Developmental trajectories in early-onset psychoses: open windows for prevention?

Catania, October 2016

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Disclosure: Celso Arango

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Otsuka			X
Pfizer, Inc.	X		X
Roche	X		
Sanofi			X
Servier	X		
Schering-Plough	X		
Shire	X		
Spanish Ministry of Education	X	X	
Stanley Foundation	X	X	x
Takeda			

Outline

- Prevention in psychiatry
- Psychosis (psychiatric disorders) as the reflection of abnormal developmental trajectories
- Shifting the focus towards prevention and early intervention in developmentally sensitive periods
- Implications and priorities for the future

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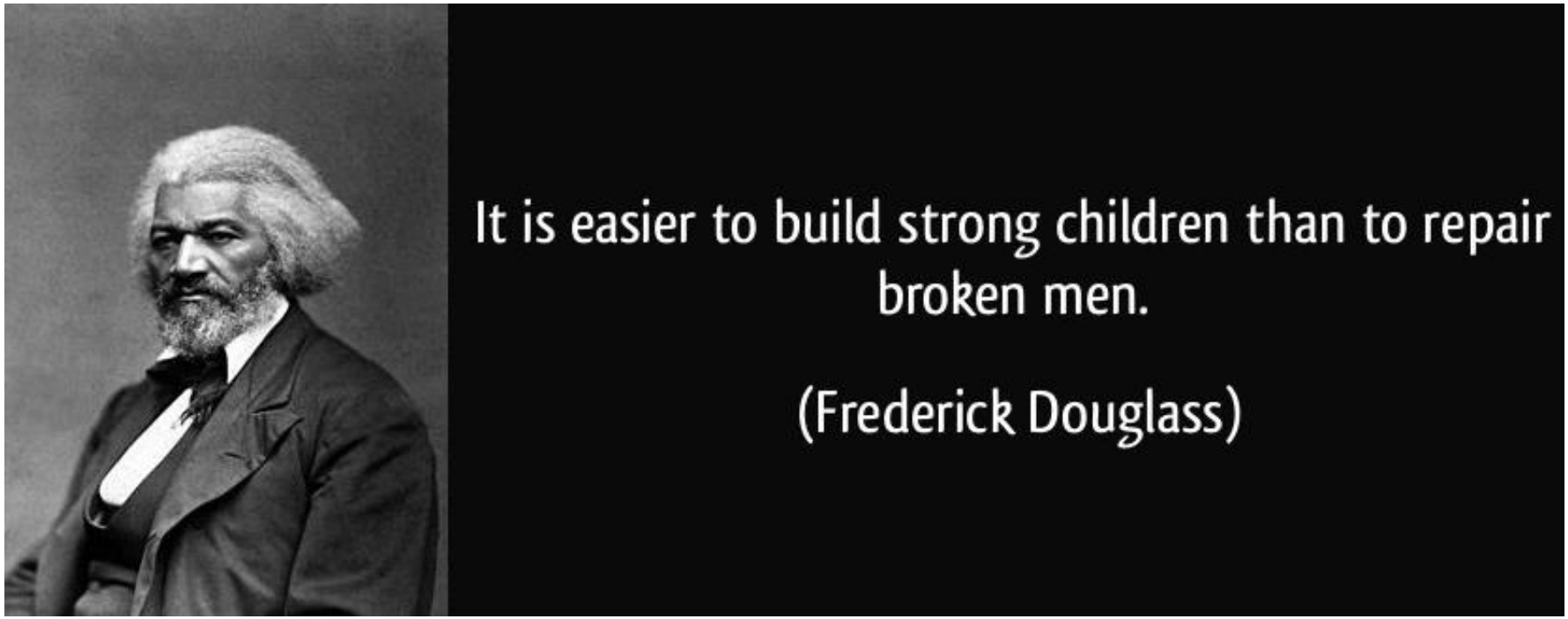
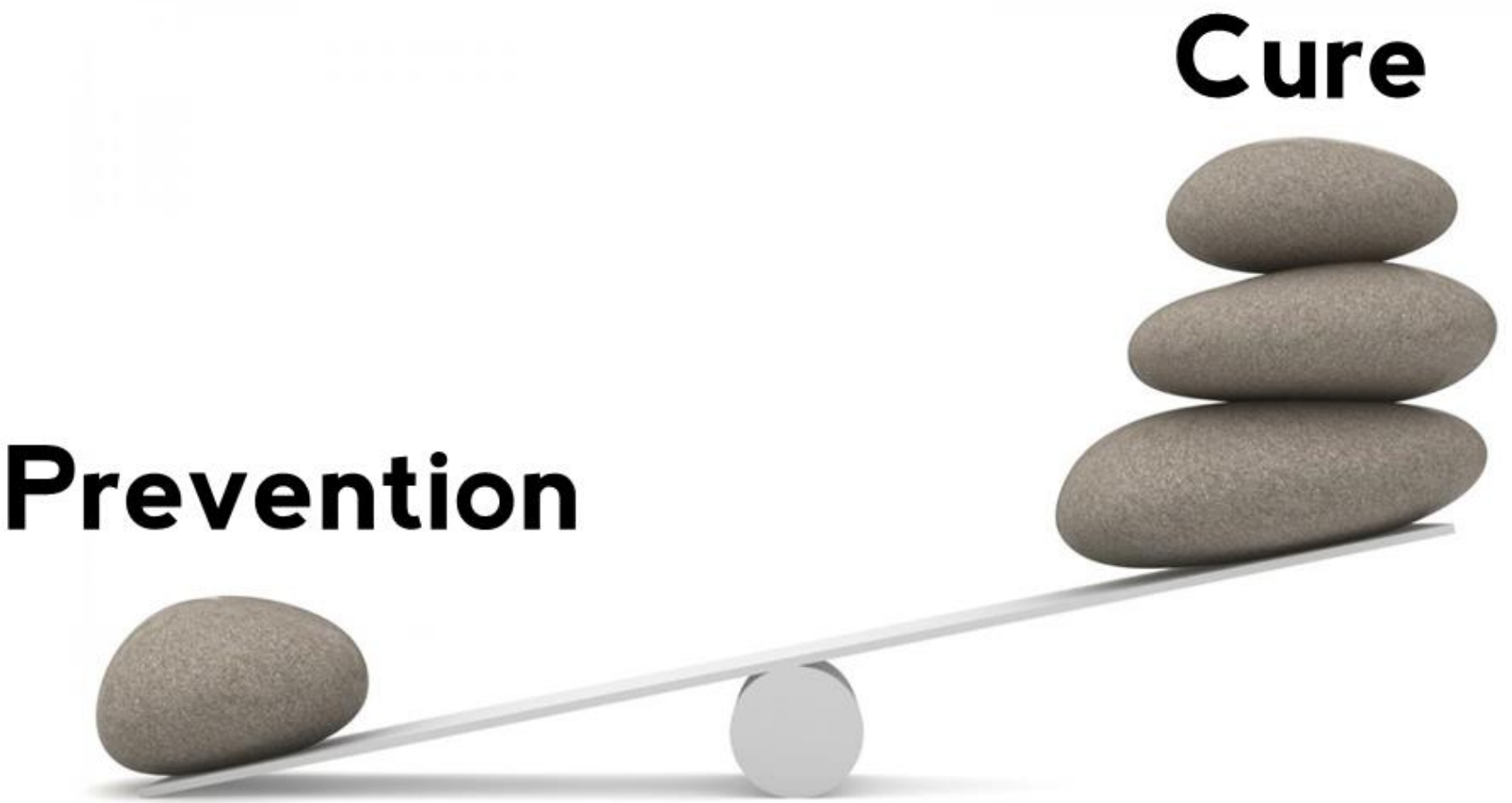

It is easier to build strong children than to repair broken men.
(Frederick Douglass)

What is prevention?

Whole population through public health policy	Whole population: selected groups and healthy individuals	Selected individuals, high risk patients	Patients
PRIMORDIAL PREVENTION Establish or maintain conditions to minimize hazards to health	**PRIMARY PREVENTION** Prevent disease well before it develops. Reduce risk factors	**SECONDARY PREVENTION** Early detection of disease (screening and intervention for pre-diabetes)	**TERTIARY PREVENTION** Treat established disease to prevent deterioration
Advocacy for social change to make physical activity easier	Primary care advice as part of routine consultation	e.g. primary care risk factor reduction for those at risk of chronic disease, falls, injury	e.g. exercise advice as part of cardiac rehabilitation


Cure
Prevention

Efficacy of preventive interventions in medicine: Prevention of diabetes

The New England Journal of Medicine

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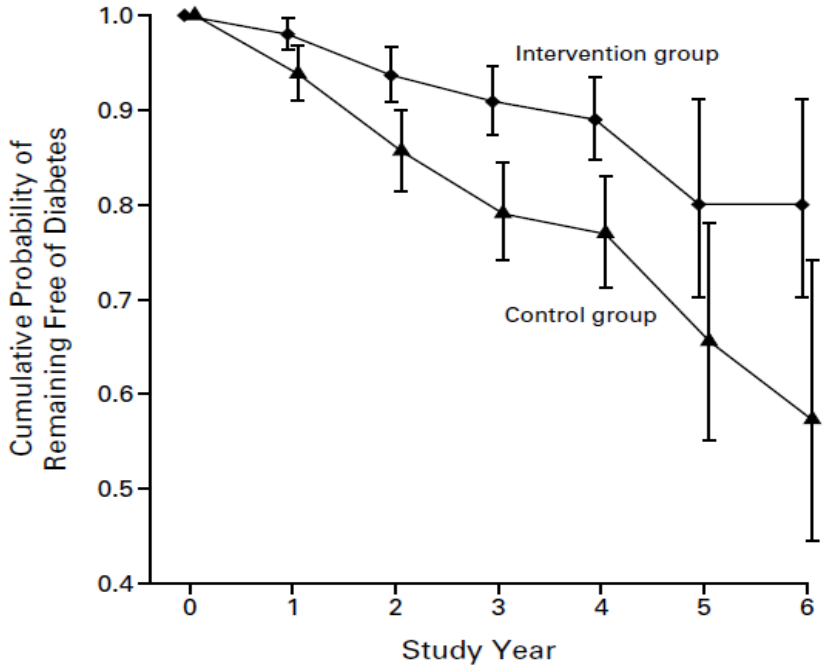
VOLUME 344 · MAY 3, 2001 · NUMBER 18

PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

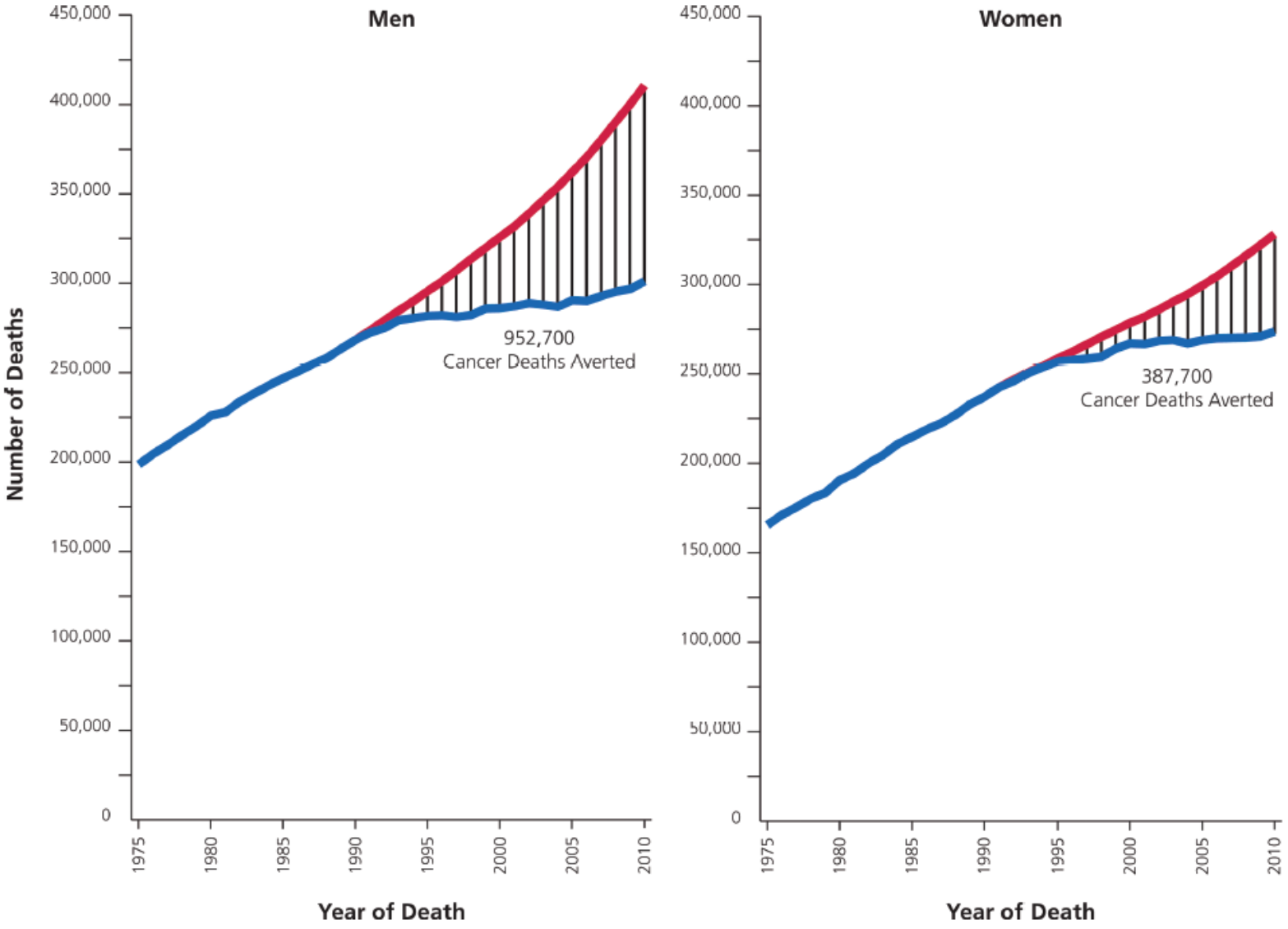
JAAKKO TUOMILEHTO, M.D., PH.D., JAANA LINDSTRÖM, M.S., JOHAN G. ERIKSSON, M.D., PH.D., TIMO T. VALLE, M.D., HELENA HÄMÄLÄINEN, M.D., PH.D., PIRJO ILANNE-PARIKKA, M.D., SIRKKA KEINÄNEN-KIUKAANNIEMI, M.D., PH.D., MAURI LAAKSO, M.D., ANNE LOUHERANTA, M.S., MERJA RASTAS, M.S., VIRPI SALMINEN, M.S., AND MATTI UUSITUPA, M.D., PH.D., FOR THE FINNISH DIABETES PREVENTION STUDY GROUP



SUBJECTS AT RISK						
Total no.	507	471	374	167	53	27
Cumulative no. with diabetes:						
Intervention group	5	15	22	24	27	27
Control group	16	37	51	53	57	59

Figure 1. Proportion of Subjects without Diabetes during the Trial.

The vertical bars show the 95 percent confidence intervals for the cumulative probability of remaining free of diabetes. The relative risk of diabetes for subjects in the intervention group, as compared with those in the control group, was 0.4 ($P<0.001$ for the comparison between the groups).

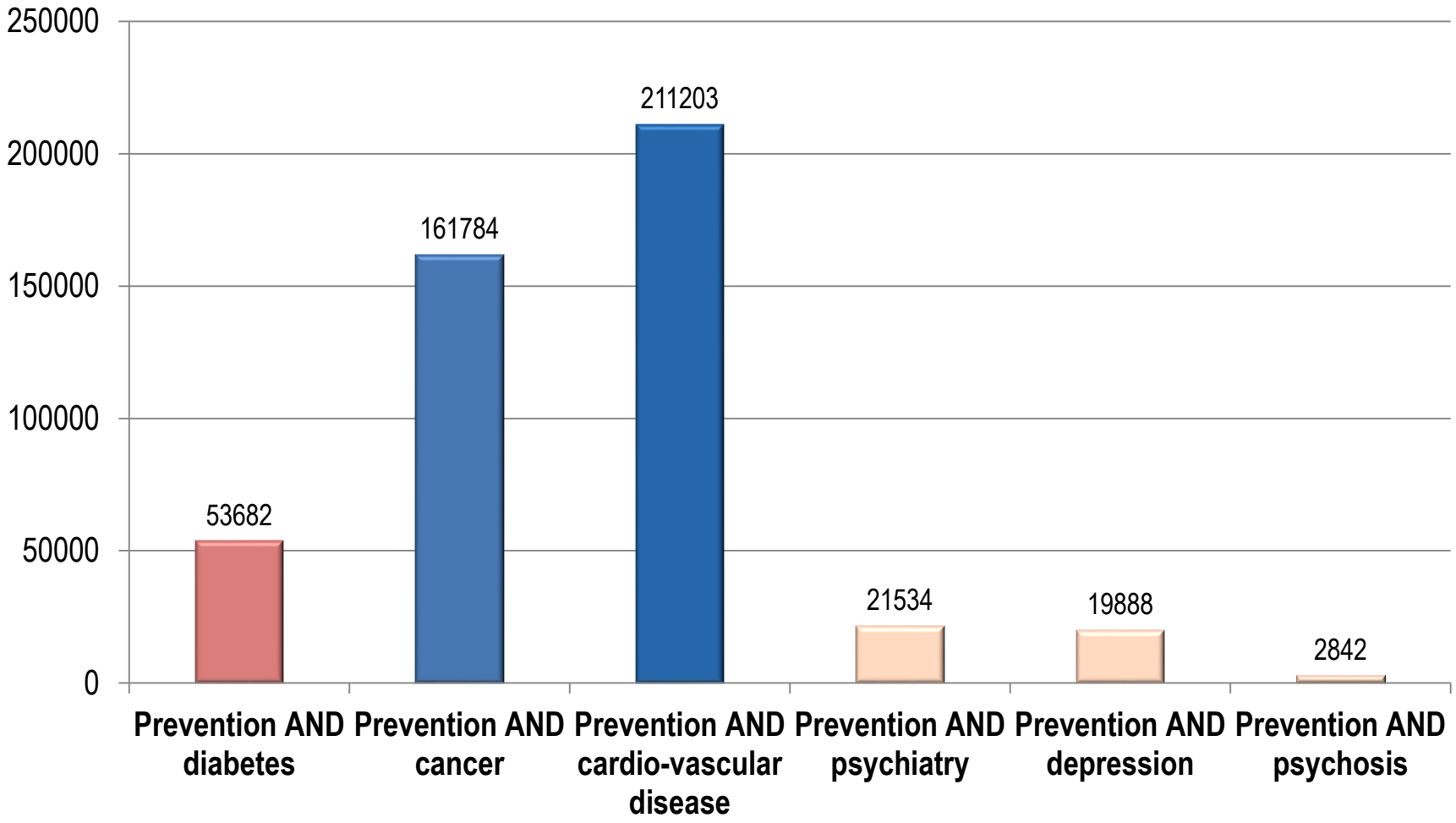


Rebecca Siegel, MPH[1]; Jiemin Ma, PhD[2,*]; Zhaohui Zou, MS[3]; Ahmedin Jemal, DVM, PhD[4]

CA CANCER J CLIN 2014;64:9–29

Prevention in psychiatry: A neglected topic?

Number of Pubmed citations for each search term



Prevention in psychiatry, a neglected topic

VIEWPOINT

Use of Clinical Preventive Services in Infants, Children, and Adolescents

Coleen A. Boyle, PhD
National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia.

James M. Perrin, MD
Division of General Pediatrics, Center for Child and Adolescent Health Research and Policy, MassGeneral Hospital for Children, Boston, Massachusetts; and Harvard Medical School, Pediatrics, Boston, Massachusetts.

Virginia A. Moyer, MD, MPH
American Board of Pediatrics, Chapel Hill, North Carolina.

At each stage from birth to young adulthood, the use of clinical preventive services (CPSs) provides an opportunity to intervene early to improve outcomes for many costly and complex conditions and to modify important disease-defining risk factors.[1] A number of important provisions of the Affordable Care Act (ACA) will provide impetus to improve the use of CPSs, in particular, the provision that such services are now covered without cost sharing.[2]

The Centers for Disease Control and Prevention (CDC) has collected baseline data and reported detailed information on a select set of CPSs for children to serve as a benchmark to measure change following ACA implementation.[3]

The selected CPSs were identified by the CDC because they represent important public health issues for which CPSs exist, the service was underused before ACA implementation, and national data (largely parent and self-report or provider office-based surveys) were available to establish a baseline (defined as prior to 2012). Other important CPSs for children were not included in the report because of the lack of

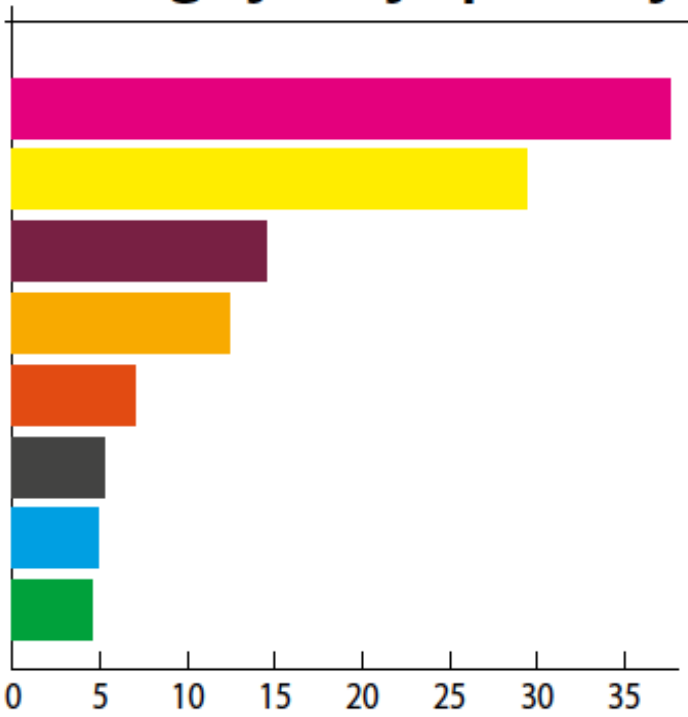
In infancy and early childhood, although 98% of all newborns were screened for hearing loss, 50% of children with a failed newborn hearing screen lacked documentation of a follow-up audiology evaluation. Without initiation of early diagnosis and subsequent communication services, the benefits of newborn hearing screening can be diminished.[4] Only 21% of all infants and toddlers were assessed in a standardized way for developmental delays. A higher percentage of parents (52%) reported informal monitoring (ie, discussion and questioning by the health care practitioner about parental concerns), but informal screening is less likely to result in appropriate identification of children with delays.[5] About one-third of children aged 1 to 2 years had screening for lead poisoning.

