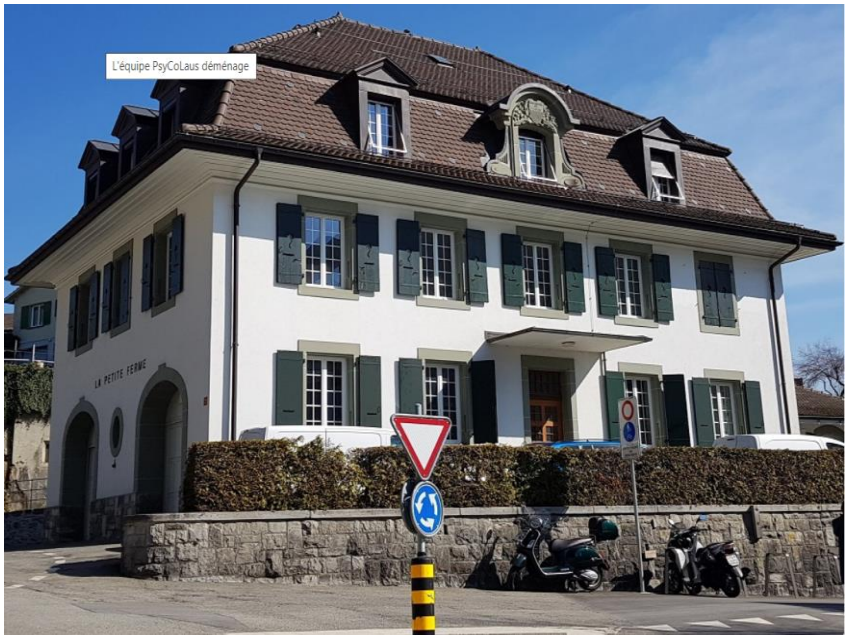
The Lausanne – Geneva High-Risk Study

Martin Preisig

Caroline Vandeleur



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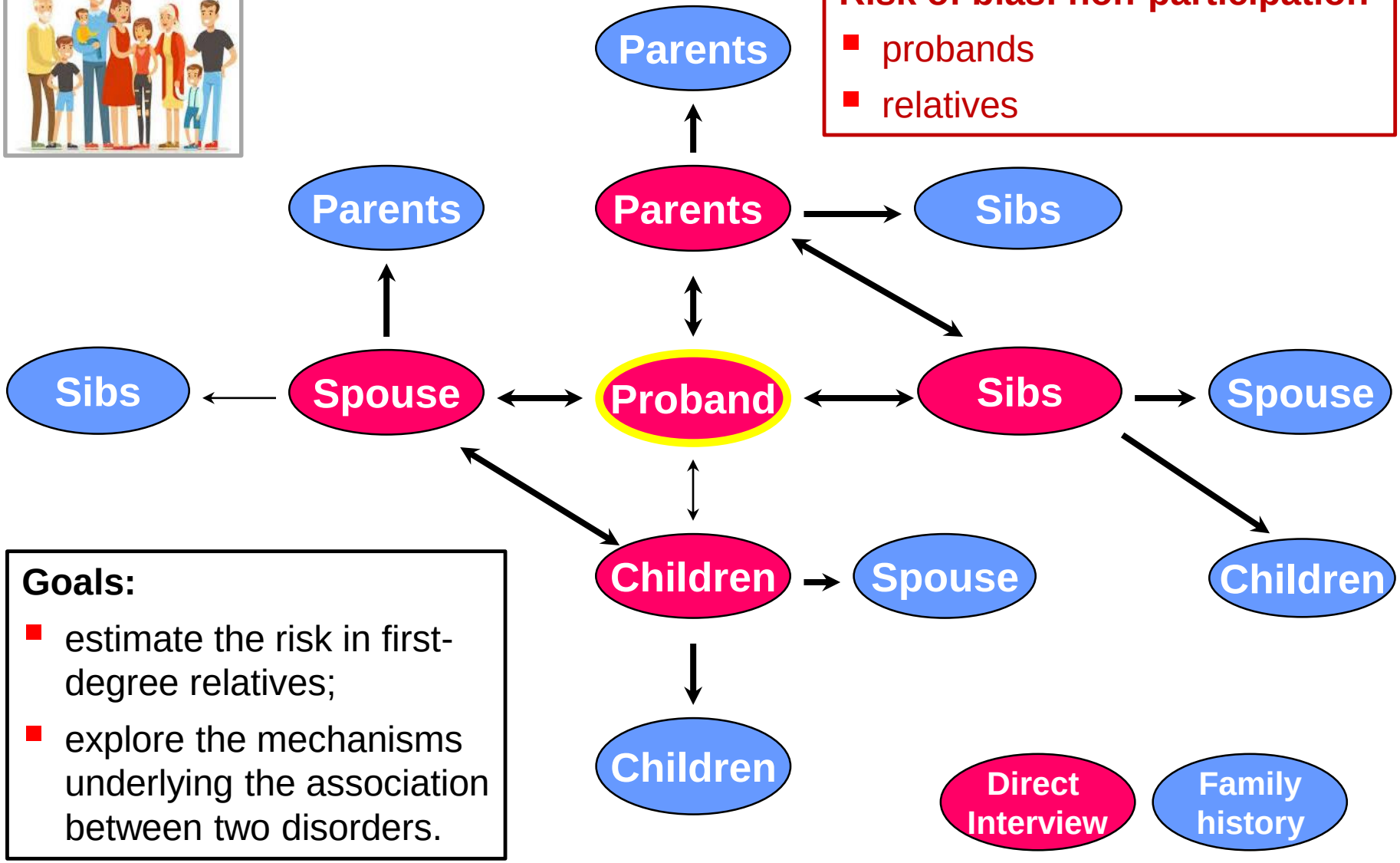
- five grants from the Swiss National Foundation (#3200-040677, #32003B-105969, #32003B-118326, #3200-049746 and #3200-061974);
- three grants for a National Centers of Competence in Research project “The Synaptic Bases of Mental Diseases” (#125759, #158776, and #51NF40 – 185897) financed by the Swiss National Foundation;
- one grant from the Swiss State Secretariat for Education, Research and Innovation (SERI #22.00170); and
- one grant from the Foundation Campus Biotech Geneva, and one grant from GlaxoSmithKline Clinical Genetics.

