
<td>4</td>
<td>Severe, persistent or unremitting illness, as judged by symptoms, neurocognition, and disability criteria Patient’s management could be fast-tracked to this stage at first presentation, based on specific clinical and functional criteria (from Stage 2), or because of failure to respond to treatment (from Stage 3a)</td>
<td>Specialised care services</td>
<td>As for Stage 3c, but with emphasis on clozapine, other tertiary treatments, and social participation despite ongoing disability</td>
</tr>
</tbody>
</table>

* This table has been reproduced in a modified form with the permission of the *Australian and New Zealand Journal of Psychiatry*. It was originally published in McGorry et al (2006).  
† The model is bidirectional, so that disorders may not only progress, but also recede and remit fully, often on a sustained and long-term basis, under the
Overview of treatments for S/R impairment

Omega-3 improve R/S impairment and may reduce the risk of progression to first episode of psychosis in 22q11ds

Original Article

Indicated prevention with long-chain polyunsaturated omega-3 fatty acids in patients with 22q11DS genetically at high risk for psychosis. Protocol of a randomized, double-blind, placebo-controlled treatment trial

Marco Armando,1,2 Franco De Crescenzo,1 Stefano Vicari,1 Maria Cristina Digilio,3 Maria Pontillo,1 Francesco Papaleo4 and G. Paul Amminger5,6
Overview of treatments for S/R impairment

✓ Non-specialist psychosocial interventions improve R/S functioning (preliminary evidences) and are well accepted by patients and parents.

Non-Specialist Psychosocial Interventions for Children and Adolescents with Intellectual Disability or Lower-Functioning Autism Spectrum Disorders: A Systematic Review

Brian Reichow¹,²,⁎, Chiara Servili³,⁴, M. Taghi Yasamy³, Corrado Barbui⁴, Shekhar Saxena³
Overview of treatments for S/R impairment

✓ Parent-training intervention showed a reduction in symptoms severity.

✓ Group psychosocial training improve R/S functioning (preliminary evidences).

The effectiveness of psychosocial interventions for children with a psychiatric disorder and mild intellectual disability to borderline intellectual functioning: A systematic literature review and meta-analysis

Lidwien Kok¹, Anne van der Waa¹, Helen Klip² and Wouter Staal²,³
Overview of treatments for S/R impairment

- Cognitive remediation improves Role functioning impairment in CAD at risk for psychosis (preliminary evidences).
- Social skills training improves Social functioning impairment in CAD at risk for psychosis (preliminary evidences).

REVIEW

Psychosocial interventions for very early and early-onset schizophrenia: a review of treatment efficacy

Marco Armando, Maria Pontillo, and Stefano Vicari
Thanks to:

**Psychologist**
- Maria Chiara Castiglioni
- Flavia Cirillo
- Lidia D'Elia
- Milena Labonia
- Deny Menghini
- Ornella Piscitelli

**PhD student and Post-Doc**
- Floriana Costanzo
- Lavinia De Peppo
- Giulia Giovagnoli
- Eleonora Napoli
- Giorgia Piccini
- Maria Pontillo
- Marialaura Pucciarini
- Cristina Varuzza
- Speech therapist
- Luigi Marotta
- Cristina Caciolo
- Serena Rossi

**MD**
- Paolo Alfieri
- Marco Armando
- Anna Maria Caramadre
- Maria Pia Casini
- Francesco De Maria
- Paola De Rose
- Luigi Mazzone
- Giovanni Valeri
- Valeria Zanna

**Researcher**
- Roberto Averna
- Michele Riborsi
- Giulia Serra

**PhD student and Post-Doc**
- Nella Lo Cascio
- Elena Monducci

**Contacts:**
- marco.armando@opbg.net
- Marco.Armando@etat.ge.ch