In early and middle childhood, when major chronic disease risk factors begin to emerge, key findings from the report indicate that between 56% and 86% of children did not receive preventive dental care, including topical fluoride application and dental sealants. Some dental services offered by physicians (eg, oral fluoride supplementation in preschool children and pediatric oral

JAMA Published online September 10, 2014

Prevention in psychiatry, a neglected topic

Average yearly spend by research activity (£m)



37.6	Underpinning research
29.4	Aetiology
14.5	Evaluation of treatments & therapeutic interventions
12.4	Health & social care services research
7.0	Development of treatments & therapeutic interventions
5.2	Detection, screening and diagnosis
4.9	Management of disease and conditions
4.5	Prevention of disease & conditions & promotion of wellbeing

On average, less than 4% of UK mental health research (£4.5m) goes directly on prevention.

UK Mental Health Research Funding Report. MQ Landscape Analysis. April, 2015

Reasons for lack of prevention in mental health

- It is not possible

- It is too expensive

Efficacy of primary prevention in child and adolescent mental health

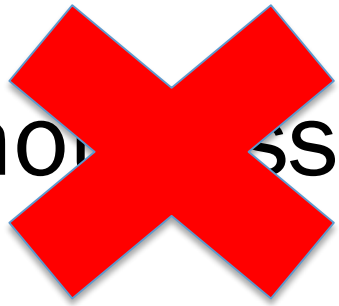
Table III. Mean Effect Sizes and 95% Confidence Intervals for Primary Prevention

Type of program	*n*	Mean effect[a]	95% CI
Environment-centered			
School-based	15	0.35	0.30–0.43
Parent training	10	0.16	–0.04–0.36
Transition programs			
Divorce	7	0.36	0.15–0.56
School entry/change	8	0.39	0.27–0.58
First-time mothers	5	0.87	0.66–1.07
Medical/dental procedure	26	0.46	0.35–0.58
Person-centered programs			
Affective education			
Children 2–7	8	0.70	0.49–0.91
Children 7–11	28	0.24[b]	0.18–0.31
Children over 11	10	0.33	0.18–0.48
Interpersonal problem solving			
Children 2–7	6	0.93	0.66–1.19
Children 7–11	12	0.36	0.23–0.48
Children over 11	0	—	—
Other person-centered programs			
Behavioral approach	26	0.49	0.38–0.59
Nonbehavioral approach	16	0.25	0.06–0.44

[a] All means differ significantly from zero except for Parent training.
[b] Only category in which mean effects are heterogeneous.

Reasons for lack of prevention in mental health

- It is not possible



- It is too expensive

Prevention in psychiatry pays off

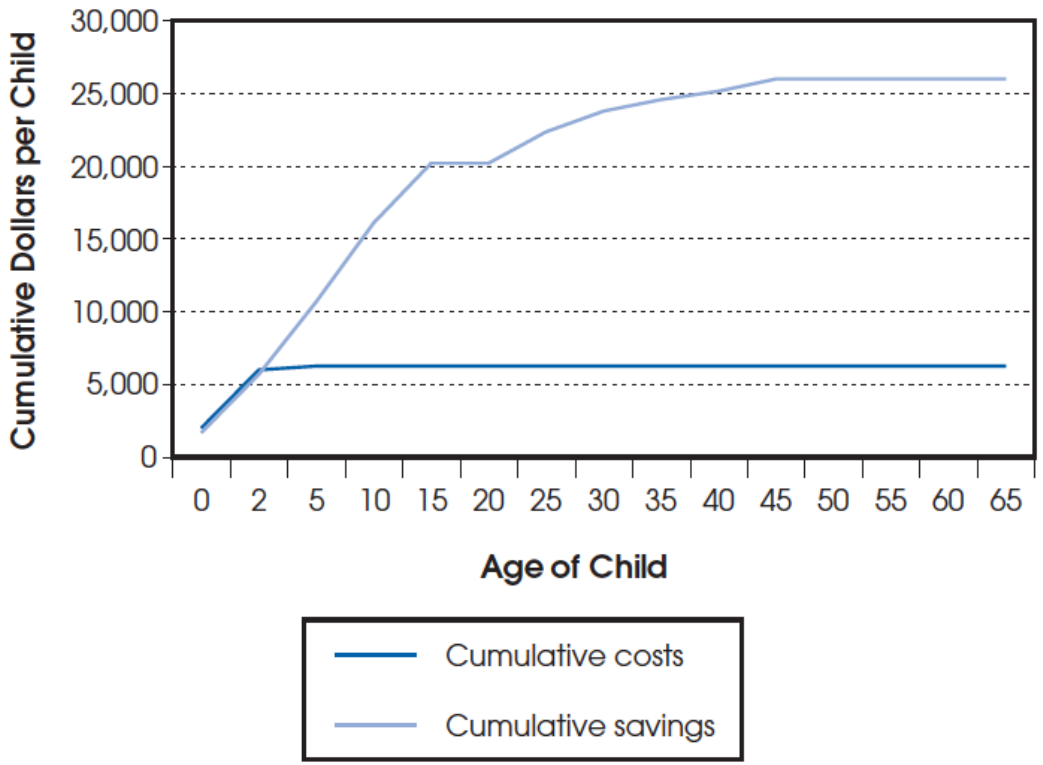
Table 13: Total returns on investment (all years): economic pay-offs per £1 expenditure [a]

	NHS	Other public sector	Non-public sector	Total
Early identification and intervention as soon as mental disorder arises				
Early intervention for conduct disorder	1.08	1.78	5.03	7.89
Health visitor interventions to reduce postnatal depression	0.40	–	0.40	0.80
Early intervention for depression in diabetes	0.19	0	0.14	0.33
Early intervention for medically unexplained symptoms [b]	1.01	0	0.74	1.75
Early diagnosis and treatment of depression at work	0.51	–	4.52	5.03
Early detection of psychosis	2.62	0.79	6.85	10.27
Early intervention in psychosis	9.68	0.27	8.02	17.97
Screening for alcohol misuse	2.24	0.93	8.57	11.75
Suicide training courses provided to all GPs	0.08	0.05	43.86	43.99
Suicide prevention through bridge safety barriers	1.75	1.31	51.39	54.45
Promotion of mental health and prevention of mental disorder				
Prevention of conduct disorder through social and emotional learning programmes	9.42	17.02	57.29	83.73
School-based interventions to reduce bullying	0	0	14.35	14.35
Workplace health promotion programmes	–	–	9.69	9.69
Addressing social determinants and consequences of mental disorder				
Debt advice services	0.34	0.58	2.63	3.55
Befriending for older adults	0.44	–	–	0.44

Knapp, McDaid and Parsonage, 2011

An example of a cost-efficient preventive intervention in children

Cumulative Costs and Savings for High-Risk Families in Elmira, NY, Nurse Home Visitation Program by Age of Child



Source: Reprinted with permission from Karoly, L.A., Greenwood, P.W., Everingham, S.S., et al. *Investing in our children: What we know and don't know about the costs and benefits of early childhood interventions.* Santa Monica, CA: RAND Corporation, 1998.

Reasons for lack of prevention in mental health

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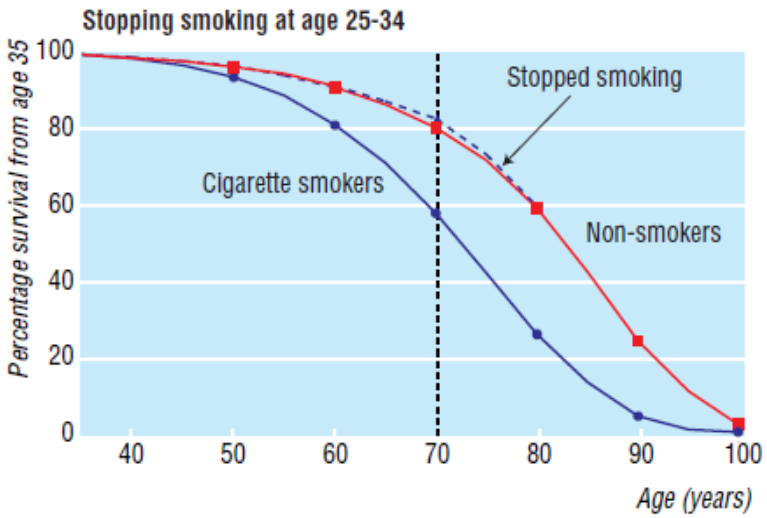
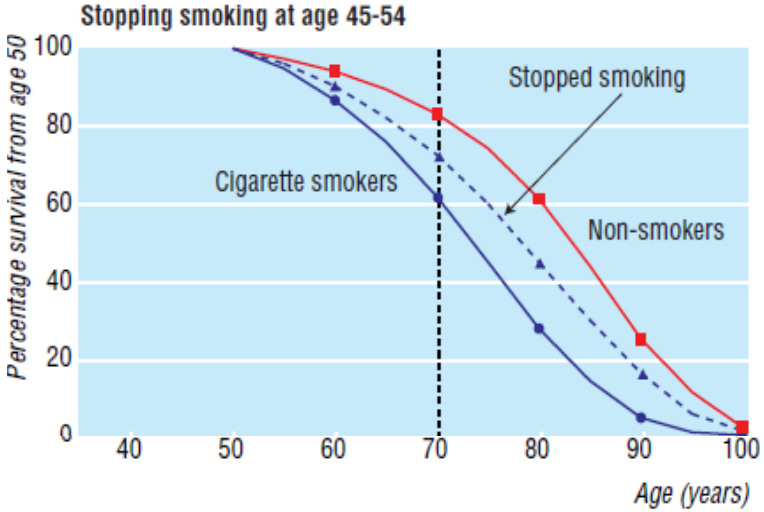
- It is too expensive

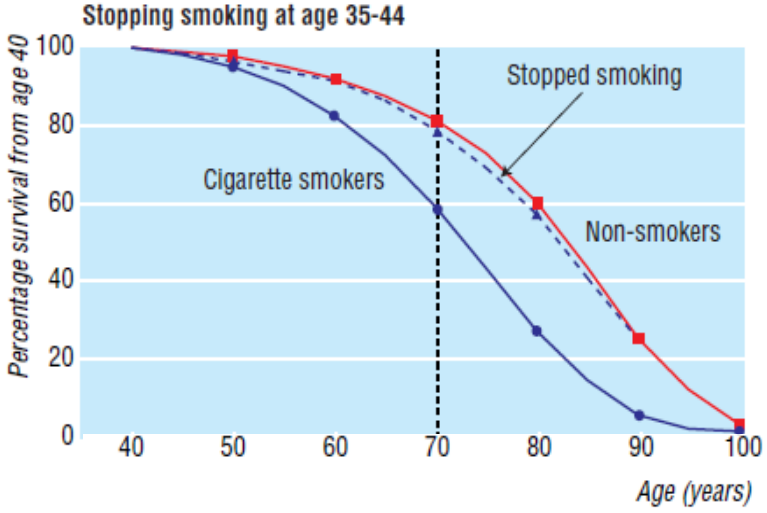
Why we get it all (or almost all) wrong?

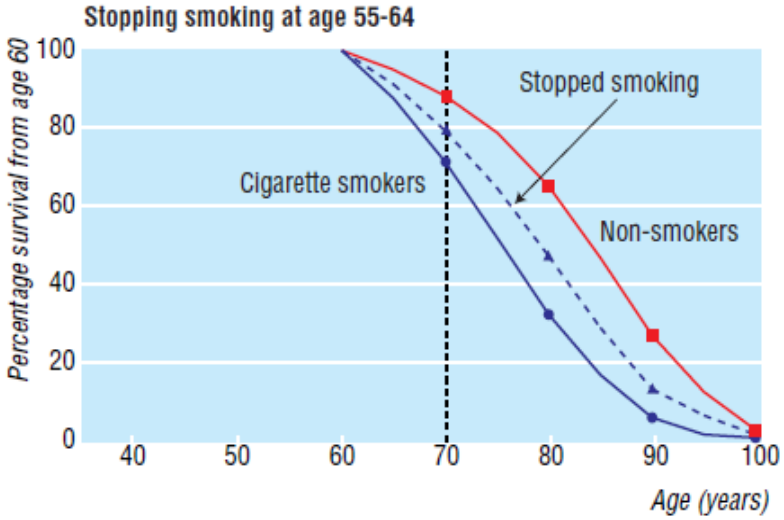
- *We act too late*

Efficacy of preventive interventions in medicine: Reduction in mortality by quitting smoking





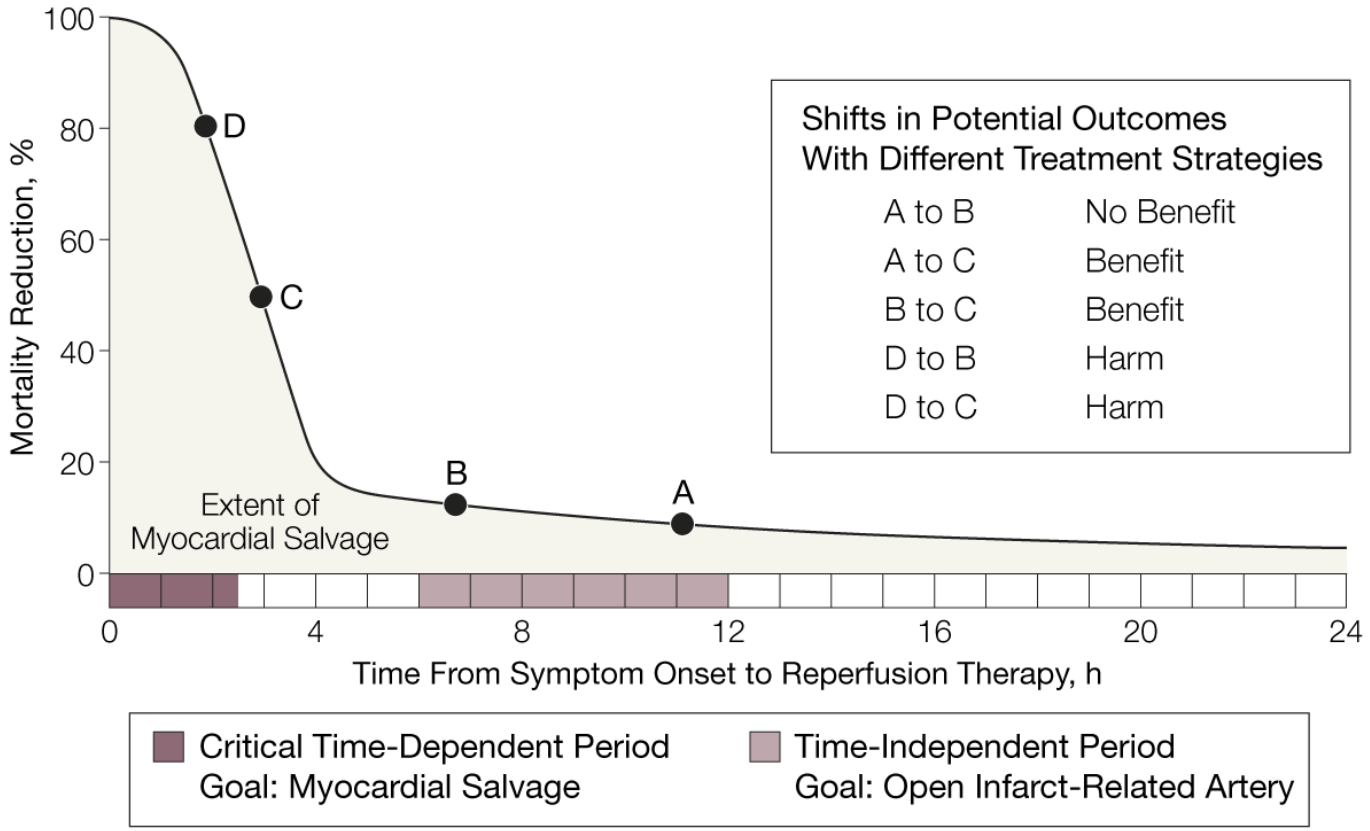




Doll et al., BMJ 2004

Critical periods for intervention

Theoretical Model of the Relationship Among the Duration of Symptoms of Acute MI Before Reperfusion Therapy, Mortality Reduction, and Extent of Myocardial Salvage



Gersh et al.,

Eur Child Adolesc Psychiatry
DOI 10.1007/s00787-013-0434-6

EDITORIAL

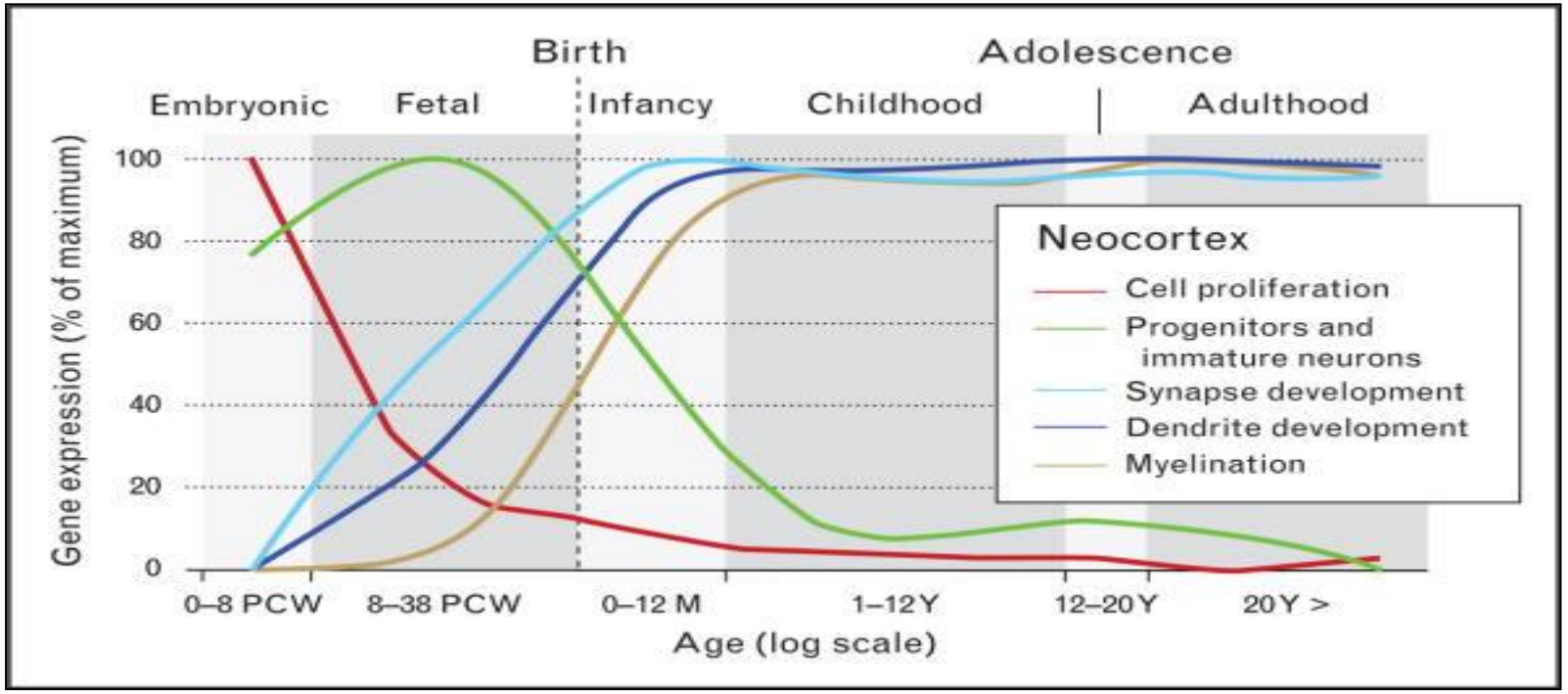
Why psychogeriatrics starts right after adolescence

Mara Parellada

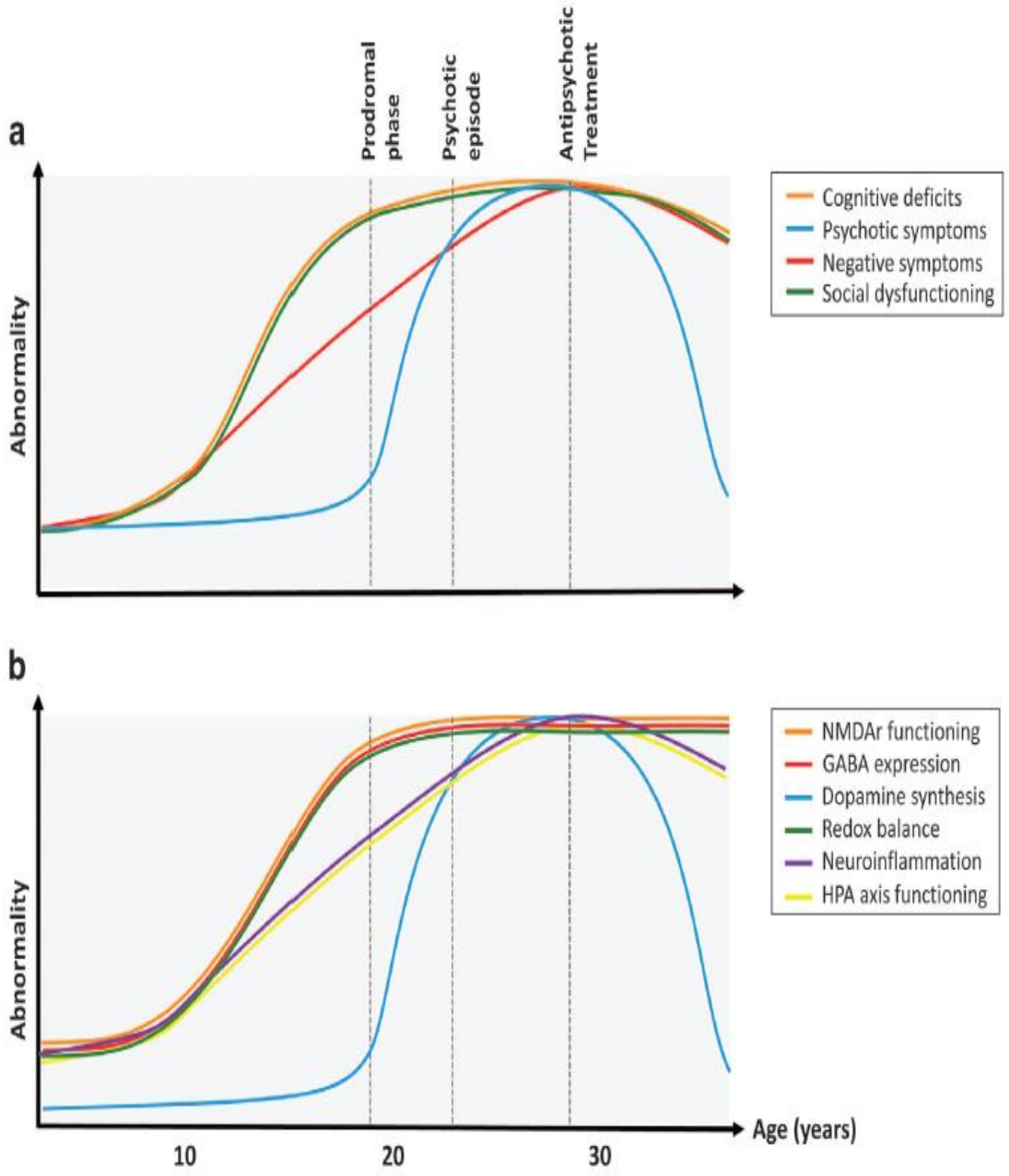
The borders between pediatric and adult medical specialties are always somewhat artificial, and based on spurious considerations, such as usually attaining the age of majority, i.e., 18 years; however, the borders between so-called child and adolescent (C&A) psychiatry and adult

females at 11.8 years [2]. The visual, auditory, and limbic cortices, which myelinate early, show a more linear pattern of aging than the frontal and parietal neocortices, which continue myelination into adulthood. Except for the posterior temporal regions, which have a more protracted

Critical periods for intervention



Graph developed by Council for Early Child Development (Nash 1997, Early Years Study 1999, Shonkoff 2000)



IE Sommer *et al*

npj Schizophrenia (2016) 16003

Critical periods for intervention

AN EXAMPLE: EARLY INTERVENTION IN AUTISM

TABLE 3.
Treatment Outcomes for Children in Groups 1 and 2 and for the Total Sample

		Percent (and number) of children who	
Group	Total	Achieved Positive Treatment Outcome	Remained in Comprehensive Intervention Program
Group 1—Program entry at 60 months or earlier	100% (9)	67% (6)	33% (3)
Group 2—Program entry after 60 months	100% (9)	11% (1)	89% (8)
Total	100% (18)	39% (7)	61% (11)

$\chi^2 (1) = 5.86, p < .02$

Fenske et al., ***Analysis and Intervention in Developmental Disabilities***, Vol. 5, pp. 49–58, 1985

Why do we get it all (or almost all) wrong?