Family studies

Risk of bias: non-participation

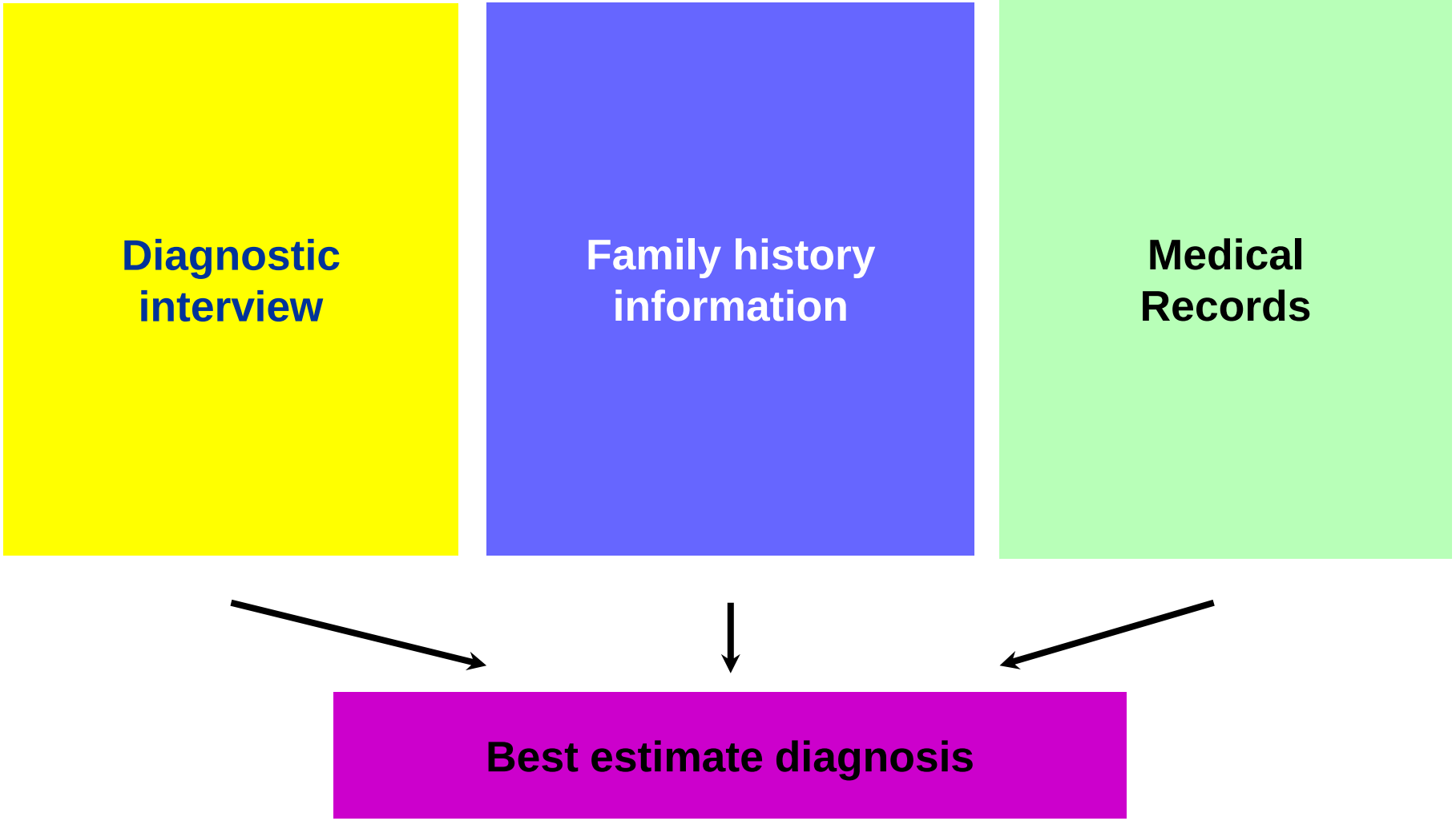
- probands
- relatives



Goals:

- estimate the risk in first-degree relatives;
- explore the mechanisms underlying the association between two disorders.

Best estimate procedure



Best estimate procedure

Journal of Affective Disorders 171 (2015) 120–127

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research report

Inter-informant agreement and prevalence estimates for mood syndromes: Direct interview vs. family history method

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[b] Department of Mental Health and Psychiatry, University Hospital of Geneva, Switzerland

Available online at www.sciencedirect.com

ScienceDirect

Drug and Alcohol Dependence 92 (2008) 9–19

DRUG and ALCOHOL DEPENDENCE

www.elsevier.com/locate/drugalcdep

Inter-informant agreement and prevalence estimates for substance use disorders: Direct interview versus family history method☆

C.L. Vandeleur [a,*], S. Rothen [a,b], N. Jeanprêtre [b], Y. Lustenberger [a,b], F. Gamma [c], E. Ayer [b], F. Ferrero [a], A. Fleischmann [b], J. Besson [b], F. Sisbane [b], M. Preisig [b]

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[b] Department of Adult Psychiatry, University Hospital of Lausanne, 1008, Prilly, Switzerland
[c] Department of Psychiatry, Harvard Medical School, Boston, MA 02115, USA

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Available online at www.sciencedirect.com

ScienceDirect

Psychiatry Research 157 (2008) 211–223

PSYCHIATRY RESEARCH

www.elsevier.com/locate/psychres

Inter-informant agreement on diagnoses and prevalence estimates of anxiety disorders: Direct interview versus family history method

Ansgar Rougemont-Buecking [a,*,1], Stéphane Rothen [a,b,1], Nicolas Jeanprêtre [a], Yodok Lustenberger [a,b], Caroline L. Vandeleur [b], Francois Ferrero [b], Martin Preisig [a]

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International Journal of Methods in Psychiatric Research
Int. J. Methods Psychiatr. Res. 18(2): 96–109 (2009)
Published online in Wiley InterScience
(www.interscience.wiley.com) **DOI:** 10.1002/mpr.281

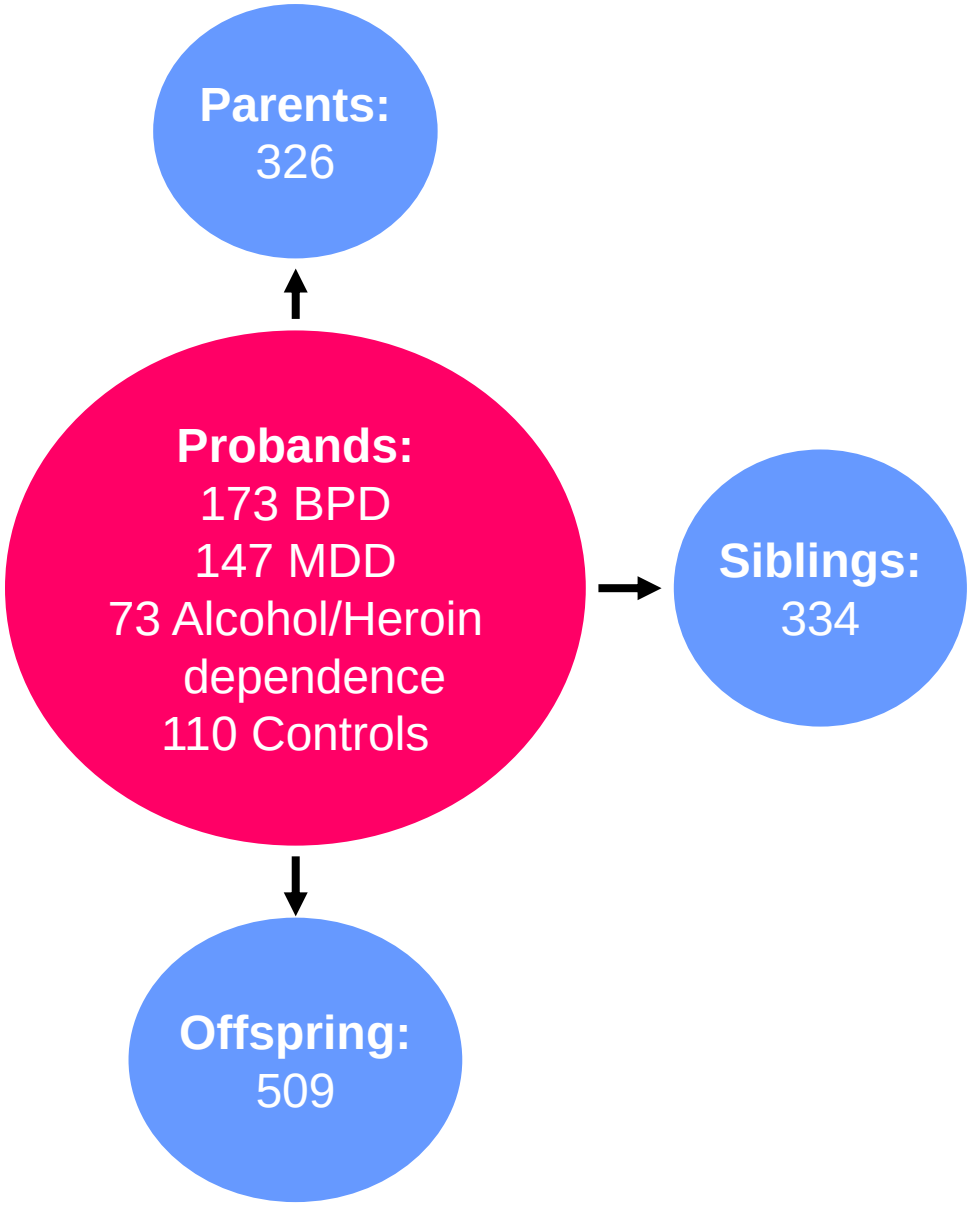
Parent–child agreement and prevalence estimates of diagnoses in childhood: Direct interview versus family history method