- *We act too late*

- *Prevention is a politician´s decision:*
  - *They are adults*
  - *They think this is something they will never use*
  - *Its pays off in the long term (and cannot be sold in the next 4 years)*

Don Juan de Palafox y Mendoza

“Kingdoms that govern with remedies rather than prevention are headed for disaster”

(June 26, 1600 – October 1, 1659)

Why do we get it all (or almost all) wrong?

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- *Lack of integration between child and adult services*


NO ADULTS
ALLOWED UNLESS
ACCOMPANIED
BY CHILDREN
SEC. 3.02 PARK CODE

Outline

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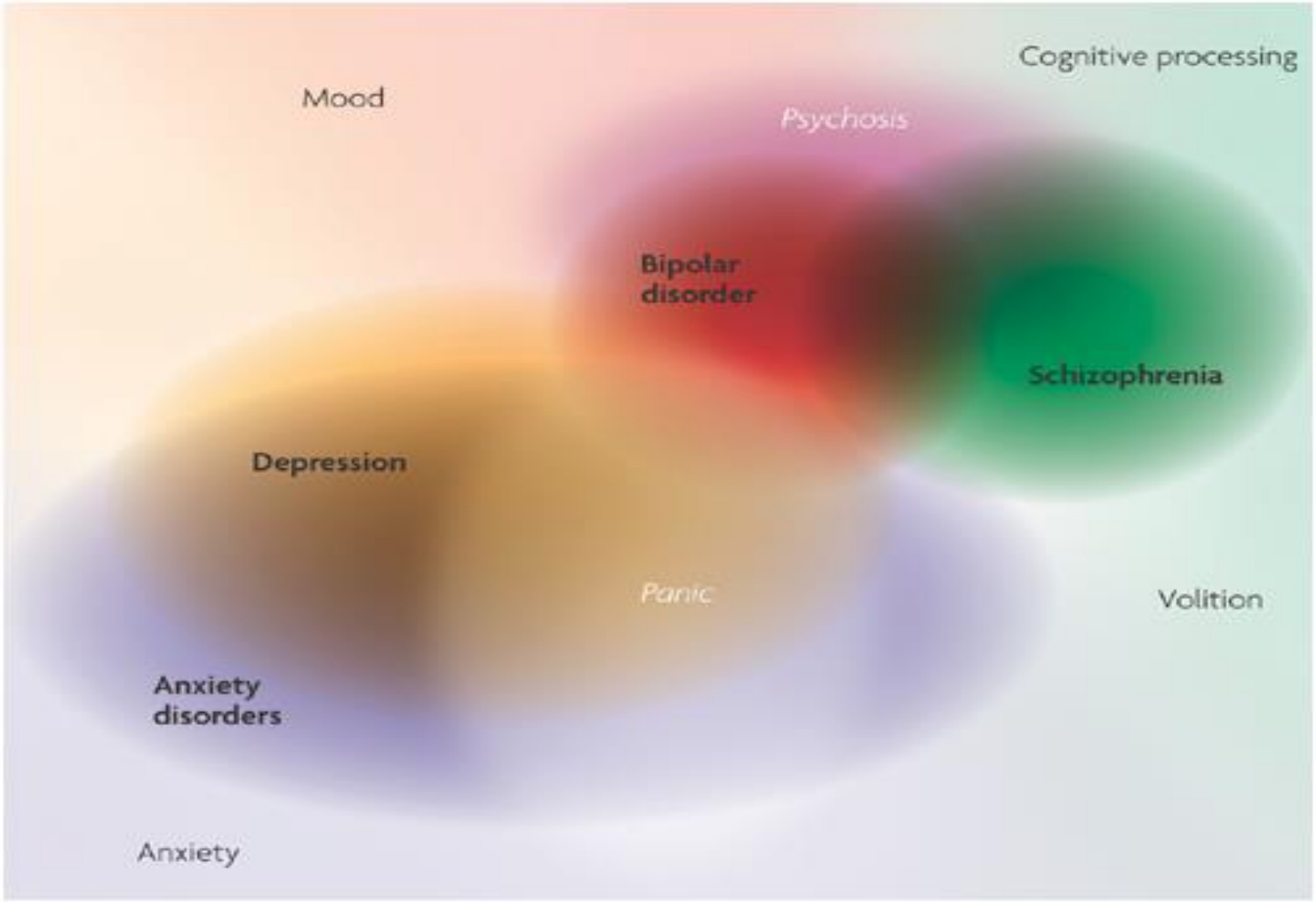
Early developmental signs in psychosis

	 Newborn-3 months	 Infancy 3-12 months	 Toddler- Pre-schooler 1-4 years	 Elementary school 5-12 years
Neuromotor and Minor Physical Anomalies		Sitting, walking, and standing delays	Potty training delays	Poor coordination and clumsiness, unusual movements
Speech/Language/ Hearing			Delays in speech and in receptive language, hearing impairments	Poor abnormal speech acquisition and quality; abnormal language including echolalia, meaningless laughter
Socioemotional Behavior			Preference for solitary play; less joy, more negative affect	More internalizing and externalizing disorders, psychotic symptoms at age 11-14
Cognition			Poorer IQ scores	Poorer IQ scores, declines in IQ scores from 4-7 years, poorer performance in other cognitive tasks

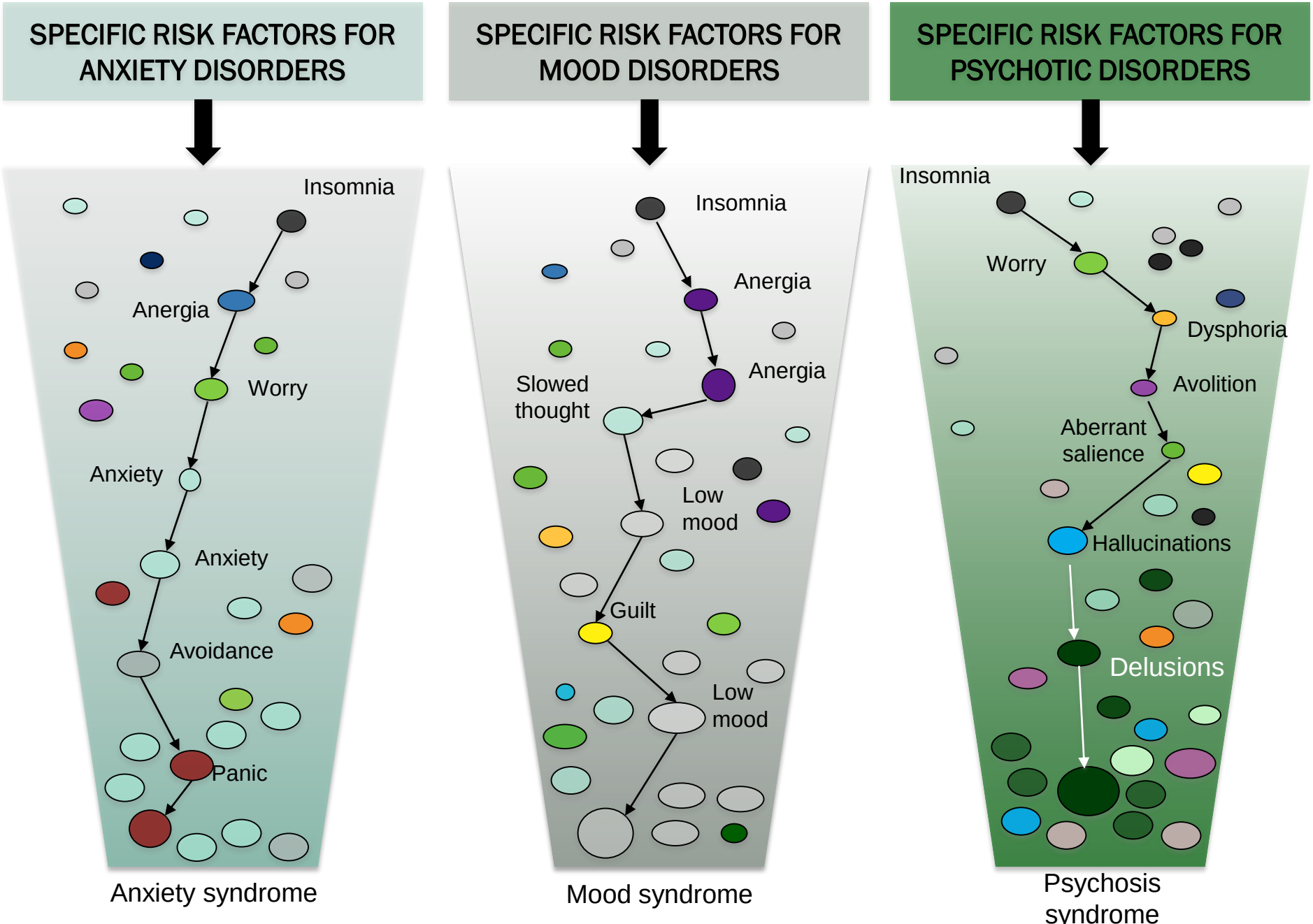
Adapted from Liu et al. Schizophrenia Bulletin, 2015.

What are we trying to prevent when we try to prevent psychosis?

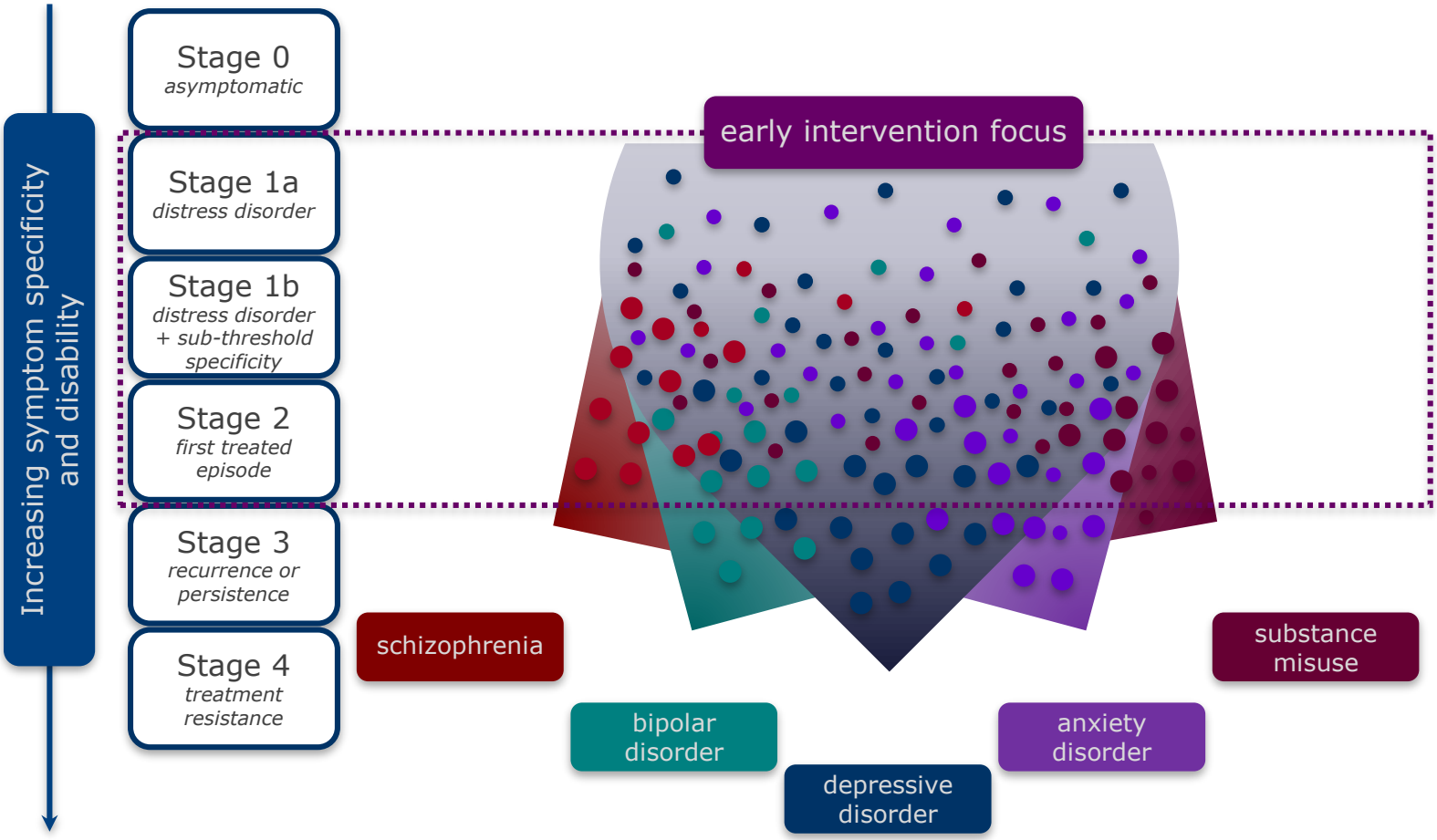


Burmeister et al.,

Risk factor silos and the pathways to specific (DSM5) conditions



Early manifestations of mental disorders are non-specific: pluripotentiality and staging



Shared genetic risk factors among neurodevelopmental disorders

Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis

*Cross-Disorder Group of the Psychiatric Genomics Consortium**

Summary

Background Findings from family and twin studies suggest that genetic contributions to psychiatric disorders do not in all cases map to present diagnostic categories. We aimed to identify specific variants underlying genetic effects shared between the five disorders in the Psychiatric Genomics Consortium: autism spectrum disorder, attention deficit-hyperactivity disorder, bipolar disorder, major depressive disorder, and schizophrenia.

Methods We analysed genome-wide single-nucleotide polymorphism (SNP) data for the five disorders in 33 332 cases and 27 888 controls of European ancestory. To characterise allelic effects on each disorder, we applied a multinomial logistic regression procedure with model selection to identify the best-fitting model of relations between genotype

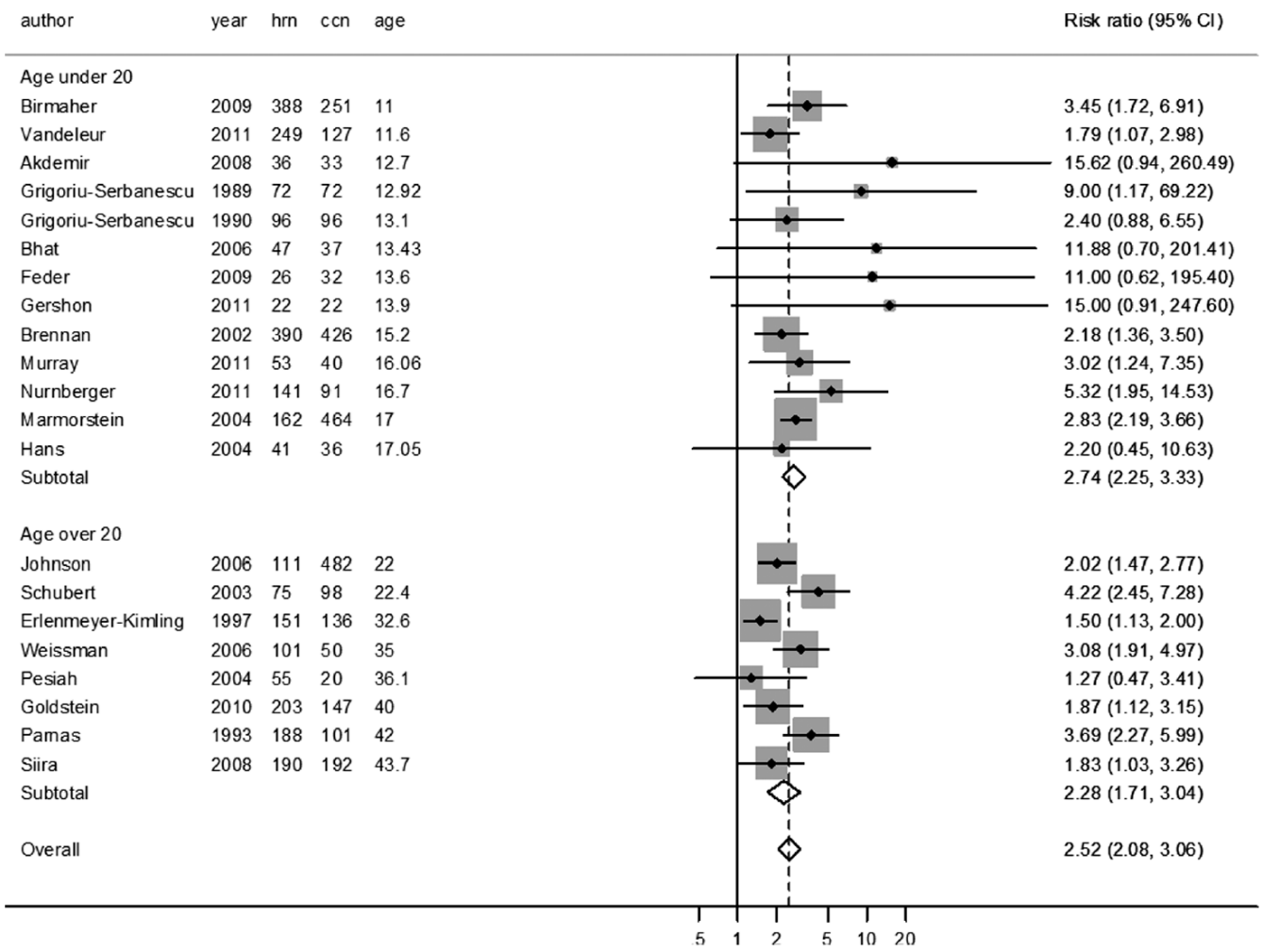
Lancet 2013; 381: 1371–79

Published Online
February 28, 2013
http://dx.doi.org/10.1016/S0140-6736(12)62129-1

This online publication has been corrected. The corrected version first appeared at thelancet.com on April 19, 2013

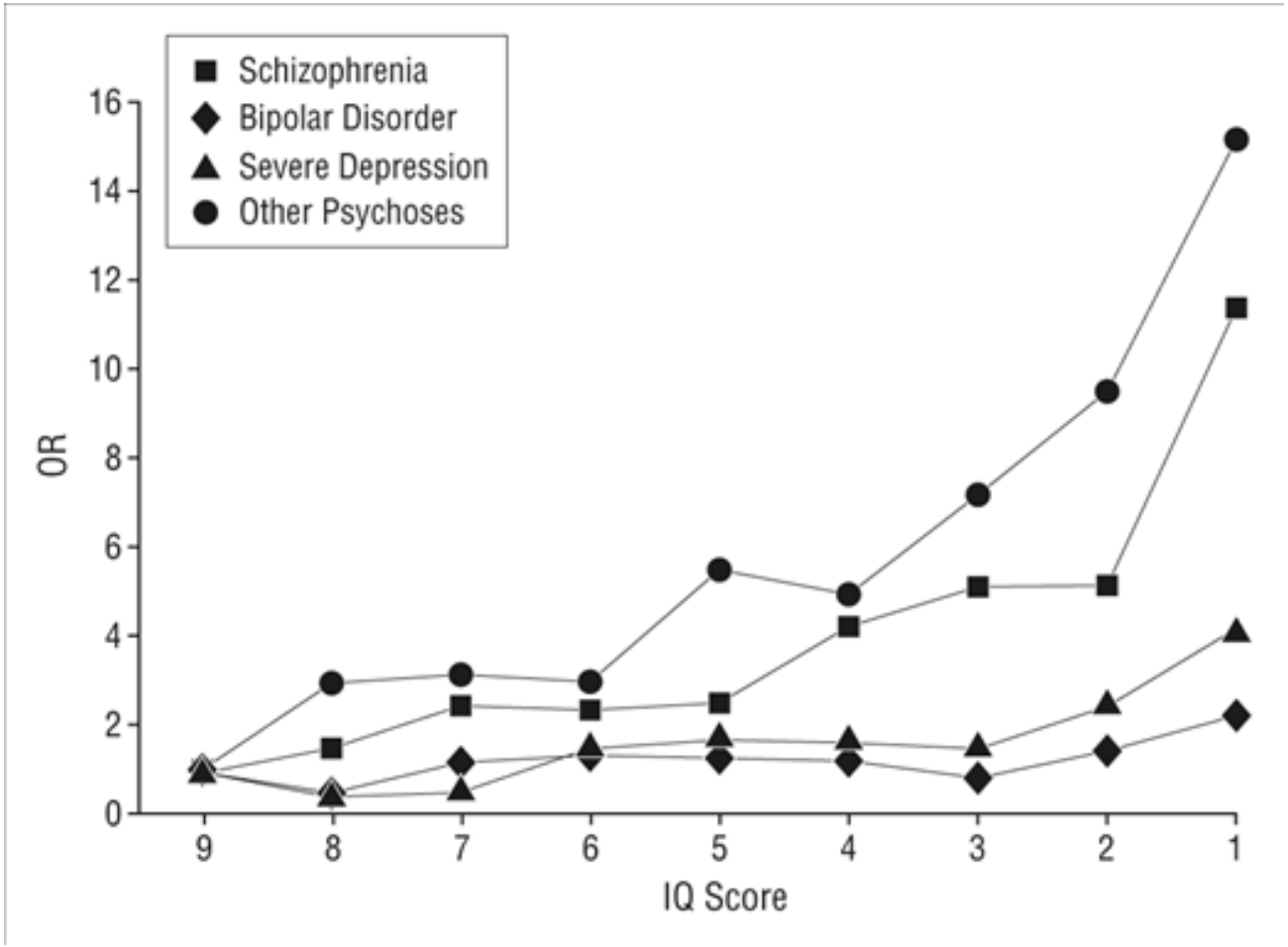
PGC, Lancet, 2013

Psychopathology in the offspring of patients with schizophrenia, bipolar disorder or depression



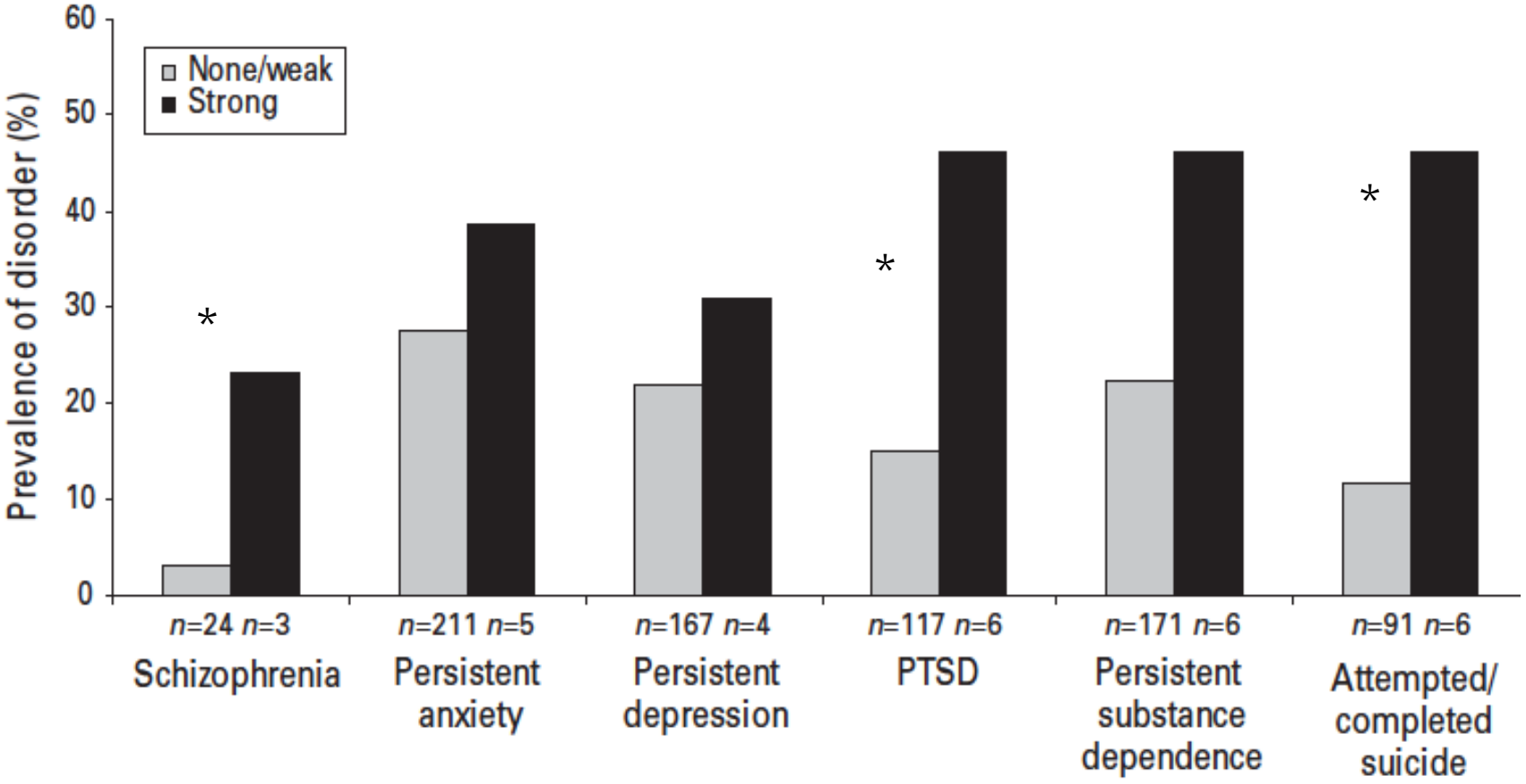
Rasic et al., Schiz Bulletin 2014

Children with low IQ are at risk of psychosis and other mental disorders



Zammit et al., Arch Gen Psychiatry. 2004;61(4):354-360.

Psychotic symptoms in childhood as a marker of general vulnerability



H. L. Fisher et al.

Psychological Medicine (2013), **43**, 2077–2086.

Schizophrenia Bulletin vol. 41 no. 4 pp. 963–970, 2015
doi:10.1093/schbul/sbu119
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Risk of Schizophrenia Increases After All Child and Adolescent Psychiatric Disorders: A Nationwide Study

Cecilie Frejstrup Maibing[*,1,4], Carsten Bøcker Pedersen[2–4], Michael Eriksen Benros[1,2,4], Preben Bo Mortensen[2,4], Søren Dalsgaard[2,4–6], and Merete Nordentoft[1,6]

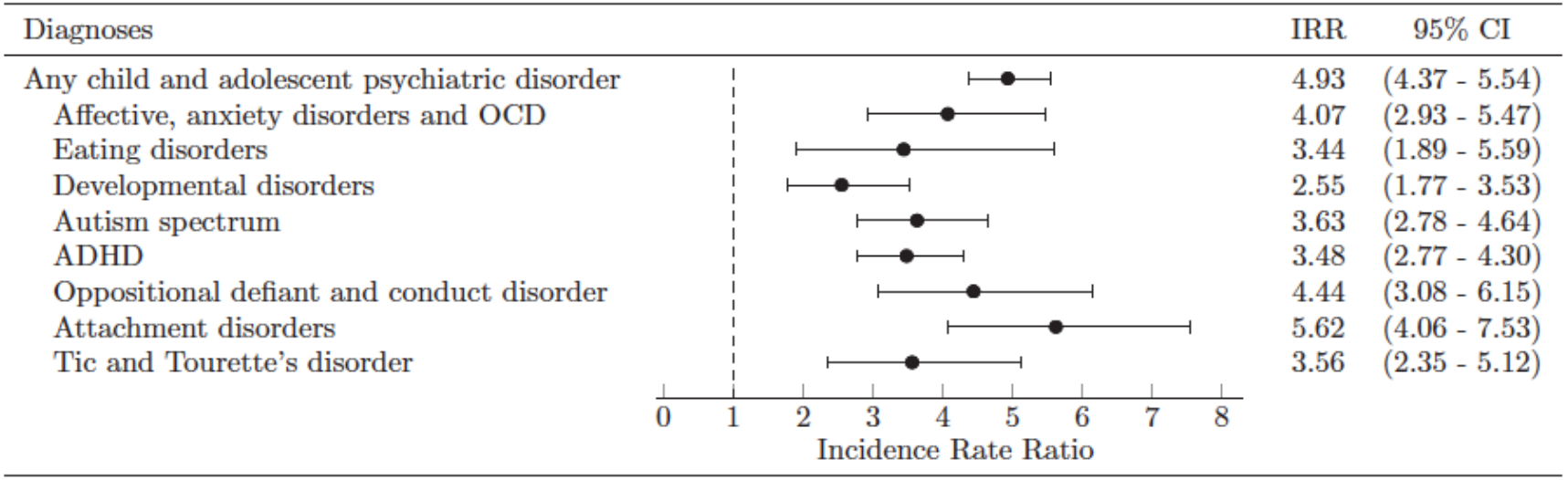


Fig. 1. Risk of schizophrenia spectrum disorders >5 years after onset of child and adolescent psychiatric disorders.

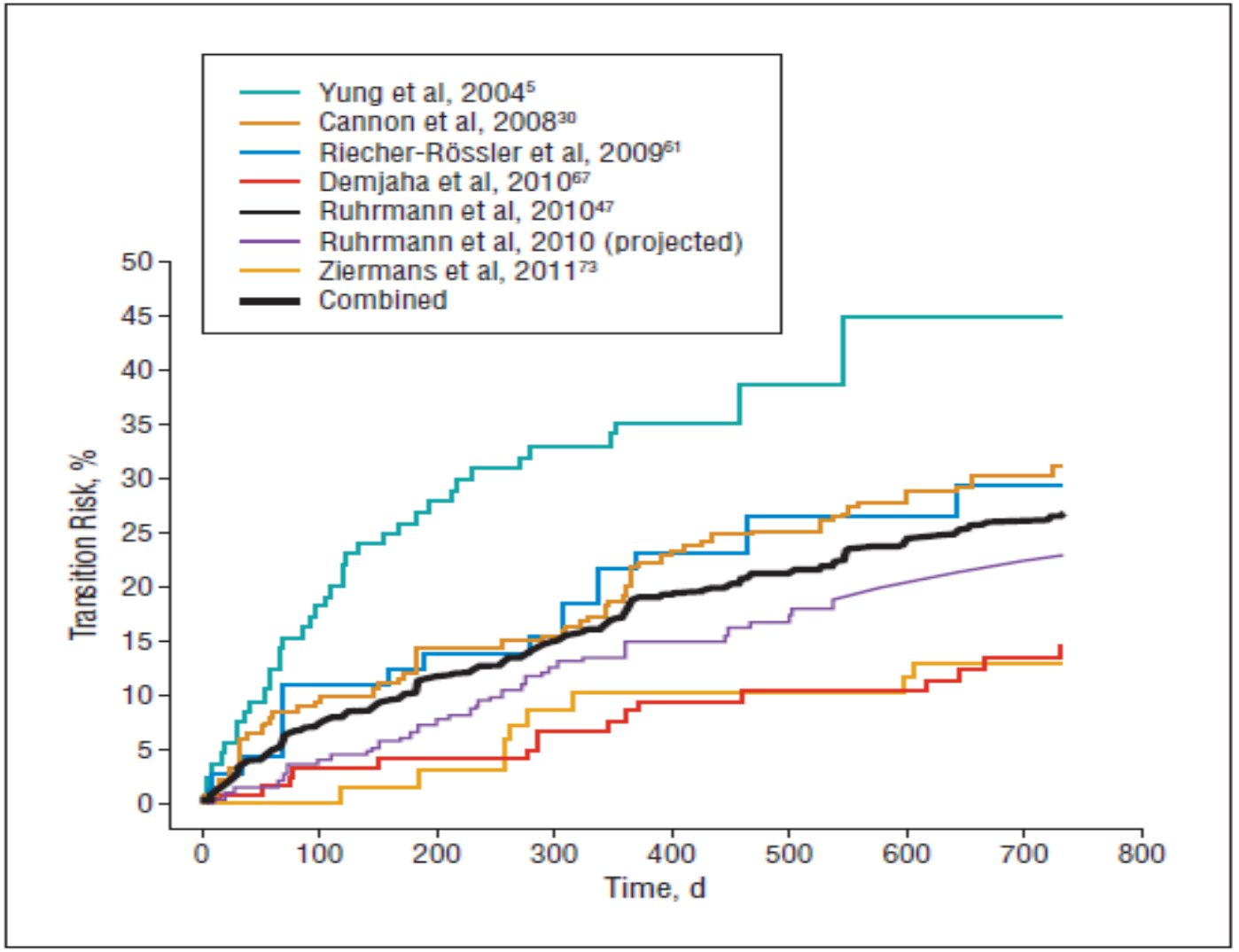
Are “prodromal” subjects healthy people at high risk for psychosis?

Table 2
SCID diagnoses.

SCID-IV diagnosis	Clinical high risk (N=360)	Control (N=108)	Significance of χ^2
Depression – current	41.4%	1.7%	<0.0001
Depression – lifetime	35.1%	5.6%	<0.0001
Lifetime alcohol	10.7%	1.1%	<0.0001
Current cannabis abuse	5.8%	1.1%	<0.05
Lifetime cannabis abuse	12.8%	2.8%	<0.001
Current OCD	7.8%	0%	<0.0001
Lifetime OCD	4.6%	0%	<0.01
Current PTSD	2.6%	0%	<0.05
Lifetime PTSD	4.1%	0%	<0.01
Current panic	13.3%	0.6%	<0.0001
Lifetime panic	9.3%	0%	<0.0001
Current social phobia	13.6%	0%	<0.0001
Lifetime social phobia	7.5%	0.6%	<0.0001
Current specific phobia	11.0%	0%	<0.0001
Lifetime specific phobia	6.4%	0.6%	<0.01
Current GAD or NOS	20.3%	2.2%	<0.0001
Lifetime GAD or NOS	9.0%	0.6%	<0.001
Current attention-deficit/hyperactivity	15.7%	1.7%	<0.0001
Lifetime attention-deficit/hyperactivity	10.8%	2.2%	<0.01
Current learning disorder NOS	2.3%	0%	<0.05
Current avoidant	10.4%	0%	<0.0001
Lifetime avoidant	4.6%	0%	<0.01
Current schizotypal	18.3%	0%	<0.0001
Lifetime schizotypal	7.2%	0%	<0.0001
Current borderline	3.8%	0%	<0.01

J. Addington et al. / Schizophrenia Research 142 (2012) 77–82

Transition rates in patients at ultra-high risk of psychosis are about one-third



Fusar-Poli et al., *Arch Gen Psychiatry. 2012;69(3):220-229*

Outcomes of Nontransitioned Cases in a Sample at Ultra-High Risk for Psychosis

TABLE 3. Course of Nonpsychotic Disorders in Young People at Ultra-High Risk for Psychosis at Baseline

	Entire Cohort (N=203)[a]		1993–2000 Subsample (N=61)[a]		2001–2003 Subsample (N=77)		2004–2006 Subsample (N=65)	
Status of Nonpsychotic Disorder	N	%	N	%	N	%	N	%
Present at baseline								
Any disorder	173	90.1	47	94.0	73	94.8	53	81.5
Any mood disorder	145	71.4	33	54.1	61	79.2	51	78.5
Any anxiety disorder	81	39.9	21	34.4	34	44.2	26	40.0
Any substance use disorder	42	21.9	17	34.0	21	27.3	4	6.1
Remitted								
Any disorder	50	26.0	12	24.0	22	28.6	16	24.6
Any mood disorder	67	33.0	13	21.3	31	40.3	23	35.4
Any anxiety disorder	48	23.6	13	21.3	22	28.6	13	20.0
Any substance use disorder	20	10.4	7	14.0	12	15.6	1	1.5
Incident								
Any disorder	72	37.5	24	48.0	24	31.2	24	36.9
Any mood disorder	19	9.3	9	14.8	4	5.2	6	9.2
Any anxiety disorder	36	17.7	13	21.3	11	14.3	12	18.5
Any substance use disorder	33	17.2	7	14.0	12	15.6	14	21.5
Persistent or recurrent								
Any disorder	99	51.6	29	58.0	40	51.9	30	46.1
Any mood disorder	78	38.4	20	32.8	30	39.0	28	43.1
Any anxiety disorder	33	16.2	8	13.1	12	15.6	13	20.0
Any substance use disorder	22	11.5	10	20.0	9	11.7	3	4.6
Never present								
Any disorder	14	7.3	5	10.0	3	3.9	6	9.2
Any mood disorder	39	19.2	19	31.1	12	15.6	8	12.3
Any anxiety disorder	86	42.3	27	44.3	32	41.6	27	41.5
Any substance use disorder	117	60.9	26	52.0	44	57.1	47	72.3

Lin, Wood, Nelson et al., Am J Psychiatry, 2015

Preventing psychosis: when?

VIEWPOINT

Mental Disorders in Childhood
Shifting the Focus From Behavioral Symptoms to Neurodevelopmental Trajectories

Thomas R. Insel, MD
National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland.

Author Reading at jama.com

The recent Global Burden of Disease Study reported on morbidity and mortality for 291 disorders and injuries across 187 countries.[1] Expressed as "years lost to disability," mental and substance abuse disorders accounted for nearly 23% of global morbidity, more than any other group of disorders.[2] Although it may seem surprising that mental and substance abuse disorders would, by this measure, be more disabling than heart disease or cancer, at least part of the explanation velopment are extraordinary. In contrast to other organ systems, the brain develops, in part, through the exuberant overproduction of cells and connections, followed by a several-year sculpting of pathways by massive elimination of much of the neural architecture along with myelination of select fibers for rapid transmission of information. The human brain continues to develop into the third decade, with cortical maturation usually not completed until age 25.

Differential Neurodevelopmental Trajectories in Patients With Early-Onset Bipolar and Schizophrenia Disorders

Celso Arango*[1,2], David Fraguas[1], and Mara Parellada[1]

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Schizophrenia and bipolar disorders share not only clinical features but also some risk factors such as genetic markers and childhood adversity, while other risk factors such as urbanicity and obstetric complications seem to be specific to schizophrenia. An intriguing question is whether the well-established abnormal neurodevelopment present in many children and adolescents who eventually develop schizo-

that the consequences of genetic predisposition and early adverse events, such as insults during gestation, would be latent throughout the first 2 decades of life and would only manifest as psychosis in early adulthood when normative maturational changes "unmask" an earlier insult. This hypothesis had been postulated some years earlier by John Strauss and William

The trajectory to schizophrenia

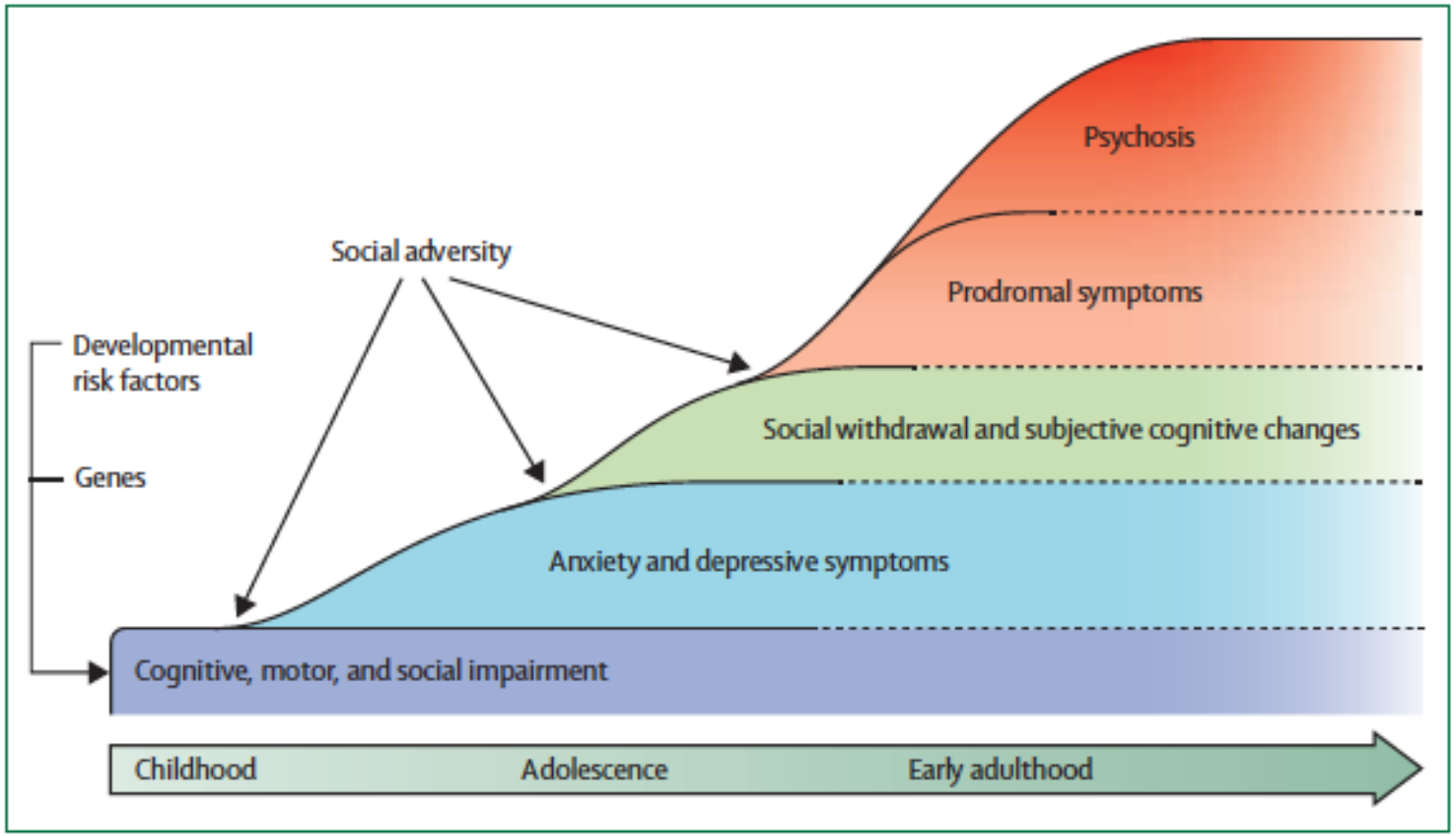


Figure 1: **The trajectory to schizophrenia showing the evolution of symptoms and the main risk factors**