STÉPHANE ROTHEN,[1,2] CAROLINE L. VANDELEUR,[2] YODOK LUSTENBERGER,[1,2] NICOLAS JEANPRÊTRE,[1] EVE AYER,[1] FRANZISKA GAMMA,[1] OLIVIER HALFON,[1] DANIEL FORNEROD,[1] FRANÇOIS FERRERO[2] & MARTIN PREISIG[1]

1 Department of Psychiatry, University Hospital Center and University of Lausanne, Lausanne, Switzerland
2 Department of Psychiatry, University Hospital of Geneva, Geneva, Switzerland

- Low sensitivity but high specificity of family history reports
- Differential reporting of participants in function of their own health status

Lausanne-Geneva Family Study



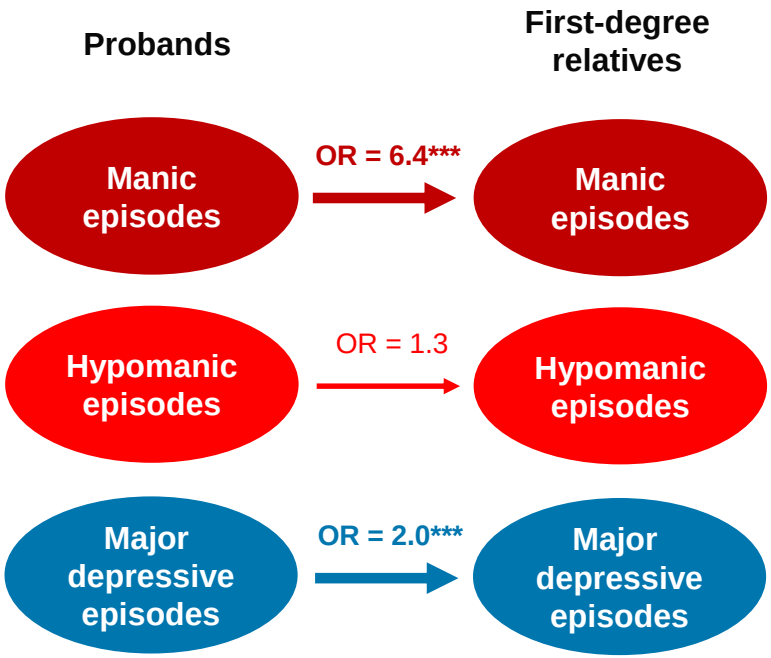
Goals:

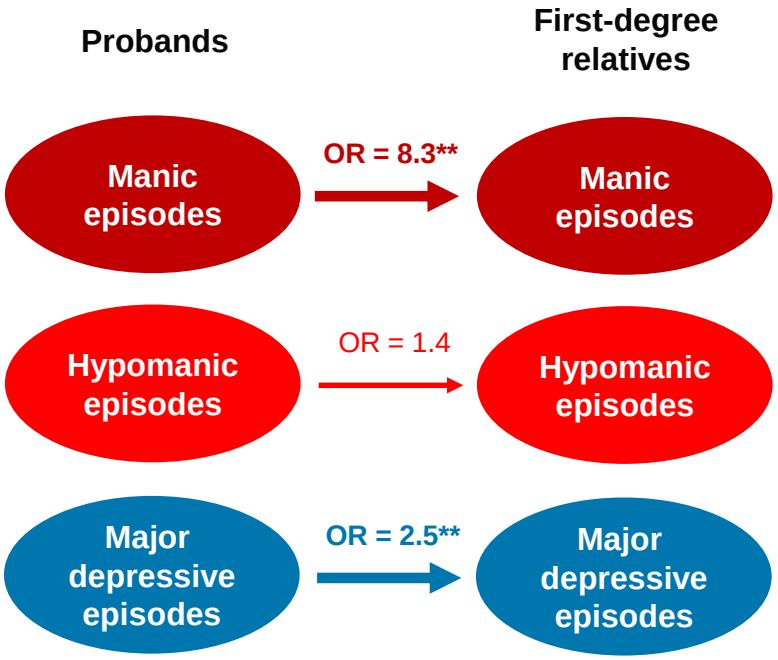
1) examine the specificity of the familial aggregation of BPD and MDD

2) assess the impact of comorbid substance use and anxiety disorders on the familial aggregation of mood disorders;

3) determine the mechanisms underlying the associations between mood disorders and comorbid conditions through the investigation of patterns of familial aggregation of these disorders.

Familial aggregation of mood episodes





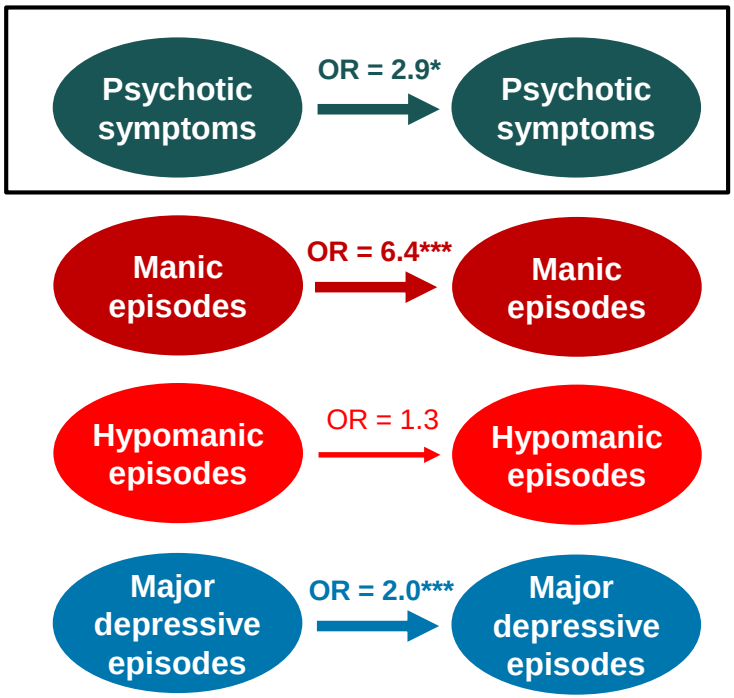
* p < 0.05; *** p < 0.001

CL Vandeleur et al (2014) Mol Psychiatry 19:209-13

* p < 0.05; * p < 0.05; *** p < 0.001

KR Merikangas et al (2014) Mol Psychiatry 19:214-19

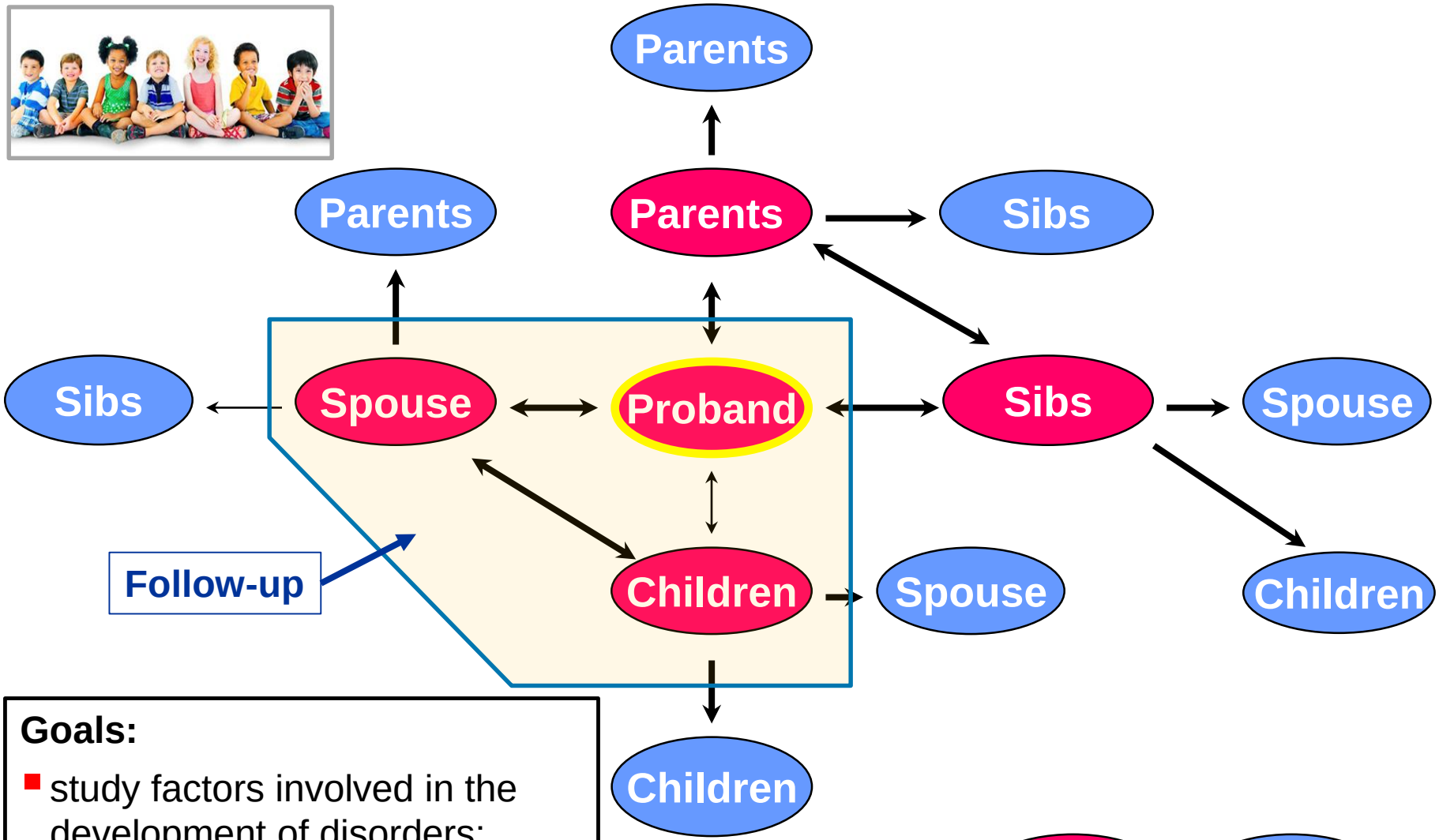
Familial aggregation of mood and psychotic episodes



* p < 0.05; *** p < 0.001

CL Vandeleur et al (2014) Mol Psychiatry 19:209-13

High-Risk Studies



Goals:

- study factors involved in the development of disorders;
- identify precursors (prodromes) of disorders.

Lausanne – Geneva High-Risk Study

Soc Psychiatry Psychiatr Epidemiol (2017) 52:1041–1058
DOI 10.1007/s00127-017-1382-0