Oliver D Howes, Robin M Murray

Lancet 2014; 383: 1677–87

Brain changes predate the onset of psychosis

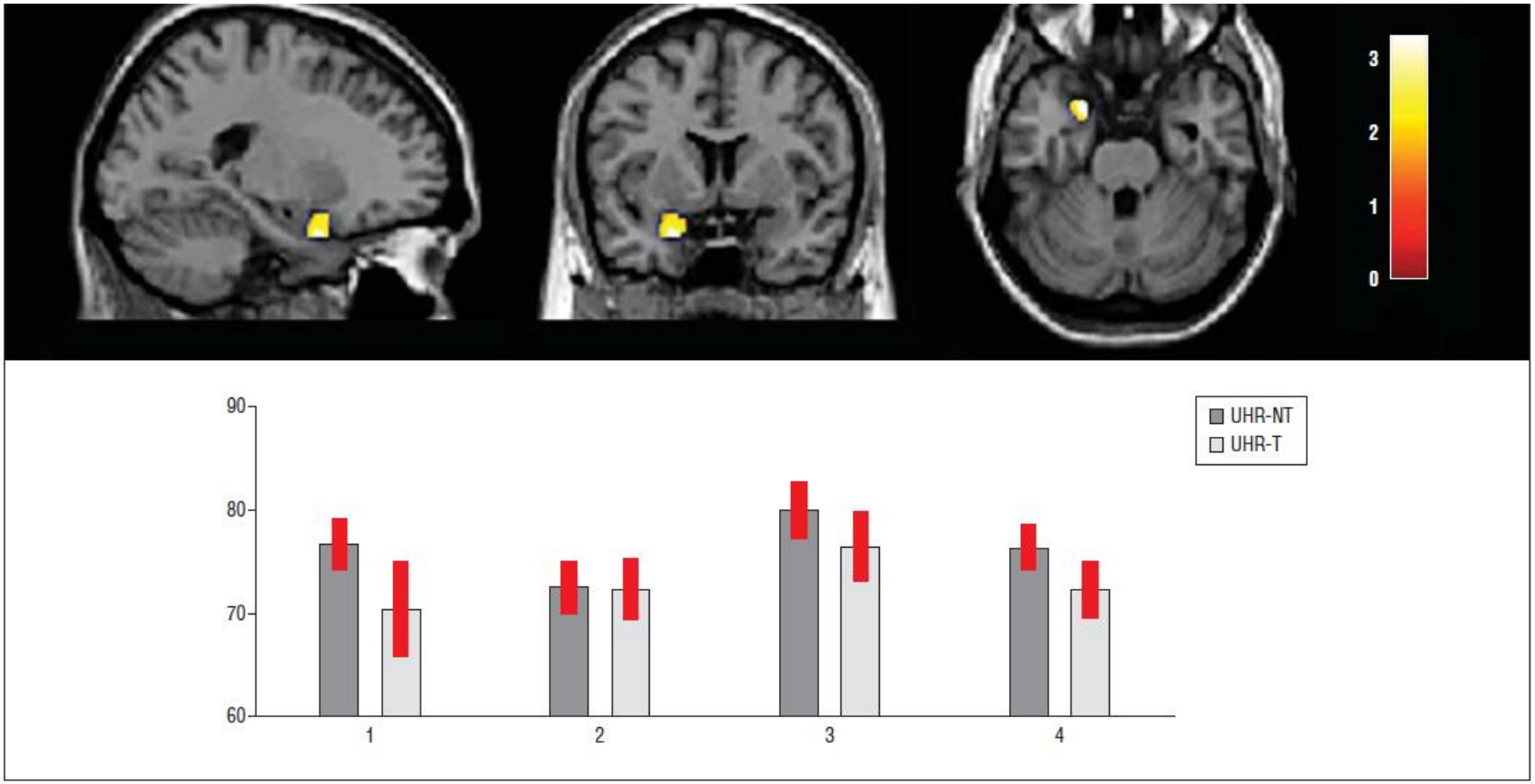


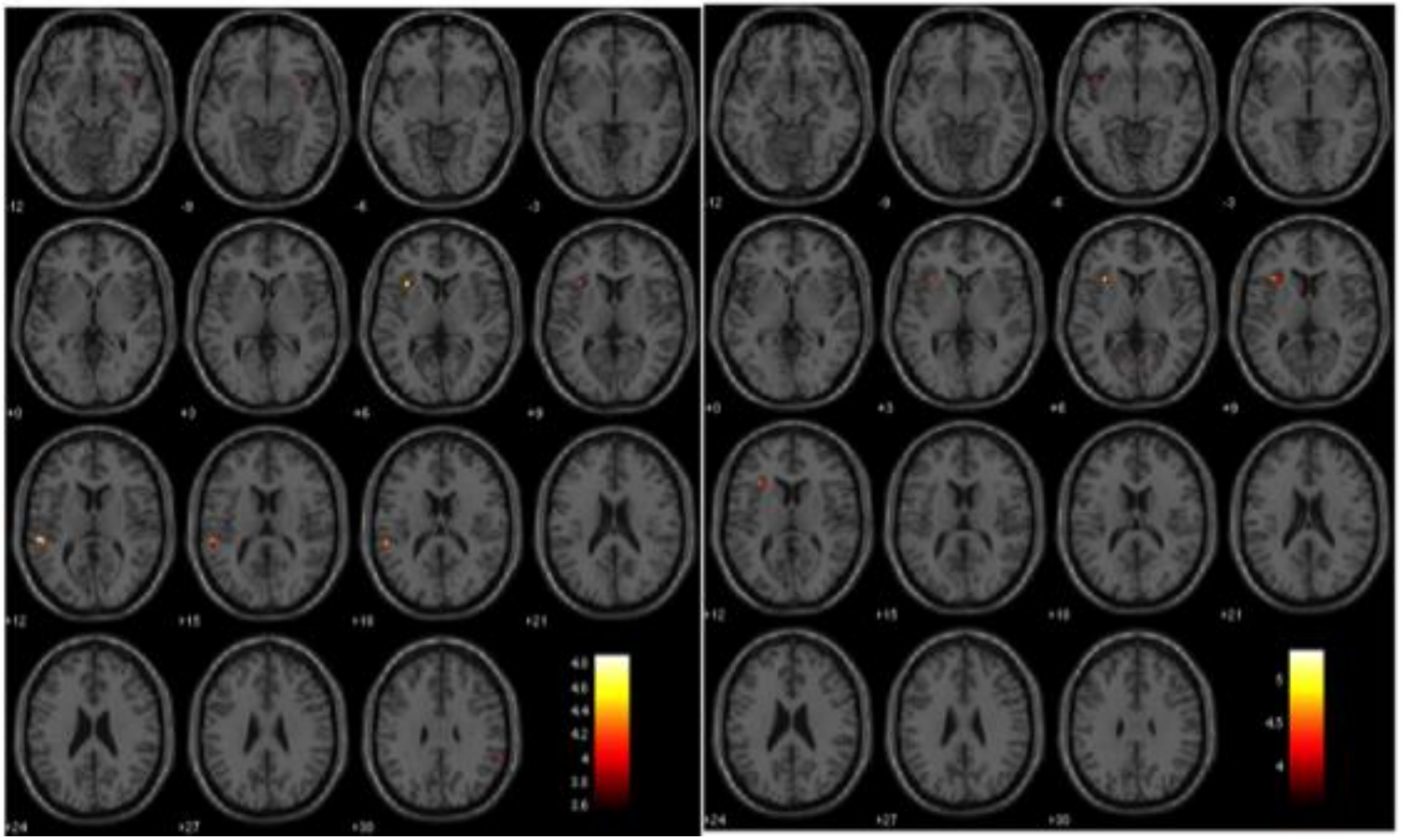
Figure 2. Differences between ultra-high-risk (UHR) individuals who did (UHR-T) and did not (UHR-NT) develop psychosis. The UHR-T individuals had less gray matter volume than did the UHR-NT individuals in the left parahippocampal gyrus, bordering the uncus (MNI [Montreal Neurological Institute] coordinates x, y, and z: –21, 6, and –27, respectively). For visualization purposes, effects are displayed at $P < .05$ uncorrected. The plot shows mean gray matter volumes for the 2

Mechelli et al.

ARCH GEN PSYCHIATRY/VOL 68 (NO. 5), MAY 2011

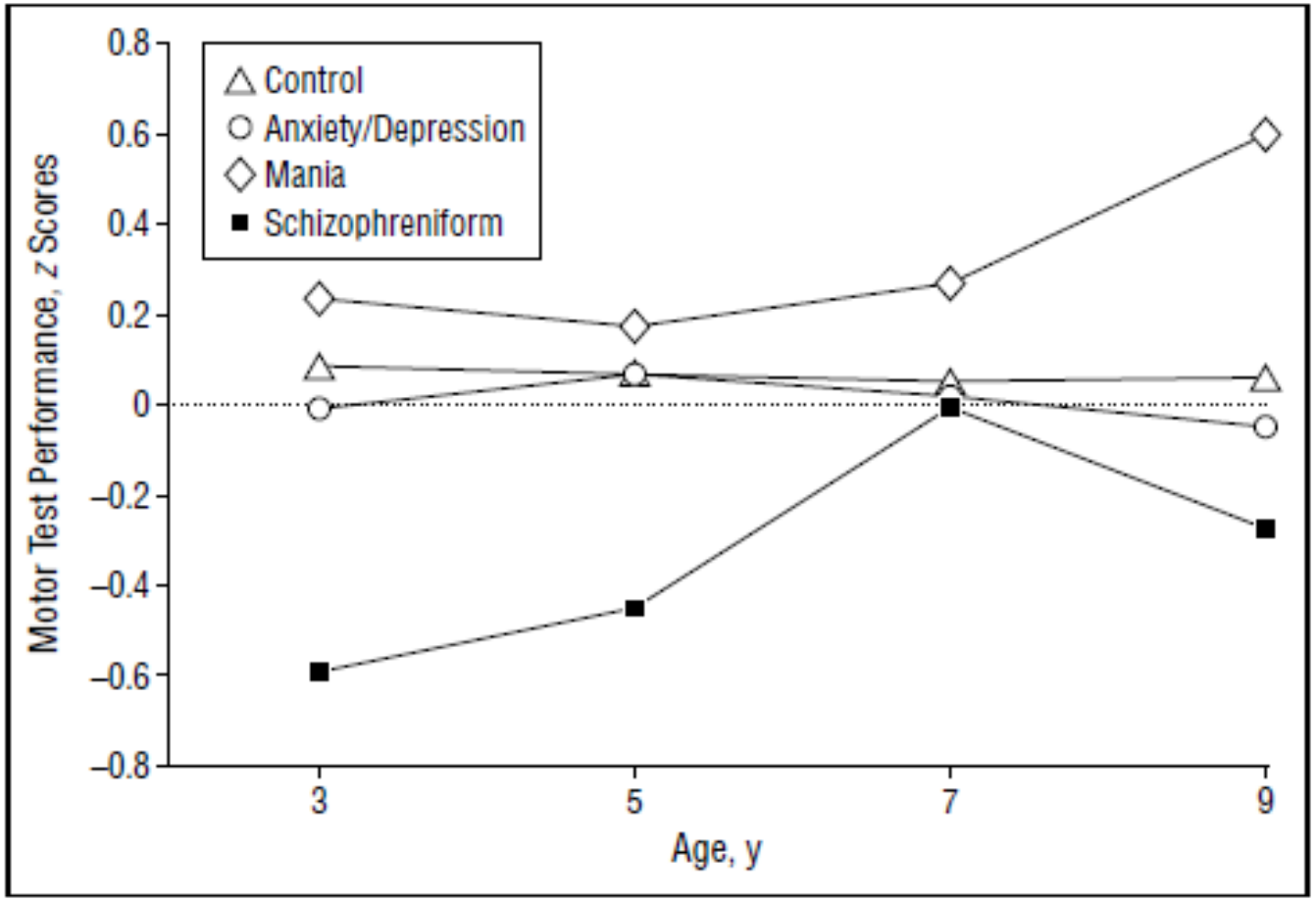
Brain changes are also present in child offspring of individuals with bipolar disorder or schizophrenia

Fig1. Significant clusters of relatively decreased gray matter volume in SzO relative to CcO and in SzO relative to BpO



Sugranyes et al., JAACAP. In press

Abnormalities in early motor development in psychosis



Cannon, Caspi et al., Arch Gen Psychiatry 2002

Premorbid adjustment difficulties in EOP

Schizophrenia Research 146 (2013) 103–110

Contents lists available at SciVerse ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Premorbid impairments in early-onset psychosis: Differences between patients with schizophrenia and bipolar disorder

Beatriz Payá [a,*], Jose Manuel Rodríguez-Sánchez [a], Soraya Otero [a], Pedro Muñoz [b], Josefina Castro-Fornieles [c], Mara Parellada [d], Ana Gonzalez-Pinto [e], Cesar Soutullo [f], Inmaculada Baeza [c], Marta Rapado-Castro [d], Margarita Sáenz-Herrero [e], Dolores Moreno [d], Celso Arango [d]

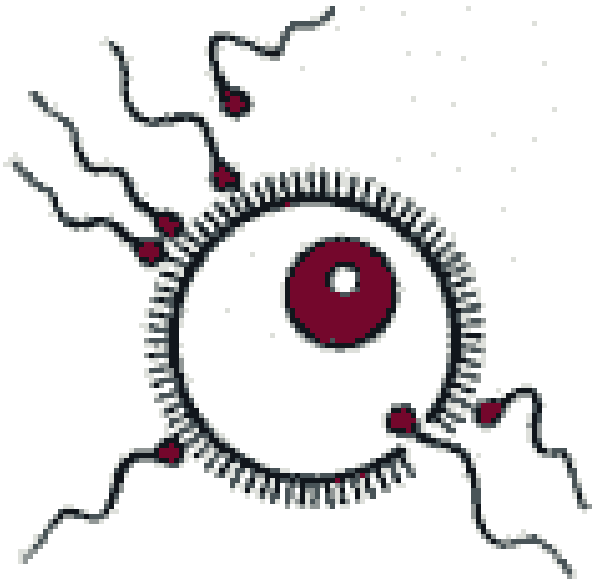
Table 3
Childhood PAS scores in schizophrenia and bipolar disorder compared with healthy control group.

	SZ (N = 46)		BP (N = 23)		Controls (N = 91)		Statistic		Comparisons[a]
	χ	SD	χ	SD	χ	SD	F[b]	p	
Total PAS-C	0.36	0.21	0.28	0.16	0.12	0.10	**18.554**	**<0.001**	Controls<SZ***; Controls<BP***
PAS Acad-C	0.36	0.21	0.35	0.20	0.16	0.13	**5.784**	**0.004**	Controls<SZ**; Controls<BP*
PAS Social-C	0.36	0.28	0.21	0.21	0.08	0.13	**20.787**	**<0.001**	Controls<SZ***; controls<BP**
PAS1-C	2.24	1.93	1.13	1.52	0.53	0.87	**16.078**	**<0.001**	Controls<SZ***; BP<SZ*
PAS2-C	2.07	1.74	1.39	1.20	0.45	0.79	**20.280**	**<0.001**	Controls<SZ***; controls<BP***
PAS3-C	3.04	1.55	3.09	1.31	1.82	1.30	1.389	0.253	
PAS4-C	1.33	1.38	1.09	1.28	0.15	0.58	**11.003**	**<0.001**	Controls<SZ***; controls<BP**

Outline

- Prevention in psychiatry
- Psychosis (psychiatric disorders) as the reflection of abnormal developmental trajectories
- Shifting the focus towards prevention and early intervention in developmentally sensitive periods
- Implications and priorities for the future

Before conception

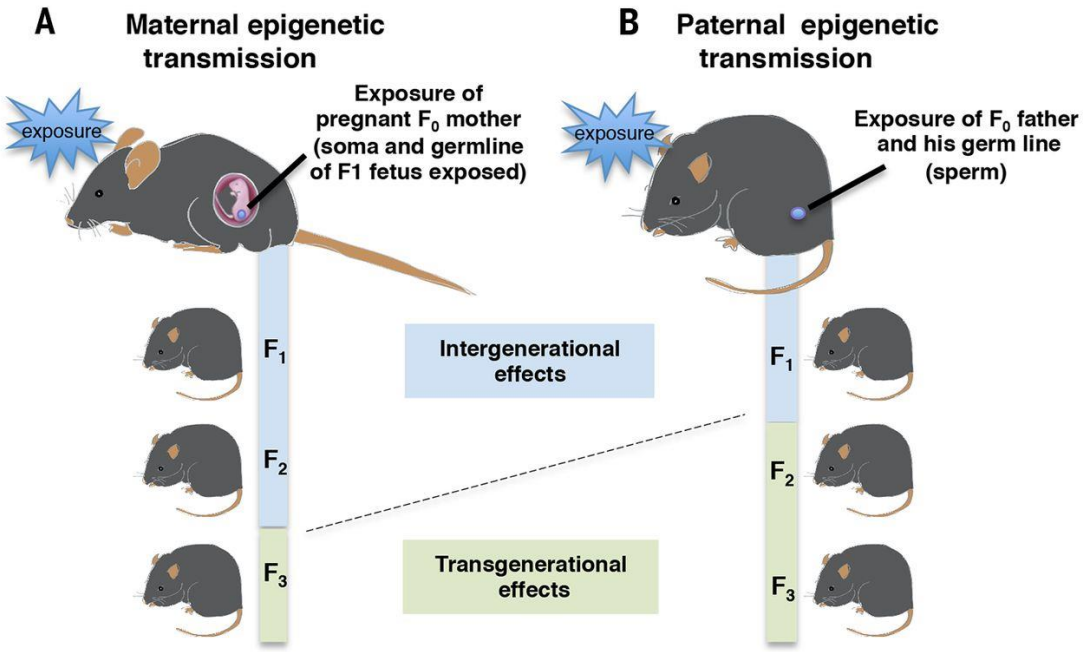


Maternal stress and delayed parenthood

Sperm protein links father's lifestyle with offspring's health

Finding suggests more attention needs to be paid to fathers' pre-conception health

By Emily Chung, CBC News Posted: Oct 09, 2015 5:00 AM ET | Last Updated: Oct 13, 2015 12:53 PM ET



Keith Siklenka et al. Science 2015;science.aab2006

Science AAAS

Parental age

Table 2. Incidence Rate Ratios (IRRs) for Schizophrenia Associated With Parental Age

Age, y	IRR (95% Confidence Interval)				
	Unadjusted Model (Model 1)*	Adjusted for Age of Both Parents (Model 2)	Adjusted for Age and Psychiatric History of Both Parents (Model 3)	Full Model Adjusted for Family Psychiatric History and Socioeconomic Factors (Model 4)†	Full Model, Family History Negative Only (Model 5)
Paternal age					
<20	1.18 (1.01-1.39)	1.14 (0.97-1.35)	1.01 (0.93-1.30)	1.04 (0.88-1.23)	1.05 (0.85-1.29)
20-24	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
25-29	0.96 (0.90-1.03)	0.97 (0.90-1.04)	0.98 (0.91-1.05)	0.99 (0.92-1.07)	1.01 (0.93-1.11)
30-34	1.02 (0.95-1.10)	1.01 (0.93-1.10)	1.02 (0.93-1.11)	1.04 (0.95-1.13)	1.03 (0.93-1.14)
35-39	1.04 (0.95-1.13)	1.01 (0.91-1.12)	1.00 (0.90-1.11)	1.02 (0.91-1.13)	1.06 (0.93-1.20)
40-44	1.20 (1.08-1.34)	1.16 (1.02-1.32)	1.14 (1.00-1.30)	1.15 (1.00-1.31)	1.21 (1.03-1.42)
45-49	1.20 (1.02-1.41)	1.14 (0.95-1.37)	1.10 (0.92-1.32)	1.09 (0.90-1.31)	1.22 (0.98-1.51)
≥50	1.75 (1.41-2.16)‡	1.65 (1.32-2.08)	1.64 (1.30-2.06)	1.51 (1.19-1.92)	1.61 (1.21-2.13)
50-54	1.42 (1.09-1.84)	1.32 (1.00-1.74)	1.29 (0.98-1.71)	1.22 (0.92-1.62)	1.33 (0.95-1.86)
≥55	2.90 (2.05-4.11)	2.71 (1.89-3.88)	2.76 (1.92-3.96)	2.45 (1.69-3.54)	2.42 (1.56-3.77)
Maternal age					
<20	1.13 (1.04-1.23)	1.07 (0.98-1.18)	1.04 (0.95-1.14)	1.03 (0.94-1.13)	1.04 (0.93-1.16)
20-24	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
25-29	1.02 (0.96-1.08)	1.03 (0.96-1.09)	1.04 (0.98-1.11)	1.02 (0.96-1.09)	1.05 (0.97-1.13)
30-34	1.09 (1.02-1.17)	1.06 (0.98-1.15)	1.09 (1.00-1.18)	1.05 (0.97-1.14)	1.08 (0.98-1.20)
35-39	1.15 (1.05-1.26)	1.05 (0.94-1.18)	1.11 (0.99-1.24)	1.07 (0.95-1.20)	1.08 (0.94-1.24)
≥40	1.39 (1.20-1.62)‡	1.15 (0.97-1.37)	1.23 (1.03-1.46)	1.18 (0.98-1.41)	1.21 (0.99-1.49)
40-44	1.34 (1.14-1.58)	1.12 (0.94-1.34)	1.20 (1.00-1.44)	1.16 (0.96-1.39)	1.20 (0.97-1.48)
≥45	1.92 (1.26-2.94)	1.45 (0.93-2.26)	1.55 (0.99-2.42)	1.41 (0.90-2.24)	1.43 (0.86-2.39)

*Two separate models were conducted: model 1a for paternal age and model 1b for maternal age.

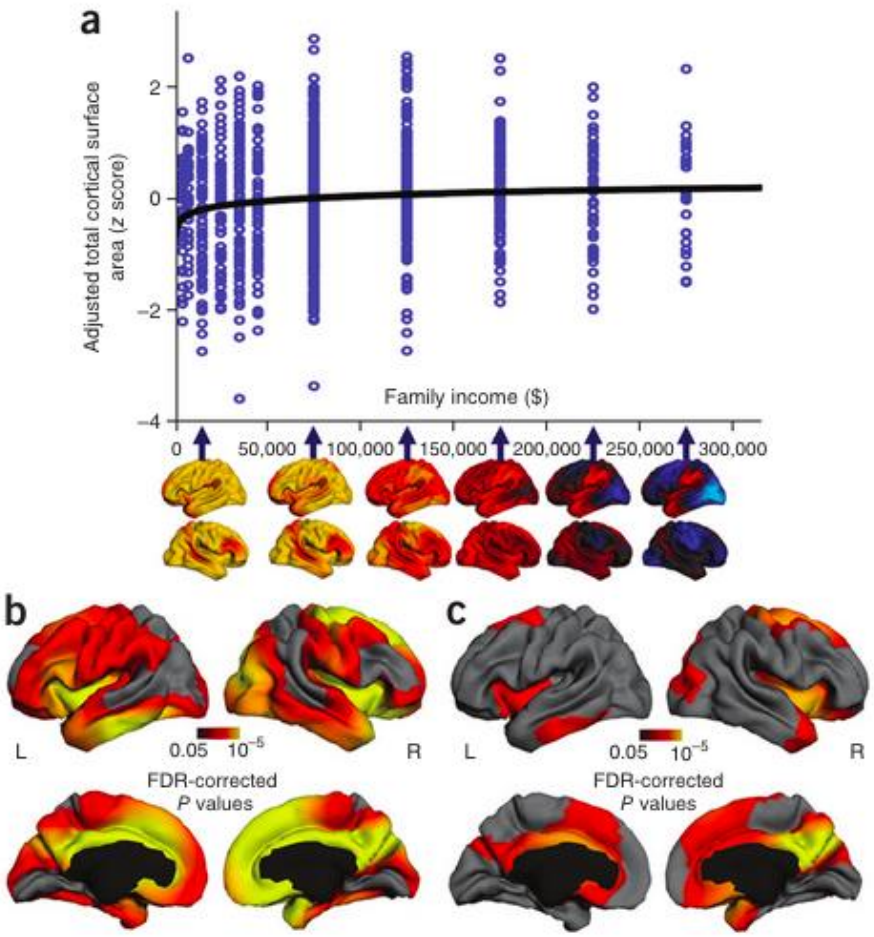
†Model adjusted for parental education, wealth, marital status, death before case admission not by suicide, family psychiatric history, history of suicide in parent or sibling, reference to father, place of birth, and sibship size.