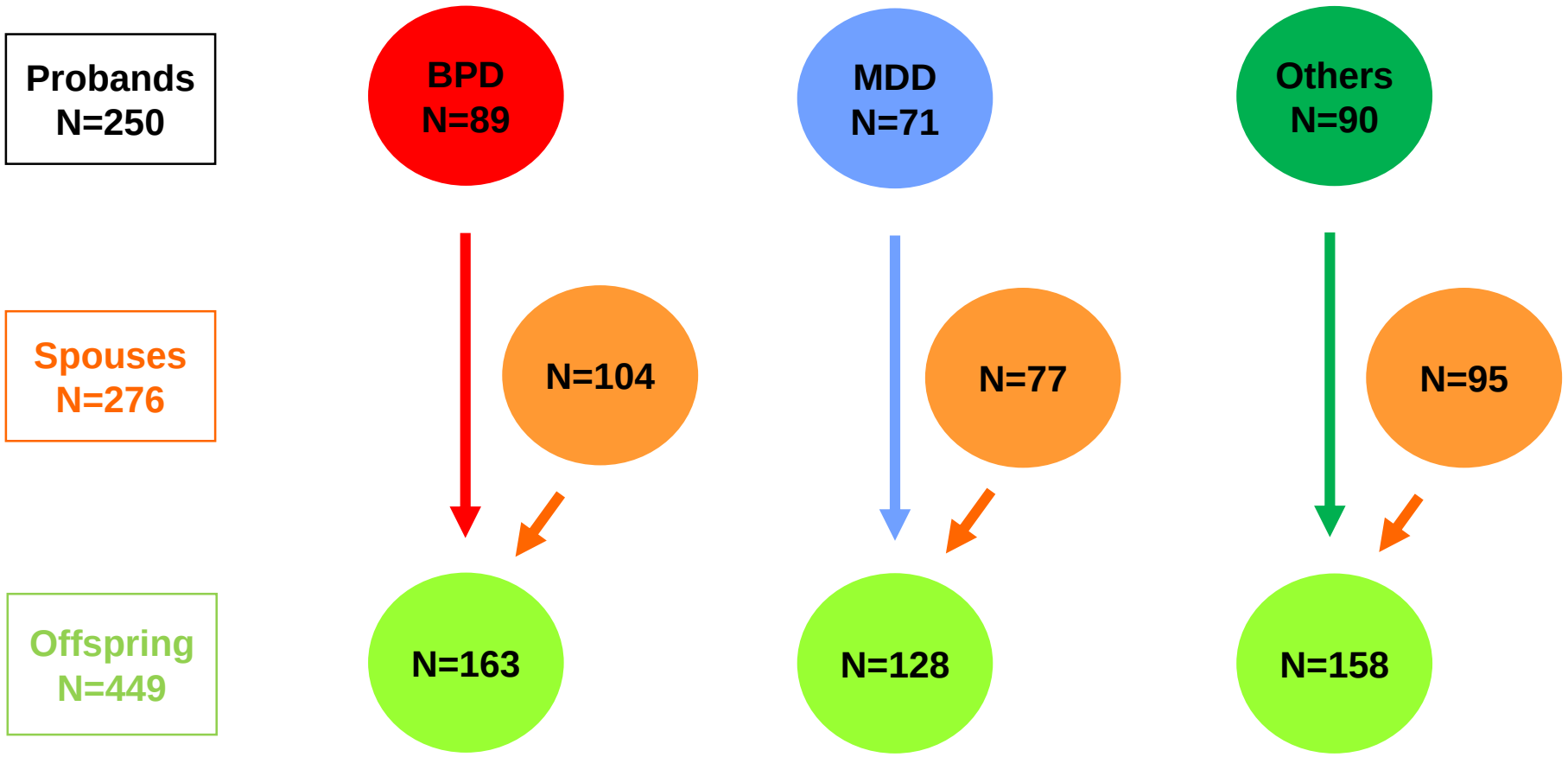
CrossMark

STUDY PROTOCOLS AND SAMPLES

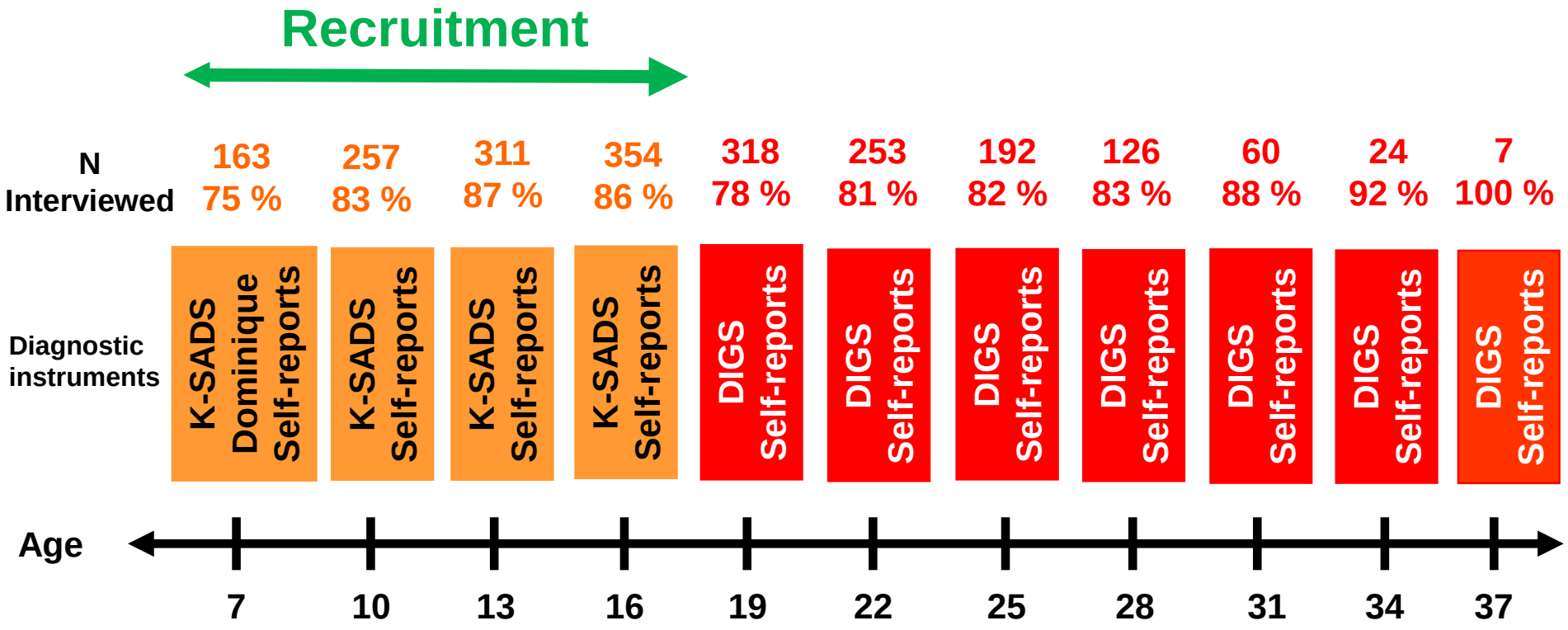
The Lausanne–Geneva cohort study of offspring of parents with mood disorders: methodology, findings, current sample characteristics, and perspectives

Caroline L. Vandeleur[1] · Marie-Pierre F. Strippoli[1] · Enrique Castelao[1] · Mehdi Gholam-Rezaee[1] · François Ferrero[2] · Pierre Marquet[1] · Jean-Michel Aubry[2] · Martin Preisig[1]

Lausanne/Geneva High Risk Study: Recruitment



Assessments in offspring (n=449)



Psychiatric assessments in adults

Psychological and environmental determinants

Diagnostic Interview for Genetic Studies (DIGS)

Diagnostic Interview for Headache Syndromes (DIHS)

Family History-Research Diagnostic Criteria (FH-RDC)

Life events questionnaires

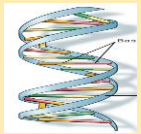
Self-reports

Neurocognitive performance

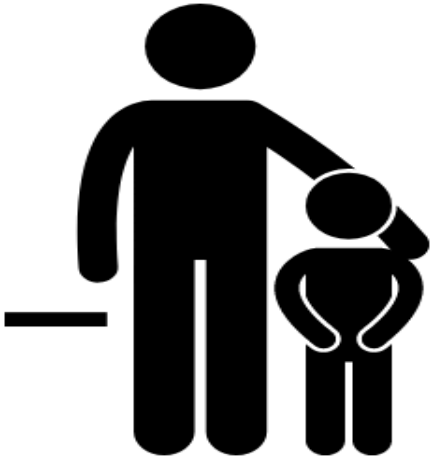
MATRICS

Physical assessments in adults

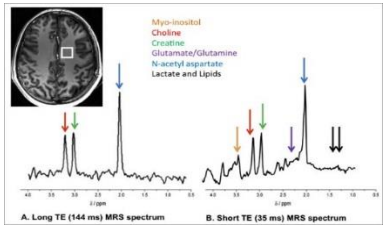
Genotyping
Dr. G. Pistis (CEPP-CHUV)



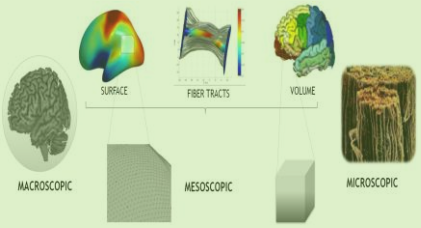
LAUSANNE-GENEVA HIGH-RISK MOOD COHORT STUDY
Prof. M. Preisig (CEPP-CHUV)



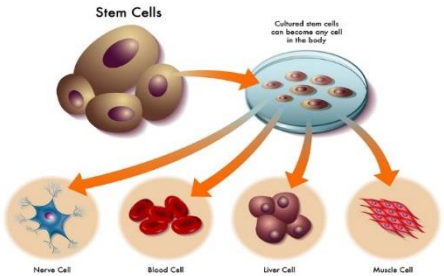
Lactate levels (MRS)
Prof. P. Magistretti (BMI-EPFL)
L. Xin (CIBM-EPFL)



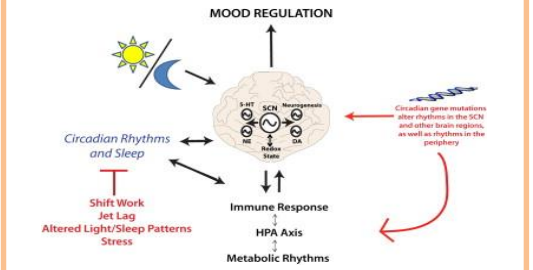
Brain morphology (MRI)
Prof. B. Draganski (LREN-CHUV)



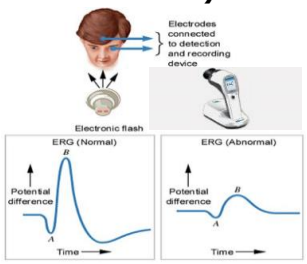
Induced pluripotent stem cells (IPSCs)
Prof. P. Marquet (CERVO, Laval, Quebec)



Physical activity/ sleep/ circadian rhythm
Prof. K. Merikangas (NIMH, USA)



Retinal response (ERG)
Dr. M. Hébert (CERVO, Laval, Quebec)



Results from baseline

BIPOLAR DISORDERS
AN INTERNATIONAL JOURNAL OF PSYCHIATRY AND NEUROSCIENCES

Bipolar Disorders 2012: 14: 641–653

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BIPOLAR DISORDERS

Original Article

Mental disorders in offspring of parents with bipolar and major depressive disorders

Vandeleur C, Rothen S, Gholam-Rezaee M, Castelao E, Vidal S, Favre S, Ferrero F, Halfon O, Fumeaux P, Merikangas KR, Aubry J-M, Burstein M, Preisig M. Mental disorders in offspring of parents with bipolar and major depressive disorders.
Bipolar Disord 2012: 14: 641–653. © 2012 The Authors.
Journal compilation © 2012 John Wiley & Sons A/S.

Objectives: There is limited information on the specificity of associations between parental bipolar disorder (BPD) and major depressive disorder (MDD) and the risk of psychopathology in offspring. The chief aim of the present study was to investigate the association between mood disorder subtypes in the two parents and mental disorders in the offspring.

Methods: A total of 376 offspring (aged 6.0–17.9 years; mean = 11.5 years) of 72 patients with BPD (139 offspring), 56 patients with MDD (110 offspring), and 66 controls (127 offspring) participated in a family study conducted in two university hospital centers in Switzerland. Probands, offspring, and biological co-parents were interviewed by psychologists blind to proband diagnoses, using a semi-structured diagnostic interview.

Results: Rates of mood and anxiety disorders were elevated among offspring of BPD probands (34.5% any mood; 42.5% any anxiety) and MDD probands (25.5% any mood; 44.6% any anxiety) as compared to those of controls (12.6% any mood; 22.8% any anxiety). Moreover, recurrent MDD was more frequent among offspring of BPD probands (7.9%) than those of controls (1.6%). Parental concordance for bipolar spectrum disorders was associated with a further elevation in the rates of mood disorders in offspring (64.3% both parents versus 27.2% one parent).

Conclusions: These findings provide unique information on the broad manifestations of parental mood disorders in their offspring. The earlier onset and increased risk of recurrent MDD in the offspring of parents with BPD compared to those of controls suggests that the episodicity characterizing BPD may emerge in childhood and adolescence.

Caroline Vandeleur[a,b], Stéphane Rothen[a,b], Mehdi Gholam-Rezaee[b], Enrique Castelao[b], Sonia Vidal[a,b], Sophie Favre[a], François Ferrero[a], Olivier Halfon[b], Pierre Fumeaux[b], Kathleen R Merikangas[c], Jean-Michel Aubry[a], Marcy Burstein[c] and Martin Preisig[b]

[a]Department of Mental Health and Psychiatry, University Hospital of Geneva, [b]Department of Psychiatry, University Hospital of Lausanne, Lausanne, Switzerland, [c]Genetic Epidemiology Research Branch, Intramural Research Program, National Institute of Mental Health, Bethesda, MD, USA

doi: 10.1111/j.1399-5618.2012.01048.x

Key words: bipolar disorder – co-parents – DSM-IV mental disorders in offspring – high-risk offspring – major depressive disorder