‡Includes older age groups.

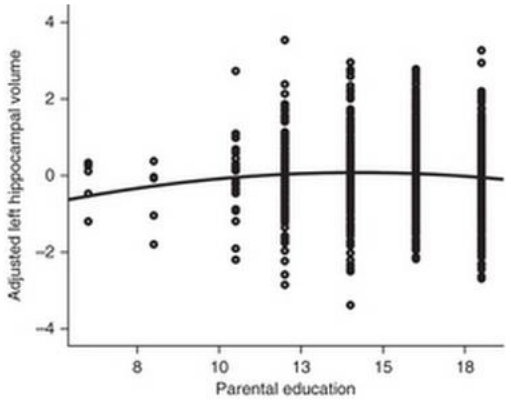
Byrne et al., Archives of General Psychiatry. July 1, 2003, Vol. 60, No. 7

Family income, parental education and brain structure in children and adolescents

Kimberly G Noble[1,2,32], Suzanne M Houston[3–5,32], Natalie H Brito[6], Hauke Bartsch[7], Eric Kan[4,5], Joshua M Kuperman[8–10], Natacha Akshoomoff[10–12], David G Amaral[10,13], Cinnamon S Bloss[10,14], Ondrej Libiger[15], Nicholas J Schork[16], Sarah S Murray[10,17], B J Casey[10,18], Linda Chang[10,19], Thomas M Ernst[10,19], Jean A Frazier[10,20], Jeffrey R Gruen[10,21–23], David N Kennedy[10,20], Peter Van Zijl[10,24,25], Stewart Mostofsky[10,25], Walter E Kaufmann[10,26,27], Tal Kenet[10,27,28], Anders M Dale[8–10,29–31], Terry L Jernigan[10–12,29] & Elizabeth R Sowell[4,5,10]



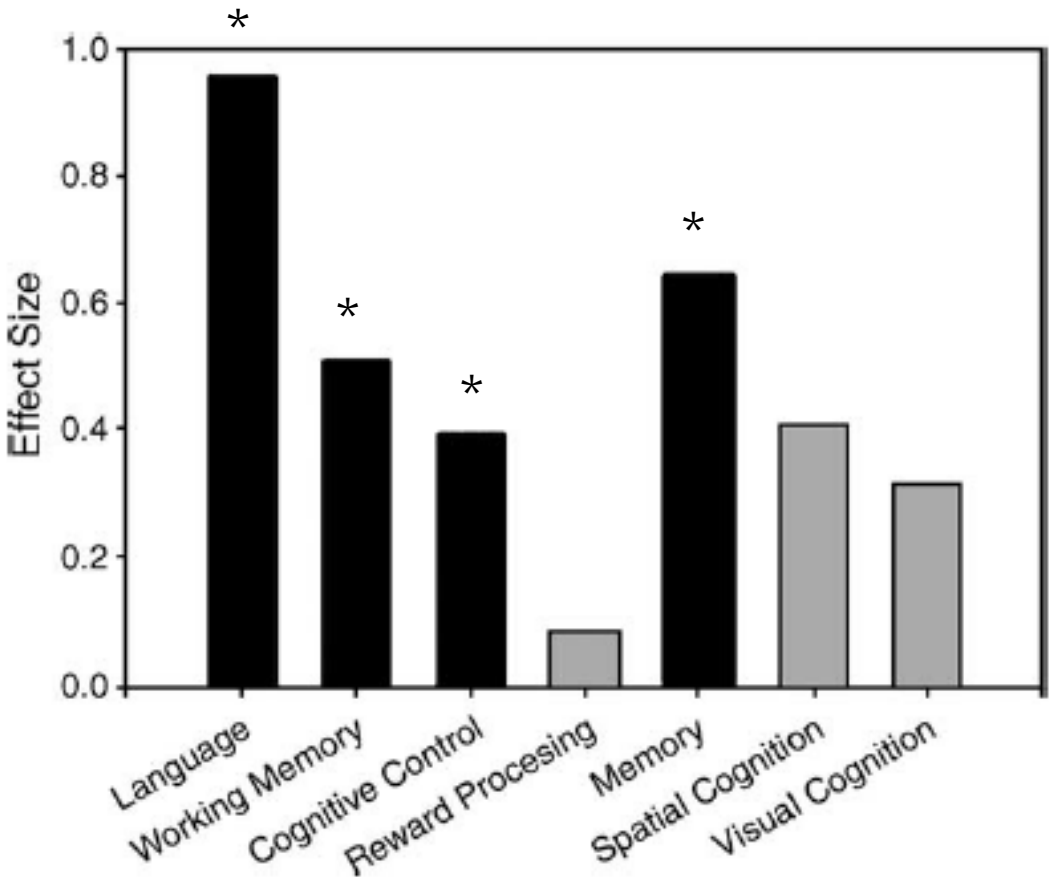
Family income is logarithmically associated with cortical surface area



Parental education is quadratically associated with left hippocampal volume

Childhood poverty: Specific associations with neurocognitive development

Martha J. Farah[a,], David M. Shera[b], Jessica H. Savage[a], Laura Betancourt[a], Joan M. Giannetta[c], Nancy L. Brodsky[c], Elsa K. Malmud[c], Hallam Hurt[c]*



* p<0.05 low vs. middle SES

Effect sizes of separation between low and middle SES

BRAIN RESEARCH 1110 (2006) 166–174

Role of cash in conditional cash transfer programmes for child health, growth, and development: an analysis of Mexico's *Oportunidades*

Lia C H Fernald, Paul J Gertler, Lynnette M Neufeld

Lancet 2008; 371: 828–37

See Comment page 789

School of Public Health (L C H Fernald PhD, P J Gertler PhD) **and Haas School of Business** (P J Gertler), **University of California, Berkeley, CA, USA; and Instituto Nacional de Salud Pública, Cuernavaca, Mexico** (L M Neufeld PhD)

Correspondence to: Dr Lia C H Fernald, School of Public Health, University of California, Berkeley, 50 University Hall, MC 7360, Berkeley, CA 94720-7360, USA **fernald@berkeley.edu**

Summary

Background Many governments have implemented conditional cash transfer (CCT) programmes with the goal of improving options for poor families through interventions in health, nutrition, and education. Families enrolled in CCT programmes receive cash in exchange for complying with certain conditions: preventive health requirements and nutrition supplementation, education, and monitoring designed to improve health outcomes and promote positive behaviour change. Our aim was to disaggregate the effects of cash transfer from those of other programme components.

Methods In an intervention that began in 1998 in Mexico, low-income communities (n=506) were randomly assigned to be enrolled in a CCT programme (*Oportunidades*, formerly *Progresa*) immediately or 18 months later. In 2003, children (n=2449) aged 24–68 months who had been enrolled in the programme their entire lives were assessed for a wide variety of outcomes. We used linear and logistic regression to determine the effect size for each outcome that is associated with a doubling of cash transfers while controlling for a wide range of covariates, including measures of household socioeconomic status.

Findings A doubling of cash transfers was associated with higher height-for-age *Z* score (β 0·20, 95% CI 0·09–0·30; p<0·0001), lower prevalence of stunting (–0·10, –0·16 to –0·05; p<0·0001), lower body-mass index for age percentile (–2·85, –5·54 to –0·15; p=0·04), and lower prevalence of being overweight (–0·08, –0·13 to –0·03; p=0·001). A doubling of cash transfers was also associated with children doing better on a scale of motor development, three scales of cognitive development, and with receptive language.

Interpretation Our results suggest that the cash transfer component of *Oportunidades* is associated with better outcomes in child health, growth, and development.

Pregnancy

Substance use during pregnancy and risk of psychosis

BJPsych | The British Journal of Psychiatry (2009) 195, 294–300. doi: 10.1192/bjp.bp.108.062471

Maternal tobacco, cannabis and alcohol use during pregnancy and risk of adolescent psychotic symptoms in offspring

Stanley Zammit, Kate Thomas, Andrew Thompson, Jeremy Horwood, Paulo Menezes, David Gunnell, Chris Hollis, Dieter Wolke, Glyn Lewis and Glynn Harrison

Table 2 Crude and adjusted[a] odds ratios (OR) and 95% CI for psychosis-like symptoms (PLIKS) by maternal substance use during pregnancy

	n	Suspected or definite PLIKS Crude OR (95% CI)	Suspected or definite PLIKS Adjusted OR (95% CI)	Definite PLIKS Crude OR (95% CI)	Definite PLIKS Adjusted OR (95% CI)
Tobacco					
None	3579	1	1	1	1
1–9 cigarettes/day	295	1.15 (0.79–1.66)	0.92 (0.63–1.36)	1.53 (0.92–2.53)	1.25 (0.73–2.14)
10–19 cigarettes/day	266	1.88 (1.35–2.61)	1.47 (1.02–2.12)	2.33 (1.48–3.66)	1.65 (0.99–2.75)
⩾20 cigarettes/day	113	2.30 (1.45–3.65)	1.84 (1.12–3.03)	2.03 (1.01–4.10)	1.54 (0.73–3.25)
Linear trend	4253	1.33 (1.18–1.49), $P<0.001$	1.20 (1.05–1.37), $P=0.007$	1.39 (1.18–1.63), $P<0.001$	1.21 (1.01–1.47), $P=0.047$
Cannabis					
None	4175	1	1	1	1
<1/week	37	0.95 (0.34–2.70)	0.58 (0.20–1.70)	0.57 (0.08–4.20)	0.34 (0.04–2.56)
⩾1/week	41	1.62 (0.71–3.66)	1.04 (0.45–2.43)	1.63 (0.50–5.32)	1.12 (0.33–3.84)
Linear trend	4253	1.22 (0.83–1.79), $P=0.317$	0.94 (0.62–1.41), $P=0.755$	1.16 (0.65–2.09), $P=0.616$	0.91 (0.49–1.71), $P=0.776$
Alcohol					
None	2522	1	1	1	1
⩽7 units/week	1293	0.92 (0.74–1.14)	0.92 (0.74–1.15)	0.67 (0.48–0.94)	0.68 (0.48–0.96)
8–21 units/week	410	1.05 (0.77–1.48)	1.00 (0.71–1.39)	0.58 (0.33–1.04)	0.56 (0.31–1.02)
⩾22 units/week	28	2.58 (1.09–6.11)	2.40 (0.99–5.83)	2.14 (0.64–7.17)	1.86 (0.54–6.42)
Linear (per 10 units)[b]	4253	0.80 (0.51–1.25)	0.75 (0.47–1.19)	0.77 (0.48–1.25)	0.73 (0.45–1.18)
Quadratic (linear^2)[b]	4253	1.21 (1.00–1.47)	1.22 (1.00–1.49)	1.04 (0.97–1.12)	1.04 (0.97–1.12)
Likelihood ratio (for overall alcohol)[b]	4253	$\chi^2=9.8$, d.f. $=2$, $P=0.008$	$\chi^2=8.3$, d.f. $=2$, $P=0.016$	$\chi^2=1.3$, d.f. $=2$, $P=0.522$	$\chi^2=1.8$, d.f. $=2$, $P=0.415$

a. Adjusted for other substances used, and all variables in Table 1; data-set with no missing data for confounders 4253.
b. Results for linear and quadratic terms for alcohol use are with both included in same model.

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Schizophrenia Research 67 (2004) 237–245
SCHIZOPHRENIA RESEARCH
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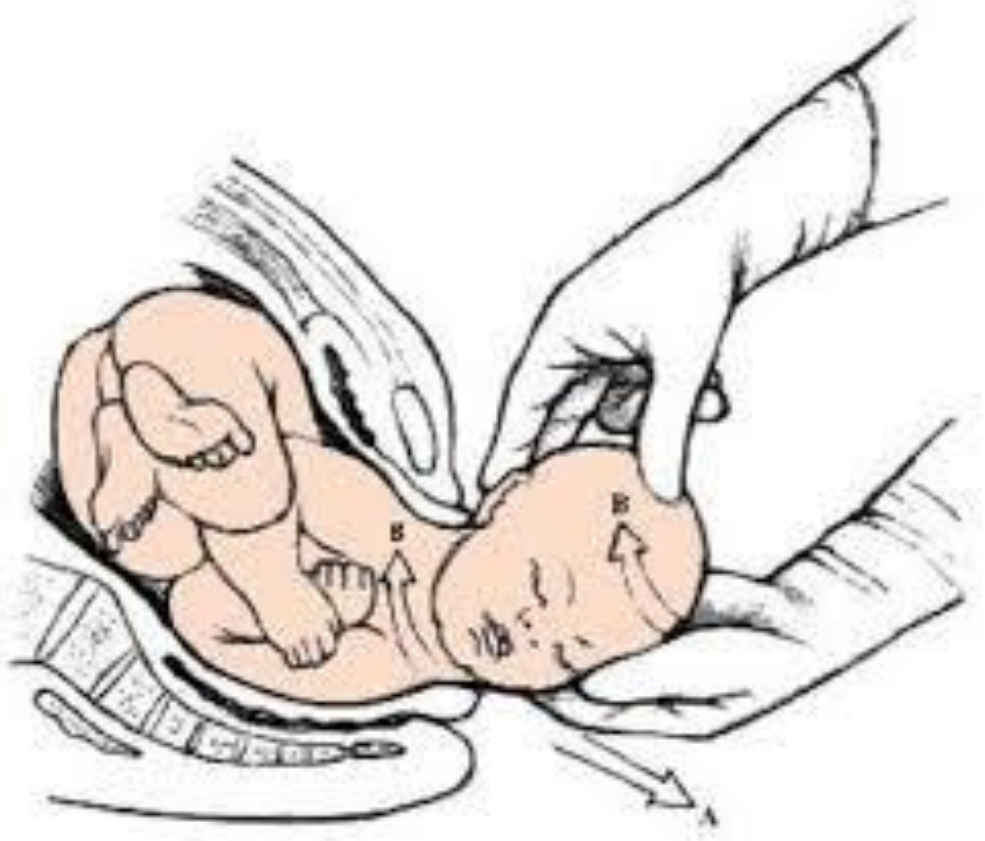
Vitamin D supplementation during the first year of life and risk of schizophrenia: a Finnish birth cohort study

John McGrath[a,b,*], Kaisa Saari[c,d], Helinä Hakko[c,d], Jari Jokelainen[c,e,f], Peter Jones[g], Marjo-Riitta Järvelin[e,h], David Chant[a], Matti Isohanni[c]

Table 2
Male cohort members only (n=4616)

		Time at risk (years)	Incidence per 100000 years at risk	RR (95% CI)	Adjusted RR (95% CI)*
Schizophrenia					
Frequency of vitamin D supplements					
None	1	411	243	1 (reference)	1 (reference)
Irregularly	4	17,034	23	0.10 (0.01–0.82)	0.08 (0.01–0.95)
Regularly	46	123,686	38	0.15 (0.02–1.02)	0.12 (0.02–0.90)
Dose of vitamin D					
Less than 2000 IU/day	2	1474	136	1 (reference)	1 (reference)
At least 2000 IU/day	49	139,657	35	0.26 (0.06–1.02)	0.23 (0.06–0.95)

Birth and perinatal period



Obstetric complications and psychosis

Eur Child Adolesc Psychiatry (2009)
18:180–184 DOI 10.1007/s00787-008-0692-x

BRIEF REPORT

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Obstetric complications as a risk factor for first psychotic episodes in childhood and adolescence

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Abstract There are reports of significant association between obstetric complications (OC) and childhood psychosis. Authors conducted a case-control study of 102 children and adolescents with a first episode psychosis (FEP) and 94 healthy controls (HC), using the obstetric complications scale (OCS) and their medical records, to examine the risk of FPE. Patients were recruited from child and adolescent psychiatry units at six university hospitals and controls from publicly-funded schools of similar characteristics and from the same geographic areas. A logistic regression was performed to quantify the risk of psychosis in childhood and adolescence, based on OC, adjusting for potential confounding factors like socio economic status (SES) and family psychiatric history (FPH). OC appeared more frequently in the records of patients. Significant differences between patients and controls were found in Prenatal OC (15.7% vs. 5.3%, $P < 0.05$) and among them, *bleeding in pregnancy* showed the greatest difference between groups (12.7% vs. 2.1%, $P < 0.01$). In the logistic regression, bleeding in pregnancy showed a crude odds ratio (OR) of 6.7 (95%CI = 1.4–30.6) and 5.1 (CI 95% = 1.0–24.9) adjusted for SES and FPH. Therefore, bleeding in pregnancy is a likely risk factor for early-onset psychosis.

Key words early psychosis – first onset – case-control – OCS

Risk of psychosis in pre-term children

Table 3. Crude and Adjusted HRs ("Relative Risks") for Incidence of First Hospitalization With a Selected Psychiatric Diagnosis After an Individual's 16th Birthday in Relation to Pregnancy Outcomes

	HR (95% CI)					
	Nonaffective Psychosis		Depressive Disorder		Bipolar Affective Disorder	
Exposure	Crude	Fully Adjusted[a]	Crude	Fully Adjusted[a]	Crude	Fully Adjusted[a]
Gestational age, wk						
<32	2.8 (1.2-6.7)	2.5 (1.0-6.0)	3.0 (1.9-4.7)	2.9 (1.8-4.6)	7.2 (2.7-19.6)	7.4 (2.7-20.6)
32-36	1.8 (1.2-2.5)	1.6 (1.1-2.3)	1.4 (1.1-1.7)	1.3 (1.1-1.7)	2.6 (1.6-4.4)	2.7 (1.6-4.5)
37-41	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
≥42	1.0 (0.8-1.2)	1.0 (0.8-1.3)	1.1 (1.0-1.3)	1.1 (1.0-1.2)	1.0 (0.7-1.5)	1.0 (0.7-1.5)
Birth weight for gestational age, SDS						
≤2	1.1 (0.7-1.6)	1.0 (0.7-1.5)	1.1 (0.8-1.3)	1.1 (0.9-1.4)	1.0 (0.5-2.1)	1.0 (0.5-2.0)
−1.99 to 1.99	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
≥2	0.9 (0.5-1.6)	0.9 (0.5-1.5)	0.8 (0.6-1.1)	0.7 (0.5-1.0)	0.9 (0.3-2.4)	0.8 (0.3-2.1)
Apgar score at 5 min						
0-3	0.8 (0.1-5.8)	0.7 (0.1-4.8)	2.4 (1.3-4.4)	2.2 (1.2-4.0)	5.3 (1.3-21.2)	3.8 (0.9-15.5)
4-6	1.6 (0.8-3.4)	1.3 (0.6-2.8)	1.2 (0.8-2.0)	1.1 (0.7-1.7)	0.7 (0.1-5.2)	0.5 (0.1-3.6)
7-10	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]

	HR (95% CI)					
	Eating Disorders		Drug Dependency		Alcohol Dependency	
Exposure	Crude	Fully Adjusted[a]	Crude	Fully Adjusted[a]	Crude	Fully Adjusted[a]
Gestational age, wk						
<32	3.7 (1.4-10.0)	3.5 (1.3-9.6)	1.2 (0.7-2.3)	1.2 (0.6-2.2)	1.5 (0.9-2.3)	1.3 (0.8-2.3)
32-36	1.4 (0.8-2.3)	1.4 (0.9-2.4)	1.3 (1.1-1.6)	1.2 (1.0-1.4)	1.4 (1.2-1.7)	1.3 (1.1-1.5)
37-41	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
≥42	1.2 (0.9-1.5)	1.1 (0.9-1.5)	1.0 (0.9-1.1)	1.0 (0.9-1.1)	1.1 (1.0-1.2)	1.1 (1.0-1.2)
Birth weight for gestational age, SDS						
≤2	0.7 (0.4-1.4)	0.7 (0.4-1.3)	1.5 (1.3-1.8)	1.4 (1.2-1.6)	1.3 (1.1-1.5)	1.2 (1.0-1.4)
−1.99 to 1.99	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
≥2	0.7 (0.3-1.6)	0.7 (0.3-1.5)	0.8 (0.6-1.0)	0.8 (0.6-1.1)	0.9 (0.7-1.1)	0.9 (0.7-1.1)
Apgar score at 5 min						
0-3	3.1 (0.8-12.5)	3.0 (0.8-12.3)	1.1 (0.5-2.4)	1.0 (0.4-2.2)	1.5 (0.8-2.9)	1.3 (0.7-2.6)
4-6	1.6 (0.6-4.4)	1.6 (0.6-4.4)	0.8 (0.5-1.3)	0.7 (0.4-1.0)	1.3 (0.9-1.9)	1.1 (0.8-1.6)
7-10	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: HR, hazard ratio; SDS, standard deviation score.
[a]The HRs are adjusted for the other variables in the table and for sex, parity, maternal age at delivery, maternal education, and maternal psychiatric family history.

Nosarti et al., JAMA Psychiatry 2012

Prevention of adverse obstetric outcomes in at-risk populations: women with severe mental illness

Schizophrenia Research 157 (2014) 305–309

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Adverse obstetric and neonatal outcomes in women with severe mental illness: To what extent can they be prevented?

Fiona Judd [a,b,*], Angela Komiti [a,b], Penny Sheehan [c], Louise Newman [d], David Castle [a,e], Ian Everall [a,f,g]

Table 1
Antenatal care: Comparing study and control groups.

	Study (n = 112)	Control (n = 19,755)	χ^2/t-test	p
Mean age (SD)	31.7 (6.1)	30.4 (5.3)	−2.3	.02
Alcohol use (%)	20.6	0.6	625	<.001
Smoking—<20 weeks (%)	38.3	6.6	171	<.001
Illicit drug use (%)	17.9	2.6	95.5	<.001
Mean gestation at 1st AN appt. (SD)	18.8 (7.8)	15.1 (6.6)	−5.0	<.001

Note: AN = antenatal.

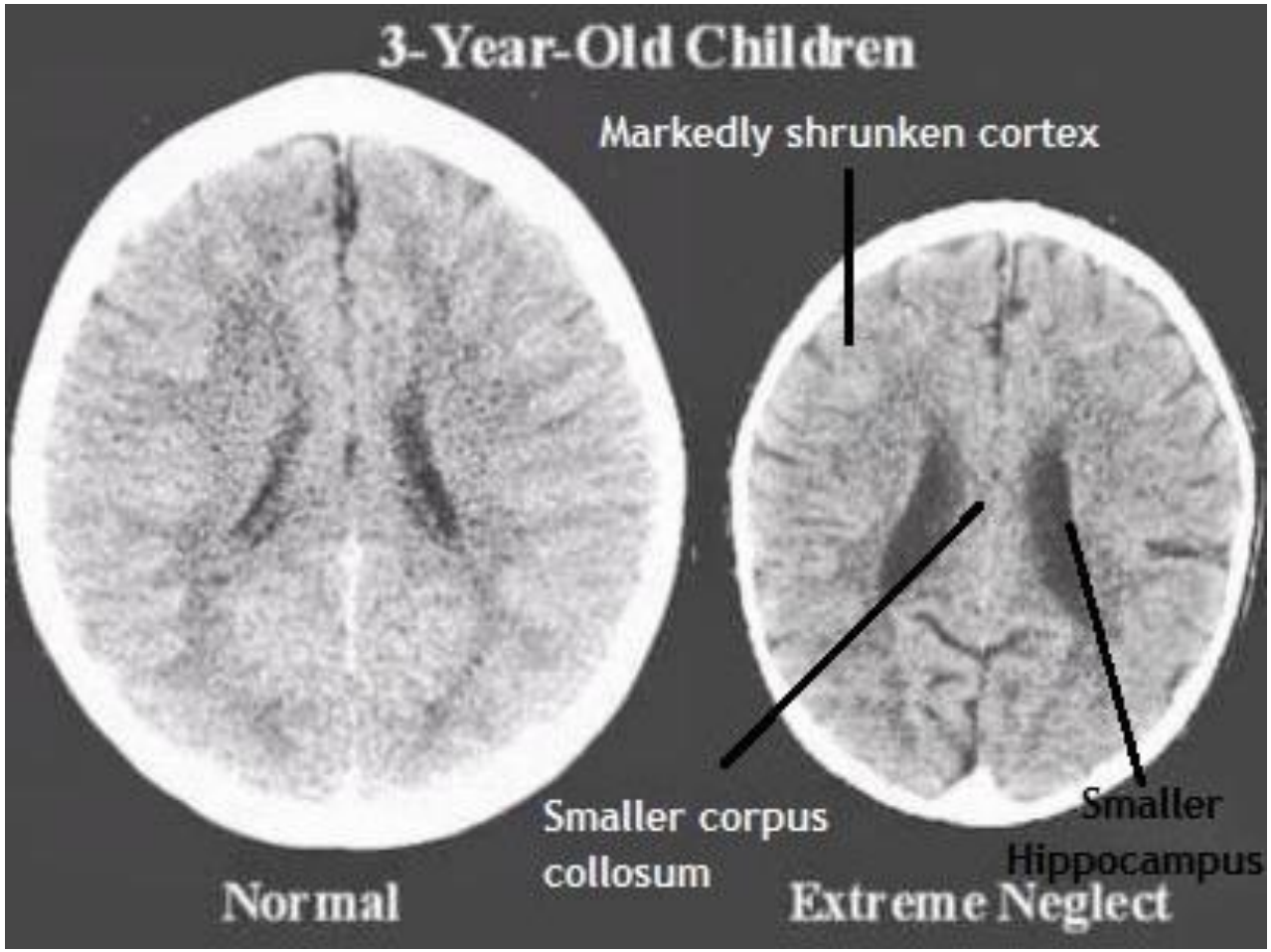
Table 3
Neonatal outcomes: comparing study and control groups.

	Study (n = 112)	Control (n = 19,755)	χ^2/t-test	p
Apgar score 8–10 at 1 min (%)	69.6	79.8	7.08	.008
Apgar score <4 at 1 min (%)	5.4	5.7	0.02	.88
Apgar score 8–10 at 5 min (%)	86.6	92.5	5.43	.02
Mean infant weight, grams (SD)	3172 (680)	3247 (719)	1.10	.27
- Excluding smokers	3262 (711)	3275 (699)	0.15	.88
Mean gestation at birth, weeks (SD)	38.4 (2.7)	38.5 (3.0)	0.46	.64
Pre-term births (<37 weeks) (%)	17.9	10.9	5.52	.02
NISC admission (%)	27.7	12.5	23.38	<.001

Note: NISC = neonatal intensive special care.

Toddlerhood and pre-school age

Effects of neglect on brain development

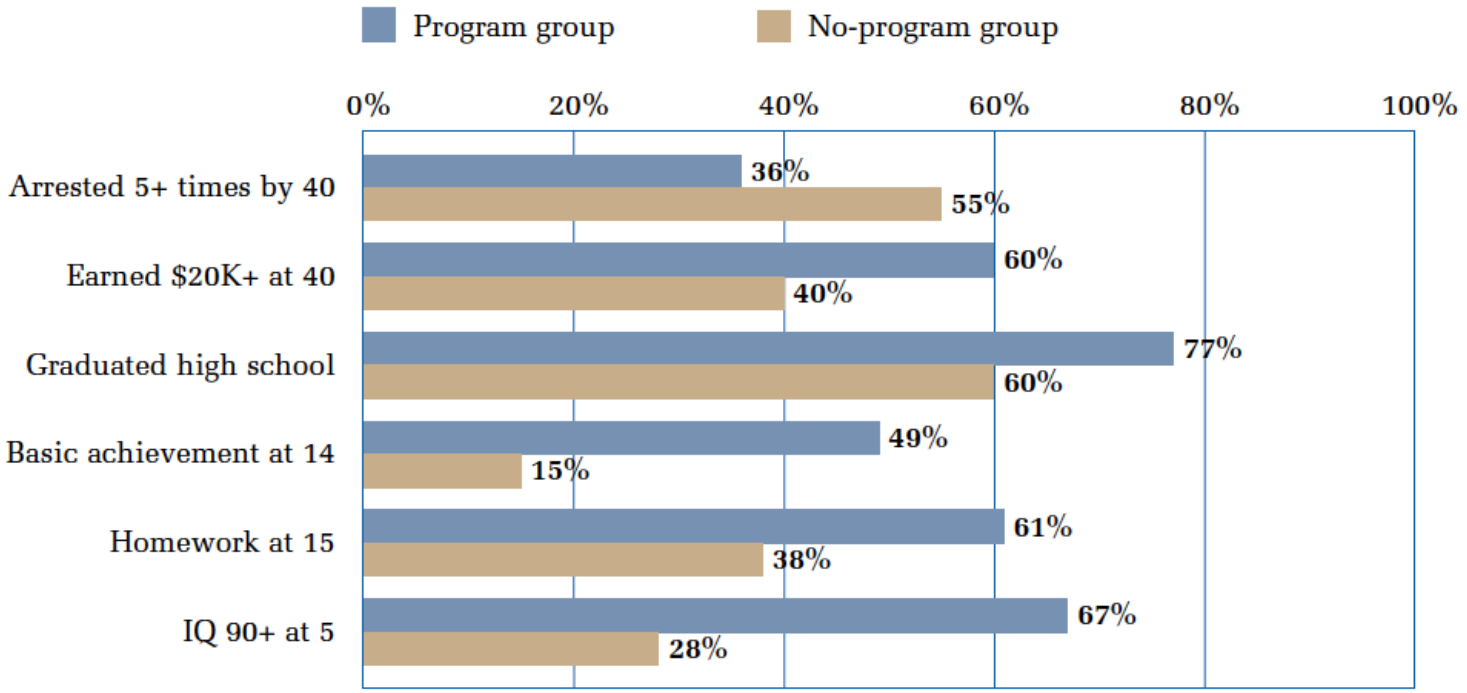


Effective preventive interventions in preschool age children

The High/Scope Perry Preschool Study Through Age 40

Figure 1

Major Findings: High/Scope Perry Preschool Study at 40

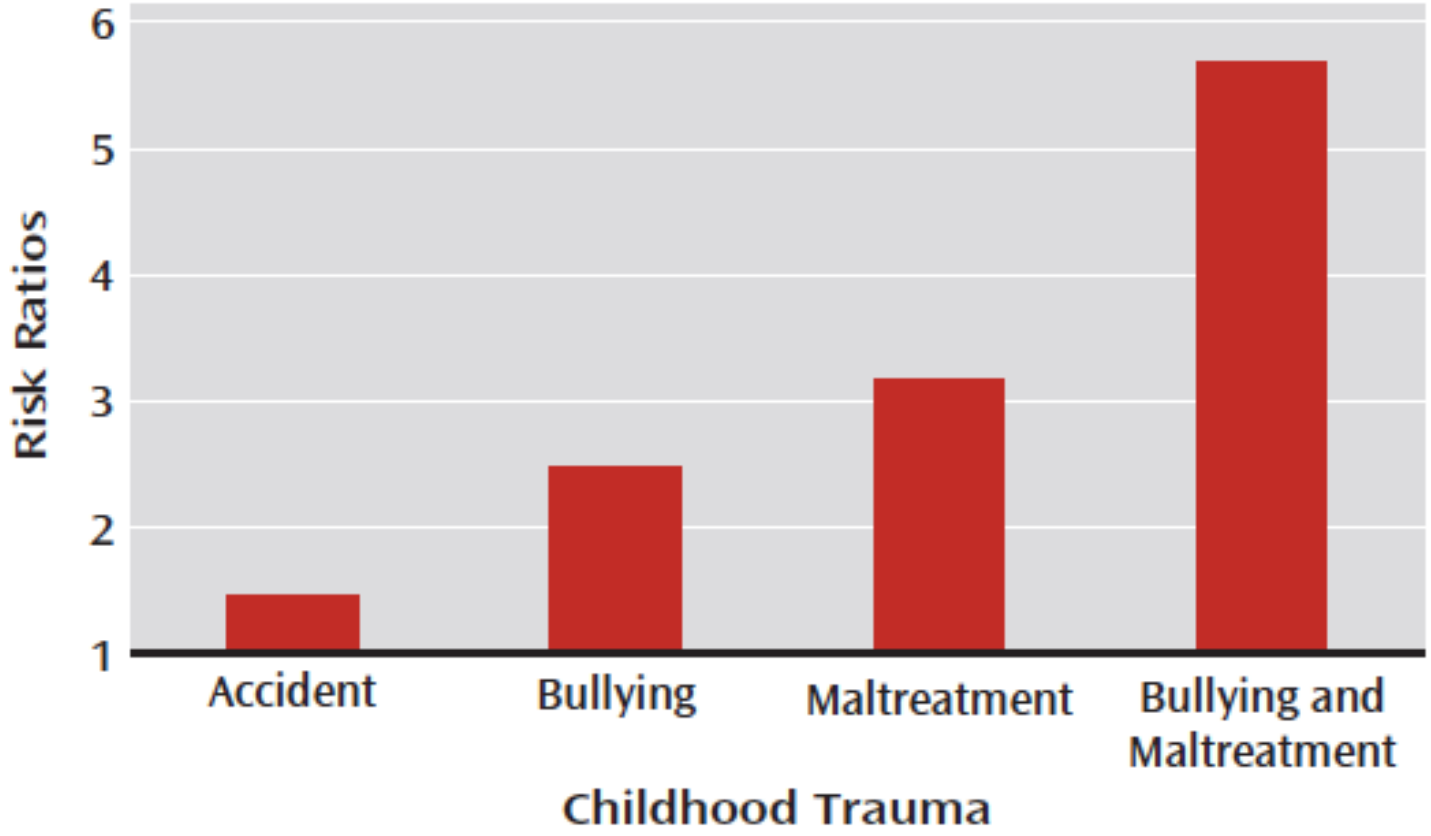


Schweinhart et al.

Primary school

Child abuse and risk for psychosis

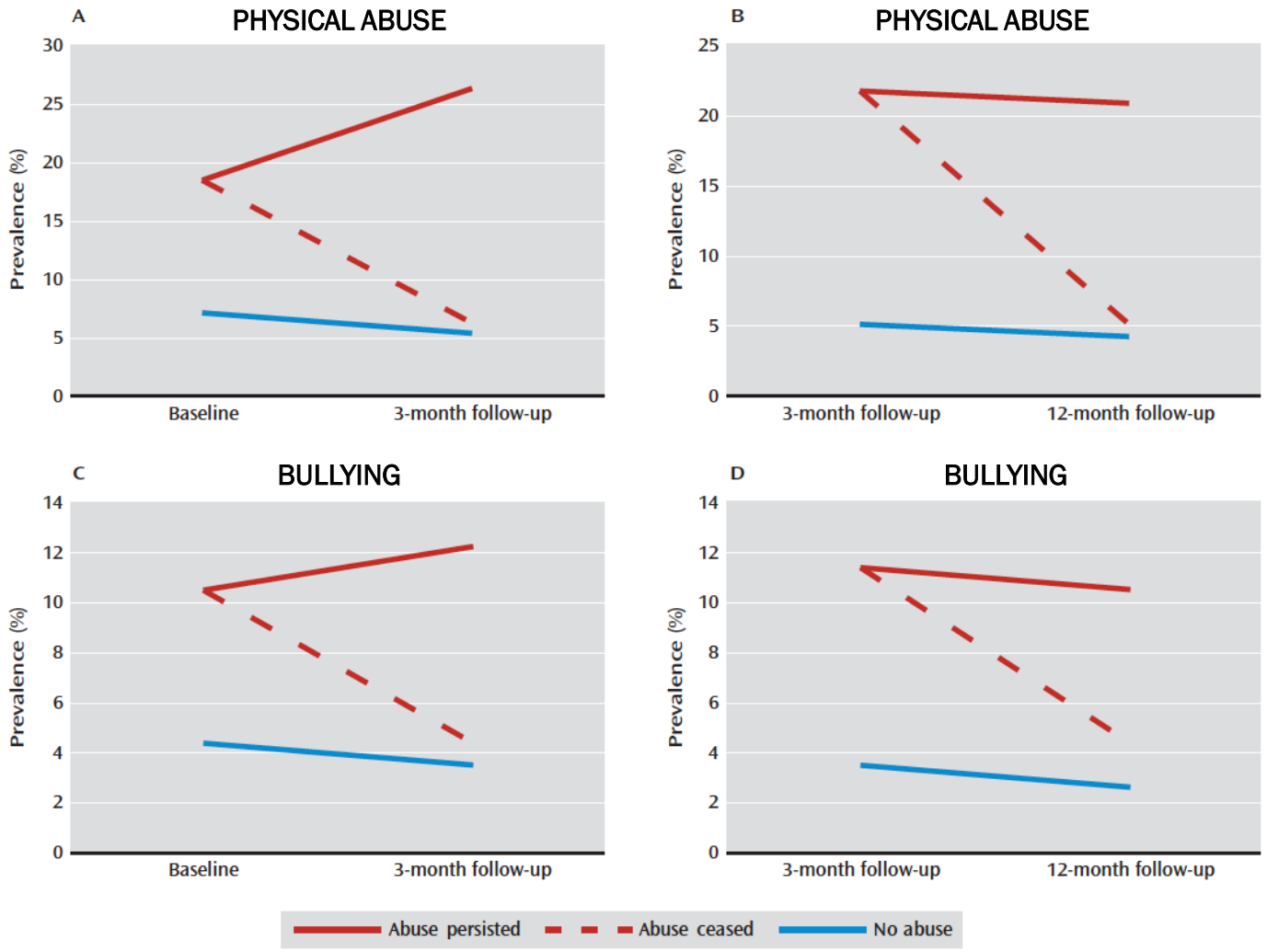
FIGURE 1. Risk of Psychotic Symptoms at Age 12 Associated With Cumulative Childhood Trauma



ARSENEAULT, CANNON, FISHER, ET AL.

Am J Psychiatry 168:1, January 2011

Effects on psychotic experiences of ceasing maltreatment and bullying



Children with low IQ and disabilities are also at risk of experiencing bullying and maltreatment

Prevalence and risk of violence against children with disabilities: a systematic review and meta-analysis of observational studies

Lisa Jones, Mark A Bellis, Sara Wood, Karen Hughes, Ellie McCoy, Lindsay Eckley, Geoff Bates, Christopher Mikton, Tom Shakespeare, Alana Officer

	Any disability			Mental or intellectual disability		
	Studies	Odds ratio (95% CI)	Heterogeneity	Studies	Odds ratio (95% CI)	Heterogeneity
Any maltreatment	4	3·68 (2·56–5·29)	91·8% (87·7–94·1)	3	4·28 (2·12–8·62)	94·0% (90·2–95·9)
Physical violence	6	3·56 (2·80–4·52)	50·6% (0–73·0)	4	3·08 (2·08–4·57)	50·8% (0–77·2)
Sexual violence	9	2·88 (2·24–3·69)	86·9% (78·8–90·9)	4	4·62 (2·08–10·23)	84·7% (64·4–91·2)
Emotional abuse	4	4·36 (2·42–7·87)	94·4% (91·4–96·0)	3	4·31 (1·37–13·56)	96·2% (94·2–97·3)
Neglect	3	4·56 (3·23–6·43)	73·8% (27·7–86·0)	2	..	..

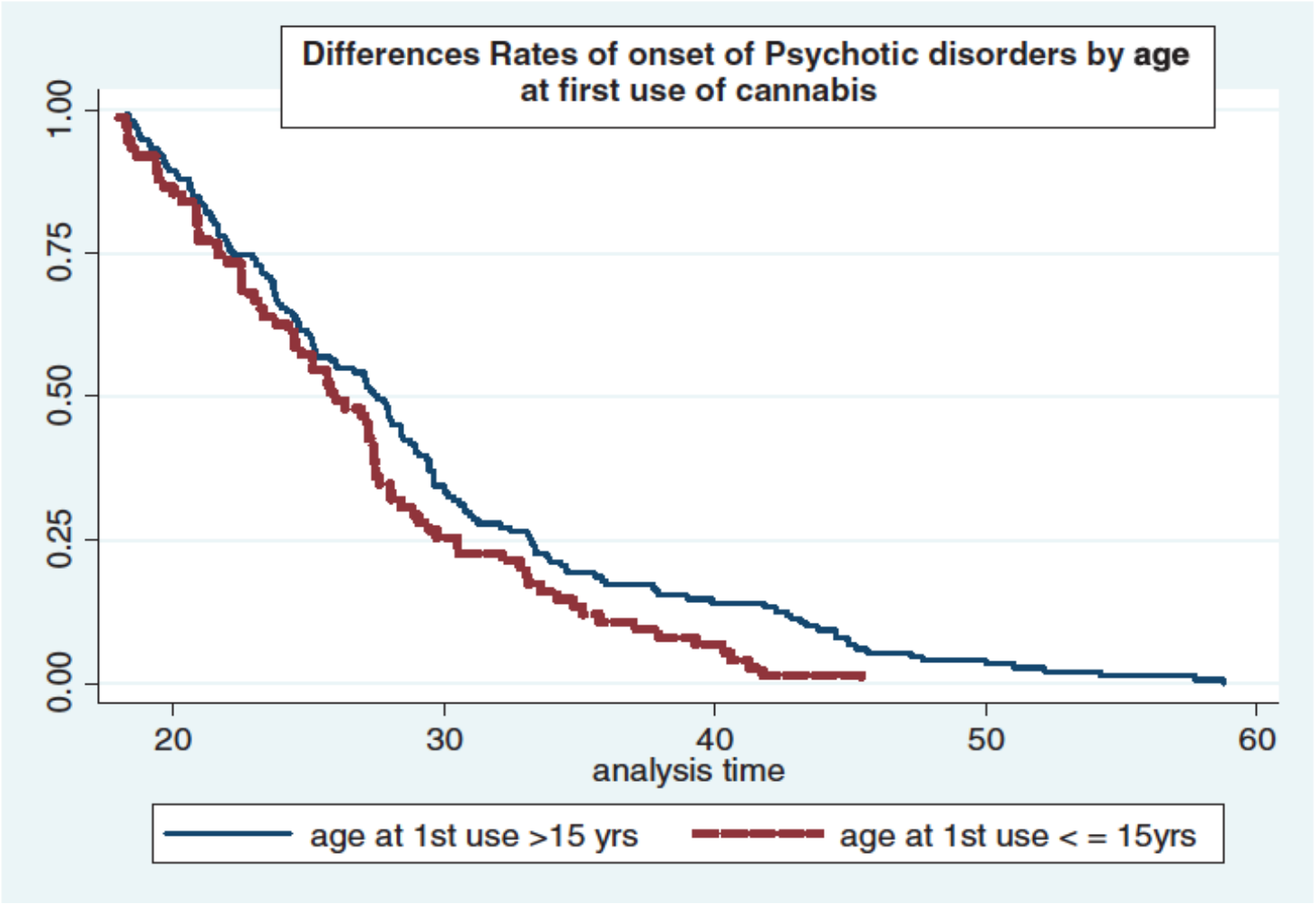
We used the I^2 statistic (95% CI) to estimate heterogeneity between pooled studies. .. = insufficient sample.

Table 3: Random-effects pooled odds ratios for risk of violence

Lancet 2012; 380: 899–907

Adolescence

Earlier onset of cannabis use associated with earlier onset of psychosis



Di Forti et al., Schizophr Bull (2014) 40 (6): 1509-1517.