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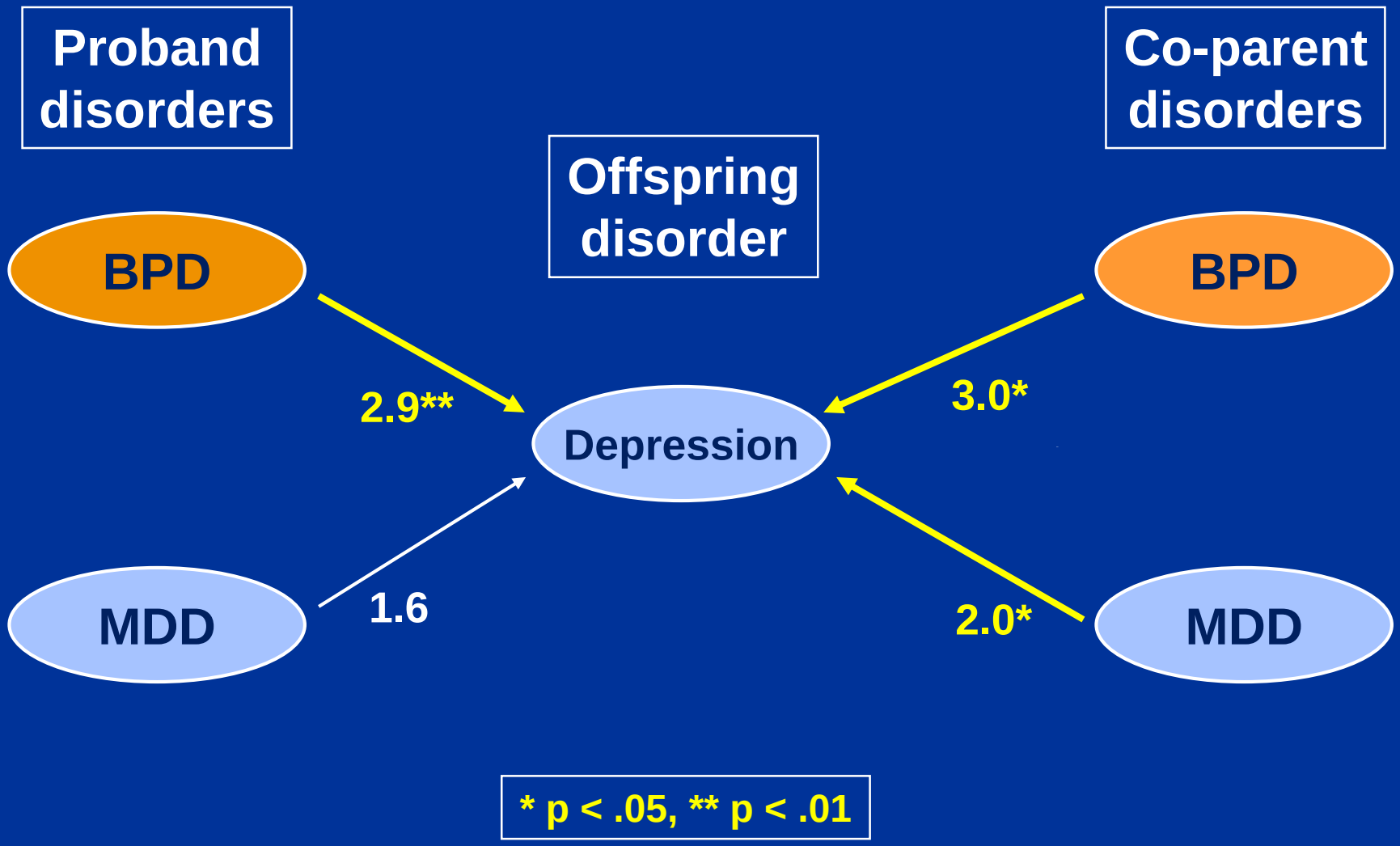
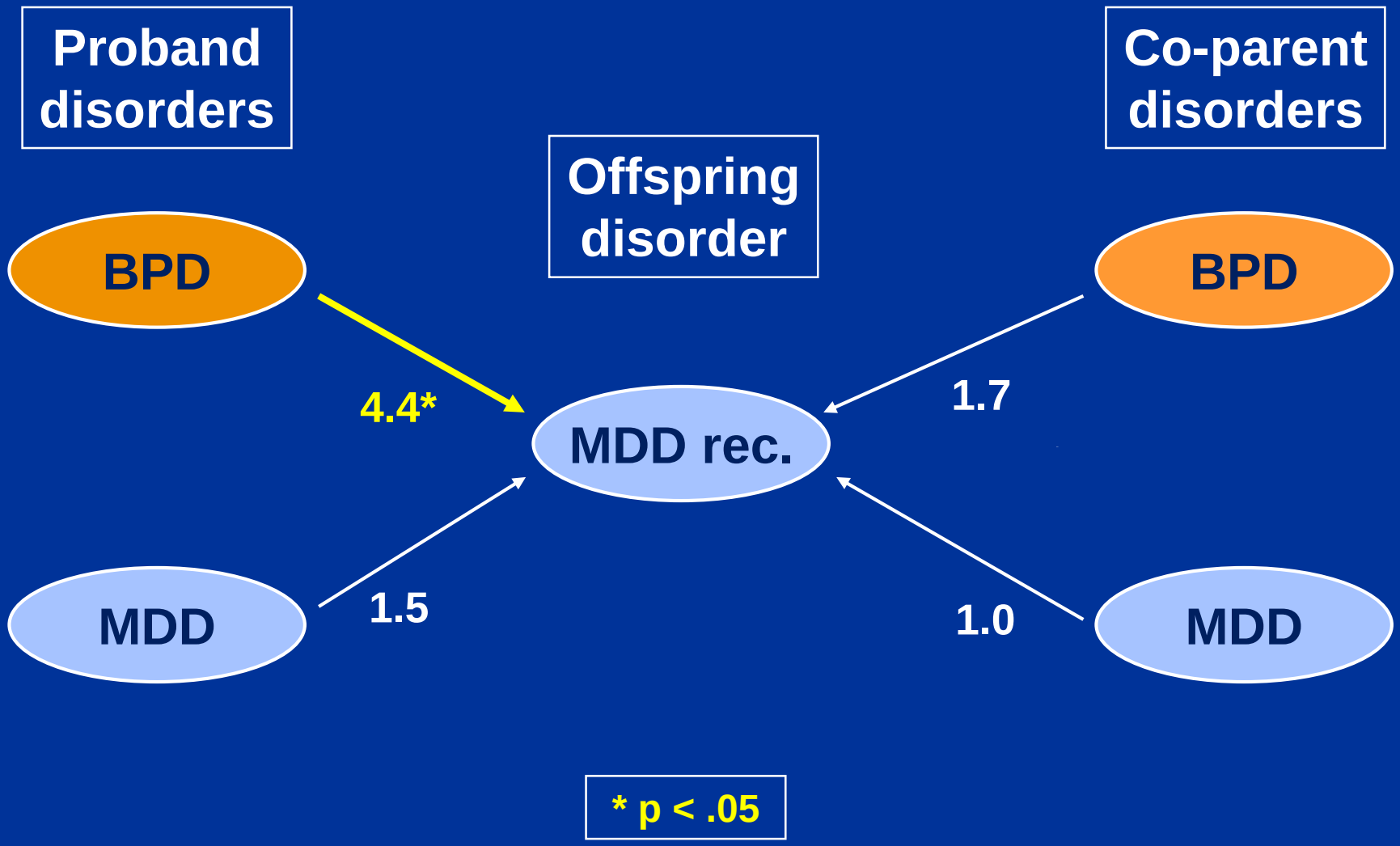
Depression in offspring (OR)



* p < .05, ** p < .01

Recurrent MDD in offspring (OR)



Results from follow-up: Specificity of familial aggregation of mood disorders

Journal of Affective Disorders 190 (2016) 26–33

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research report

The specificity of the familial aggregation of early-onset bipolar disorder: A controlled 10-year follow-up study of offspring of parents with mood disorders

Martin Preisig [a], Marie-Pierre F. Strippoli [a], Enrique Castelao [a], Kathleen Ries Merikangas [b], Mehdi Gholam-Rezaee [a], Pierre Marquet [a], Jean-Michel Aubry [c], Caroline L. Vandeleur [a,*]