OPEN ACCESS Freely available online

PLOS | ONE

Primary Prevention of Cannabis Use: A Systematic Review of Randomized Controlled Trials

Melissa M. Norberg*, Sarah Kezelman, Nicholas Lim-Howe

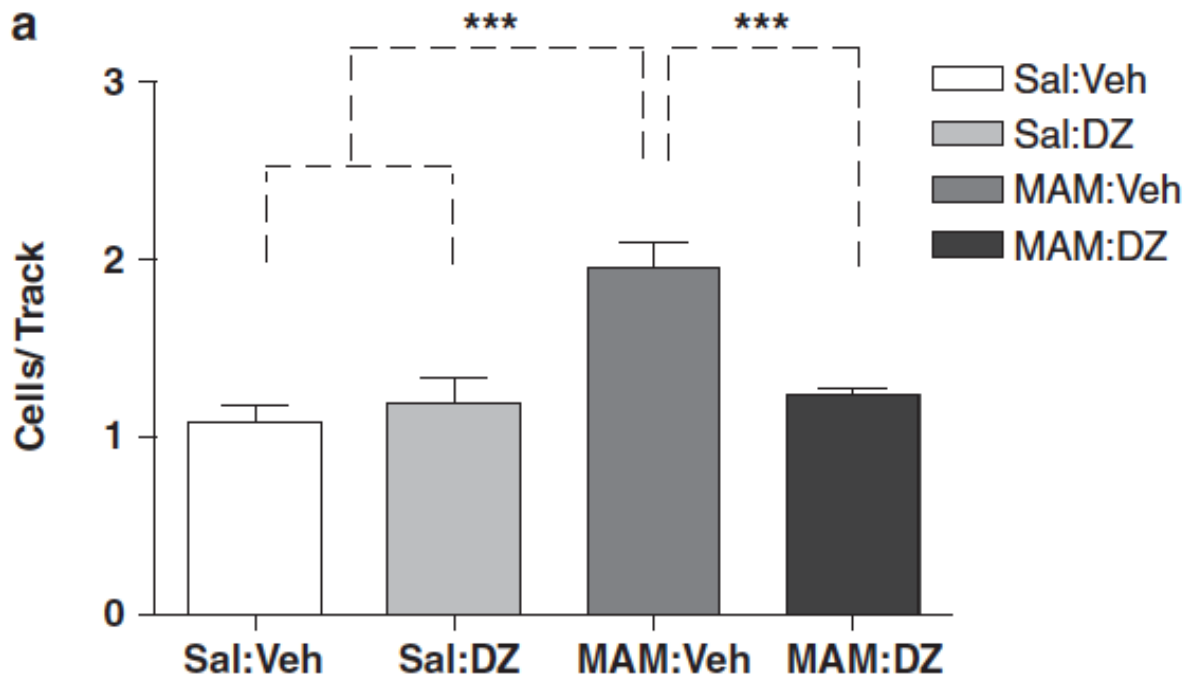
National Cannabis Prevention and Information Centre, University of New South Wales, Randwick, New South Wales, Australia

Abstract

A systematic review of primary prevention was conducted for cannabis use outcomes in youth and young adults. The aim of the review was to develop a comprehensive understanding of prevention programming by assessing universal, targeted, uni-modal, and multi-modal approaches as well as individual program characteristics. Twenty-eight articles, representing 25 unique studies, identified from eight electronic databases (EMBASE, MEDLINE, CINAHL, ERIC, PsycINFO, DRUG, EBM Reviews, and Project CORK), were eligible for inclusion. Results indicated that primary prevention programs can be effective in reducing cannabis use in youth populations, with statistically significant effect sizes ranging from trivial (0.07) to extremely large (5.26), with the majority of significant effect sizes being trivial to small. Given that the preponderance of significant effect sizes were trivial to small and that percentages of statistically significant and non-statistically significant findings were often equivalent across program type and individual components, the effectiveness of primary prevention for cannabis use should be interpreted with caution. Universal multi-modal programs appeared to outperform other program types (i.e, universal uni-modal, targeted multi-modal, targeted unimodal). Specifically, universal multi-modal programs that targeted early adolescents (10–13 year olds), utilised non-teacher or multiple facilitators, were short in duration (10 sessions or less), and implemented boosters sessions were associated with large median effect sizes. While there were studies in these areas that contradicted these results, the results highlight the importance of assessing the interdependent relationship of program components and program types. Finally, results indicated that the overall quality of included studies was poor, with an average quality rating of 4.64 out of 9. Thus, further quality research and reporting and the development of new innovative programs are required.

Targeting increased stress sensitivity during adolescence

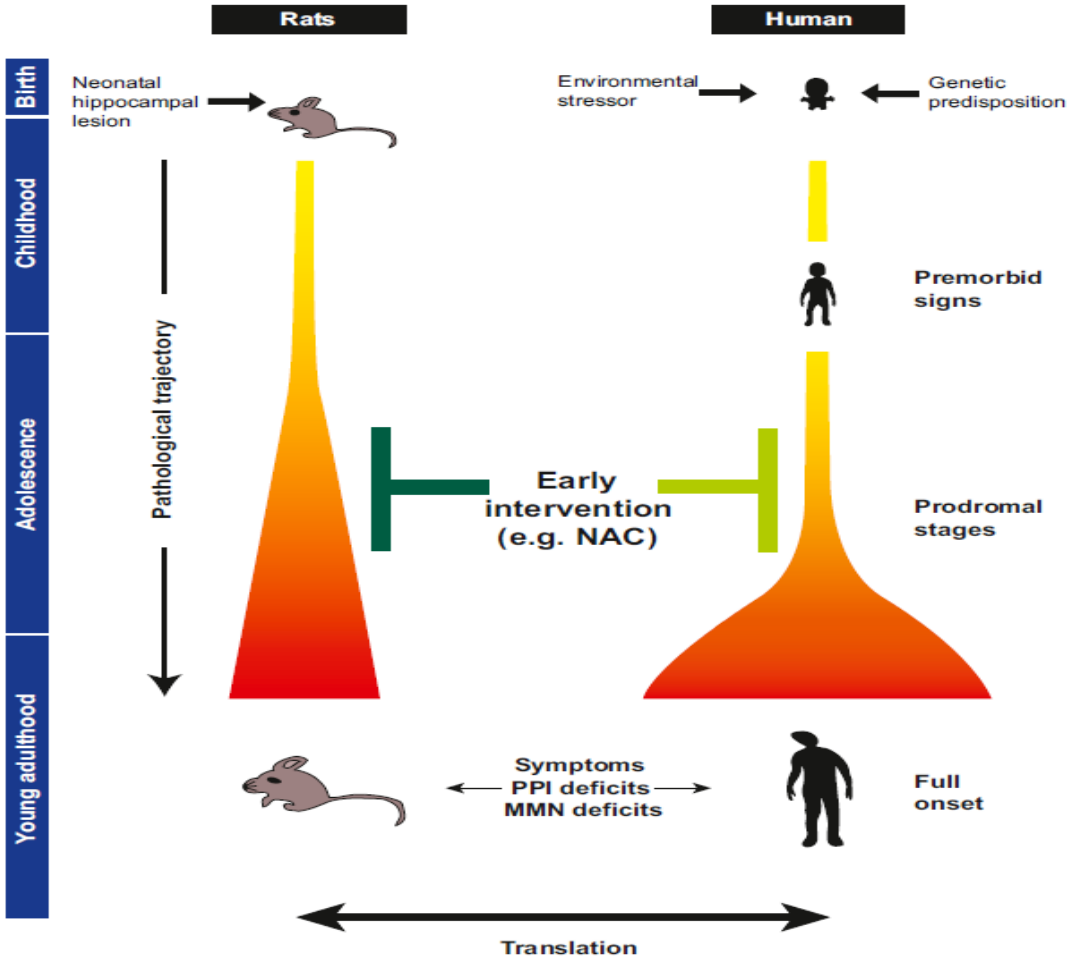
Peripubertal Diazepam Administration Prevents the Emergence of Dopamine System Hyperresponsivity in the MAM Developmental Disruption Model of Schizophrenia



Y Du and AA Grace

Neuropsychopharmacology (2013) 38, 1881–1888

Preventive interventions in adolescent oxidative stress



Akira Sawa[1,*] and Larry J. Seidman[2]

Neuron 83, September 3, 2014

Outline

- Prevention in psychiatry
- Psychosis (psychiatric disorders) as the reflection of abnormal developmental trajectories
- Shifting the focus towards prevention and early intervention in developmentally sensitive periods
- Implications and priorities for the future

ROAMER
A Roadmap for Mental Health Research in Europe

High Level Priorities

ROAMER's 6 Mental Health Research Priorities

1. Research into mental disorder prevention, mental health promotion and interventions in children, adolescents and young people
2. Focus on the development and causal mechanisms of mental health symptoms, syndromes and well-being across the lifespan (including older populations)
3. Developing and maintaining international and interdisciplinary research networks and shared databases
4. Developing and implementing better interventions using new scientific and technological advances
5. Reducing stigma, empowering service users and carers in decisions about mental health care, research
6. Health and social systems research that addresses quality of care and takes account of socio-cultural and socio-economic contexts and approaches

Prevention and very early intervention in the context of a developmental perspective

Putting science into practice for early child development

UNICEF/NYHQ2011-0721/Asselin

Published Online
September 20, 2014
http://dx.doi.org/10.1016/
S0140-6736(14)61680-9

The debate between nature and nurture as determinants of early child development is over. Today, we understand that the two are inextricably linked. The degree of their interdependence—and the impact of this interplay on the developing brains of children—is even greater than we previously imagined.[1] This knowledge has tremendous implications for how we design and deliver early child development interventions.

During the past 24 years, the united efforts and shared goals of the global community have achieved substantial progress in child survival, and child mortality worldwide has declined by 49%.[2] We can build on those gains by focusing new effort and attention not only on saving

violent conflicts and other catastrophes. Toxic stress increases the production of cortisol, a hormone that can disrupt the healthy development of the brain, affecting health, learning, and behaviour. Toxic stress also undermines the ability of the body to absorb nutrients, so potentially exacerbating malnutrition.[5]

We are just beginning to understand how environmental factors—including the quality of parenting—might modify the expression of genes, and possibly affect not just one, but multiple, generations.[6,7] This growing area of inquiry is beginning to change the way we think about development in early childhood and early childhood development interventions. As separate

Recommendations:

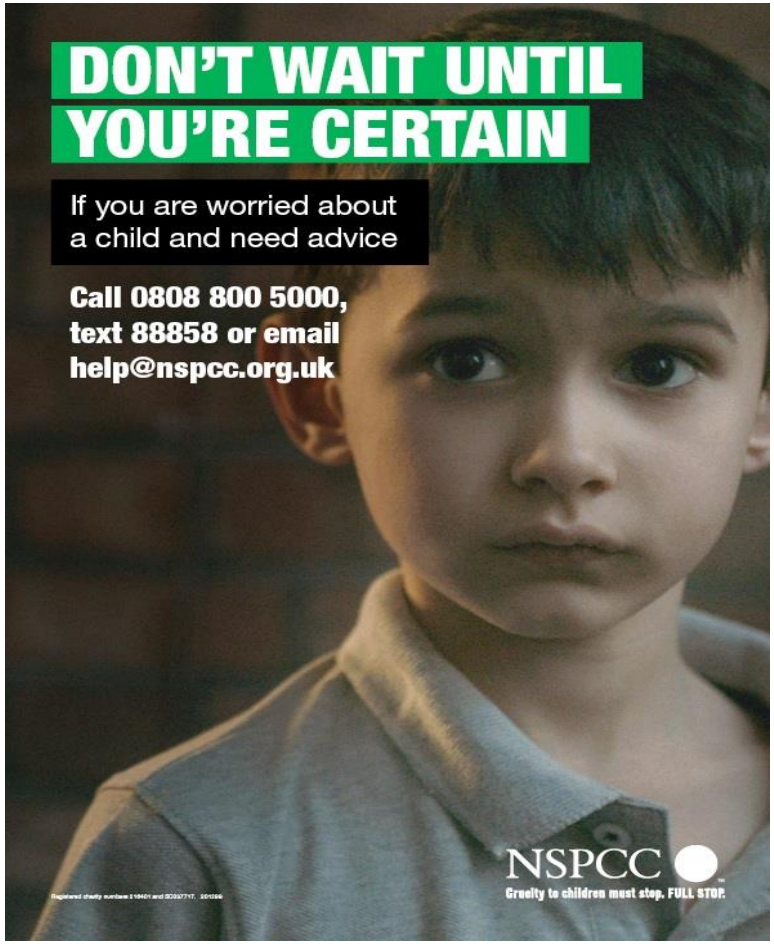
1) Early interventions should start with prenatal care, even before conception.
2) Policies and interventions should be interdisciplinary involving health, education, nutrition, high-quality caregiving and protection
3) Effective programmes should take into account brain development, with special focus on critical periods such as early childhood and adolescence.

*Anthony Lake, *Margaret Chan*

SOCIETY

Increase awareness of risk factors and implement preventive interventions

Early detection and intervention in high-risk situations



- Increase social awareness of child abuse and neglect.
- Specific education of professionals in contact with children: teachers, pediatricians, doctors working in emergency services, social workers.
- Early detection at schools.
- Create safe environments facilitating the reporting of child abuse and avoiding re-victimisation.
- Close monitoring of cases of child abuse for early detection of development of mental disorders.
- Avoid service fragmentation.

Early intervention strategies in patients at ultra-high risk of psychosis

Early interventions to prevent psychosis: systematic review and meta-analysis

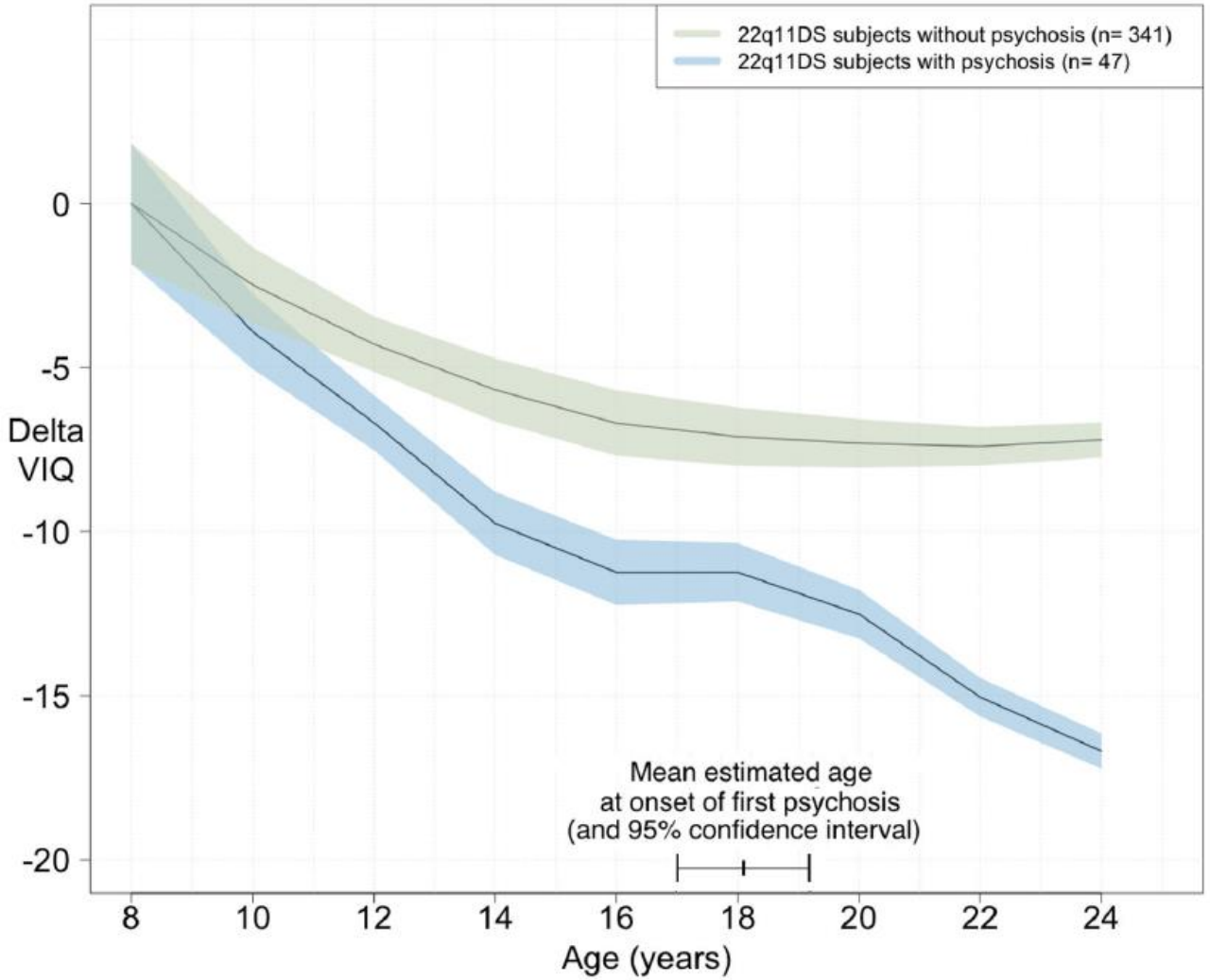
Table 2| **Summary of effects for transition to psychosis**

Comparison	Time point (months of treatment)	No (%) of trials in analysis	No (%) of participants in analysis	Risk ratio (95% CI), random effects	Heterogeneity (I^2 (%), χ^2 (P))	Quality of evidence (GRADE)
CBT *v* supportive counseling[23-25, 28, 29]	0-6	4 (80)	591 (88)	0.62 (0.29 to 1.31)	17, 3.6 (P=0.31)	Low*‡
	6-12	5 (100)	645 (71)	0.54 (0.34 to 0.86)	0, 2.51 (P=0.64) =0.P2)	Moderate*
	12+	4 (80)	570 (85)	0.63 (0.40 to 0.99)	0, 2.50(P=0.48)	Low*‡
CBT and risperidone *v* supportive counselling[24, 30]	0-6	2 (100)	130 (100)	0.35 (0.13 to 0.95)	0, 0.59 (P=0.44)	Very low*‡§
	6-12	2 (100)	130 (100)	0.63 (0.33 to 1.21)	0, 0.25 (P=0.61)	Very low*‡§
	12+	1 (50)	41 (32)	0.59 (0.34 to 1.04)	NA	Very low*‡§
Integrated psychotherapy *v* supportive counselling[37]	6-12	1 (100)	125 (100)	0.19 (0.04 to 0.81)	NA	Very low*‡¶
	12+	1 (100)	125 (100)	0.32 (0.11 to 0.92)	NA	Very low*‡¶
Integrated psychotherapy *v* standard care[35]	6-12	1 (100)	67 (85)	0.24 (0.07 to 0.81)	NA	Low*‡
	12+	1 (100)	65 (82)	0.52 (0.26 to 1.02)	NA	Low*‡
CBT and risperidone *v* CBT and placebo[24]	0-6	1 (100)	87 (100)	1.02 (0.15 to 6.94)	NA	Very low*‡§
	6-12	1 (100)	87 (100)	1.02 (0.39 to 2.67)	NA	Very low*‡§
Olanzapine *v* placebo[27]	6-12	1 (100)	60 (100)	0.43 (0.17 to 1.08)	NA	Very low*‡§
Omega 3 fatty acids *v* placebo[26]	0-6	1 (100)	76 (94)	0.13 (0.02 to 0.95)	NA	Low*§
	6-12	1 (100)	81 (100)	0.18 (0.04 to 0.75)	NA	Low*§

Stafford et al.,

BMJ 2013;346:f185

Cognitive decline preceding psychosis in 22q11 deletion syndrome



Vorstman et al.

JAMA Psychiatry. 2015 April 1; 72(4): 377–385

Effect of a supportive environment on cognitive and behavioural development in 22q11 deletion syndrome

Journal of Intellectual Disability Research doi: 10.1111/jir.12054

VOLUME 58 PART 1 pp 31–47 JANUARY 2014

Association of the family environment with behavioural and cognitive outcomes in children with chromosome 22q11.2 deletion syndrome

T. M. Allen,[1] J. Hersh,[1] K. Schoch,[2] K. Curtiss[2], S. R. Hooper[3] & V. Shashi[2]

- Modest associations were found between aspects of the family social environment and parenting styles with social-behavioural and cognitive/academic outcomes.
- Physical punishment, socioeconomic status, parental control and family organisation significantly predicted social-behavioural and cognitive outcomes in children with 22q11DS.
- Understanding the impact of environmental variables on developmental outcomes can be useful in determining more effective targets for intervention.

Supporting parenting in mothers with schizophrenia

INTERVENTIONS

- Diagnostic, neuropsychological and parenting assessments
- Outpatient, home outreach, crisis and inpatient treatment when needed
- Individual-, marital-, family- and group-treatment modalities
- Parent education
- Extensive linkages with schools, child protection and legal services
- Income supplementation
- Safe housing
- Respite and domestic aid
- Treatment accessibility for children
- Emphasis on prevention of negative impact of the mother's illness on the child (i.e. prenatal care, good obstetrics, postnatal psychiatric care, infant monitoring and early intervention with the child

Seeman et al., Primary Psychiatry 2002

Journal of the American Academy of
CHILD & ADOLESCENT
PSYCHIATRY

Effect of Preventive Interventions in Mentally Ill Parents on the Mental Health of the Offspring: Systematic Review and Meta-Analysis

Results

Thirteen trials including 1,490 children were analyzed. Interventions included cognitive, behavioral, or psychoeducational components. Seven trials assessed the incidence of mental disorders and seven trials assessed symptoms. In total 161 new diagnoses of mental illness were recorded, with interventions decreasing the risk by 40% (combined relative risk 0.60, 95% CI 0.45–0.79). Symptom scores were lower in the intervention groups: standardized mean differences were −0.22 (95% CI −0.37 to −0.08) for internalizing symptoms (p = .003) and −0.16 (95% confidence interval −0.36 to 0.04) for externalizing symptoms (p = .12).

Conclusions

Interventions to prevent mental disorders and psychological symptoms in the offspring of parents with mental disorders appear to be effective.

January 2012. Volume 51, Issue 1, Pages 8–17.e8

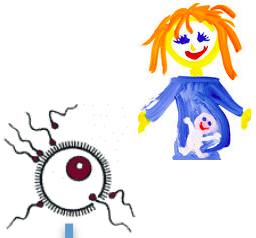
Developmentally sensitive interventions

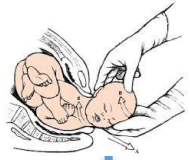
Clinical risk symptoms

Good prenatal care to improve nutrition, reduce maternal infection, substance misuse, stress, obstetric complications

- Screening for cognitive, social and motor deficits
- Prevention of trauma and bullying
- Participation in sports, art, music

- CBT, family therapy
- Medication
- Supported employment for clinical conditions







CONCEPTION | BIRTH | PRE-SCHOOL | PRIMARY SCHOOL | PUBERTY ADOLESCENCE | LATE TEENS AND 20s

Good perinatal support, good supportive parental care, early mother-child interaction support

- Support school function
- Support relationships
- Family psychoeducation
- Cognitive enhancement

- Prevention of substance use
- Management of risk taking
- Prosocial activities
- Forming identity

Familial risk for psychosis

Adapted from Seidman and Nortendoft. Schiz Bulletin, 2015

Eur Child Adolesc Psychiatry (2012) 21:475–476
DOI 10.1007/s00787-012-0313-6

EDITORIAL

Someone is not listening to the facts: there is little psychiatry outside (child and adolescent) psychiatry

preventive

Celso Arango

Published online: 2 August 2012

Given these trying economic times, let us start with some economic evidence. We have recently learned from a study funded by the European College of Neuropsychopharmacology (ECNP) and the European Brain Council (EBC) that brain disorders, and mental disorders in particular, are not only one of the main causes of burden and suffering for European countries, but they cost the EU more than cardiovascular and oncologic disorders combined. The

could be one of the plausible explanations for this finding. Another article in this issue reflects that some environmental factors, such as sexual abuse, are far more common than expected. Using data from a longitudinal randomised controlled trial of a school-based intervention programme for reducing adolescent sexual assault and related risk behaviours, Brasmen et al. (in press) assessed the prevalence of adolescent peer-on-peer sexual victimisation over

Conclusions

- There is still little interest in preventative interventions in psychiatry, as compared with other medical specialties.

- Behavioural symptoms are late manifestations of the underlying brain process. Recent knowledge about developmental risks for psychosis has shaped a promising outlook for early intervention.

- Risk factors do not seem to be disorder-specific. In psychosis, even early intervention is most often secondary prevention.

Conclusions

•A priority for the next few years will be to focus towards “very early” interventions in which the aim is not prevention of psychosis. Eventually, specific interventions in developmentally sensitive periods, may reduce the incidence of psychosis or shift the evolution towards less severe presentations.

•In those at very increased risk of presenting psychosis, narrow monitoring, parent training and training in coping skills should be mandatory.

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