[a] Department of Psychiatry, University Hospital of Lausanne, Switzerland
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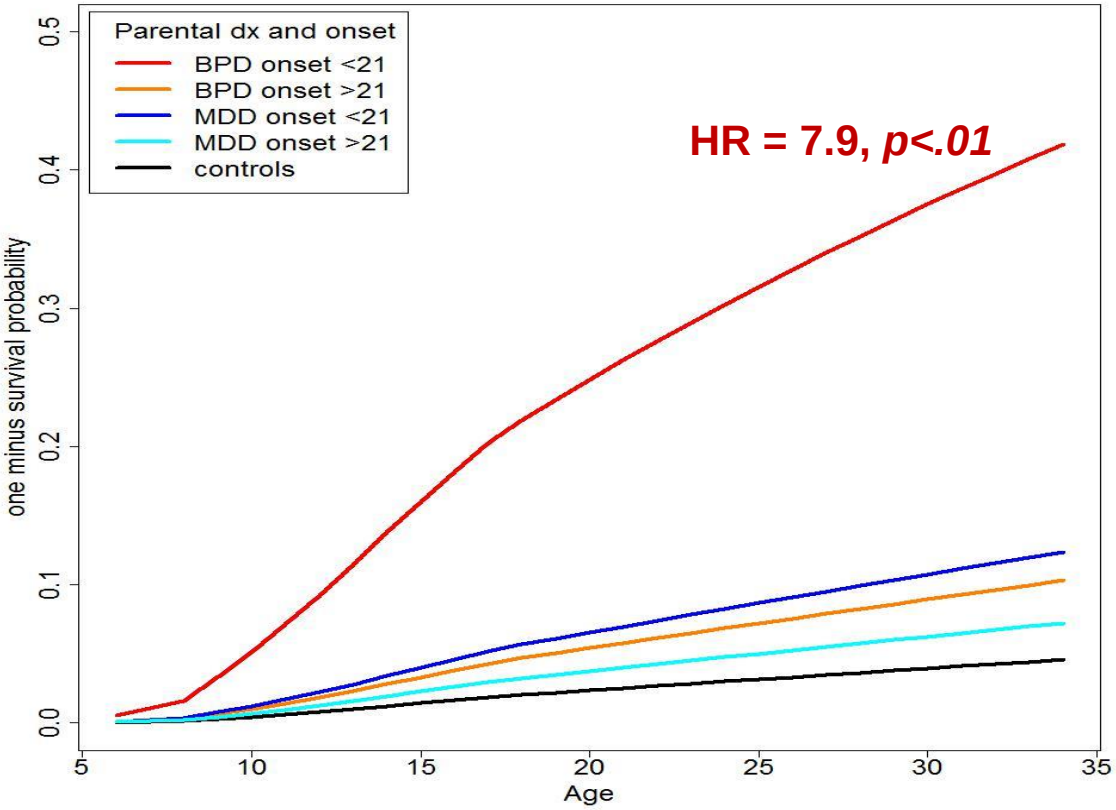
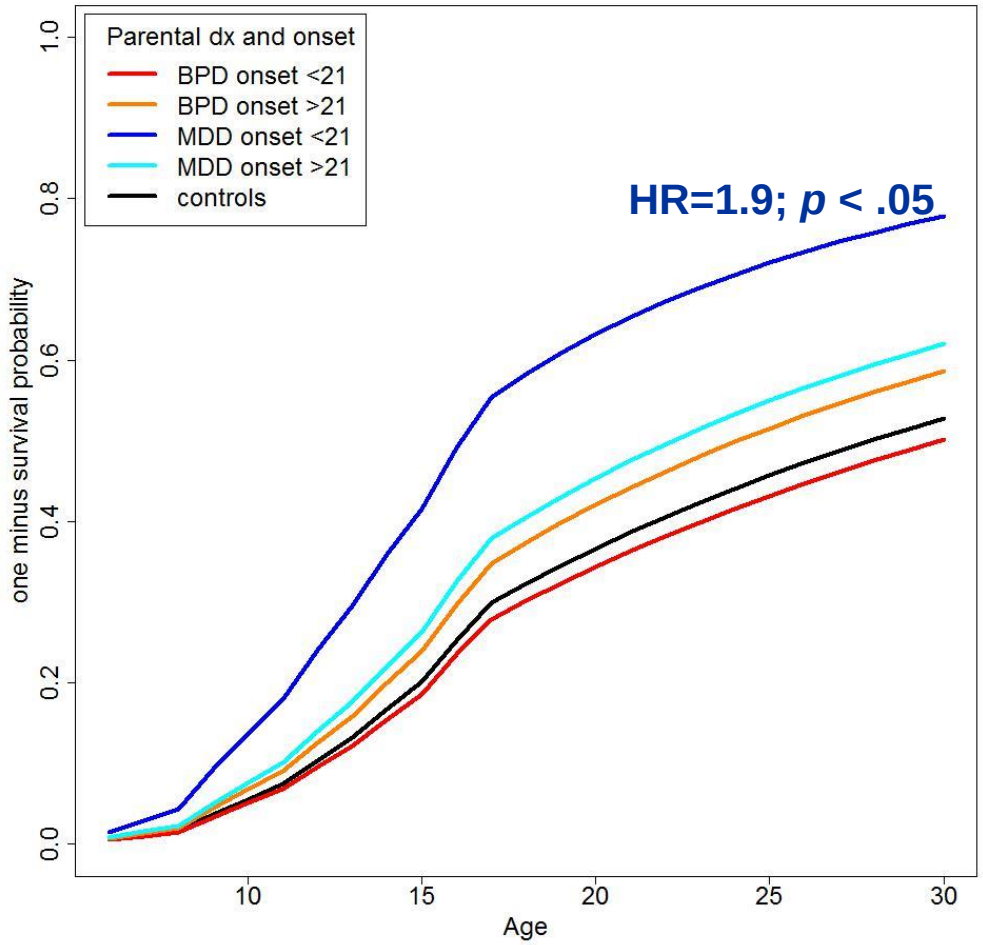
[c] Department of Mental Health and Psychiatry, University Hospital of Geneva, Switzerland

Risk of bipolar disorder by type and onset of the parental mood disorder (n=372)



Preisig M et al (2016) Journal of Affective Disorders 190:26-33

Risk of MDD in offspring as a function of the type and onset of the parental mood disorder



Moulin F et al (2022) Int J Bipolar Disord 10:11

Prospective identification of precursors of full-blown mood disorders (N=449)

The Journal of Child Psychology and Psychiatry

Journal of Child Psychology and Psychiatry 62:4 (2021), pp 404–413 doi:10.1111/jcpp.13307

Psychopathological precursors of the onset of mood disorders in offspring of parents with and without mood disorders: results of a 13-year prospective cohort high-risk study

Dominique Rudaz,[1] Caroline L. Vandeleur,[1] Mehdi Gholam,[1] Enrique Castelao,[1] Marie-Pierre F. Strippoli,[1] Pierre Marquet,[1,2] Jean-Michel Aubry,[3] Kathleen R. Merikangas,[4] and Martin Preisig[1]

[1]Department of Psychiatry, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland; [2]Institute of Mental Health, Laval University, Québec, QC, Canada; [3]Department of Psychiatry, University Hospital of Geneva, Geneva, Switzerland; [4]Genetic Epidemiology Research Branch, Intramural Research Program, National Institute of Mental Health, Bethesda, MD, USA

Prospective identification of precursors of full-blown mood disorders

Demographic characteristics of offspring by diagnostic status (n=449)

	(Hypo)mania (n=46)	MDD (n= 202)	Others (n= 201)

18 manic episodes
28 hypomanic episodes

Demographic characteristics of offspring by diagnostic status (n=449)

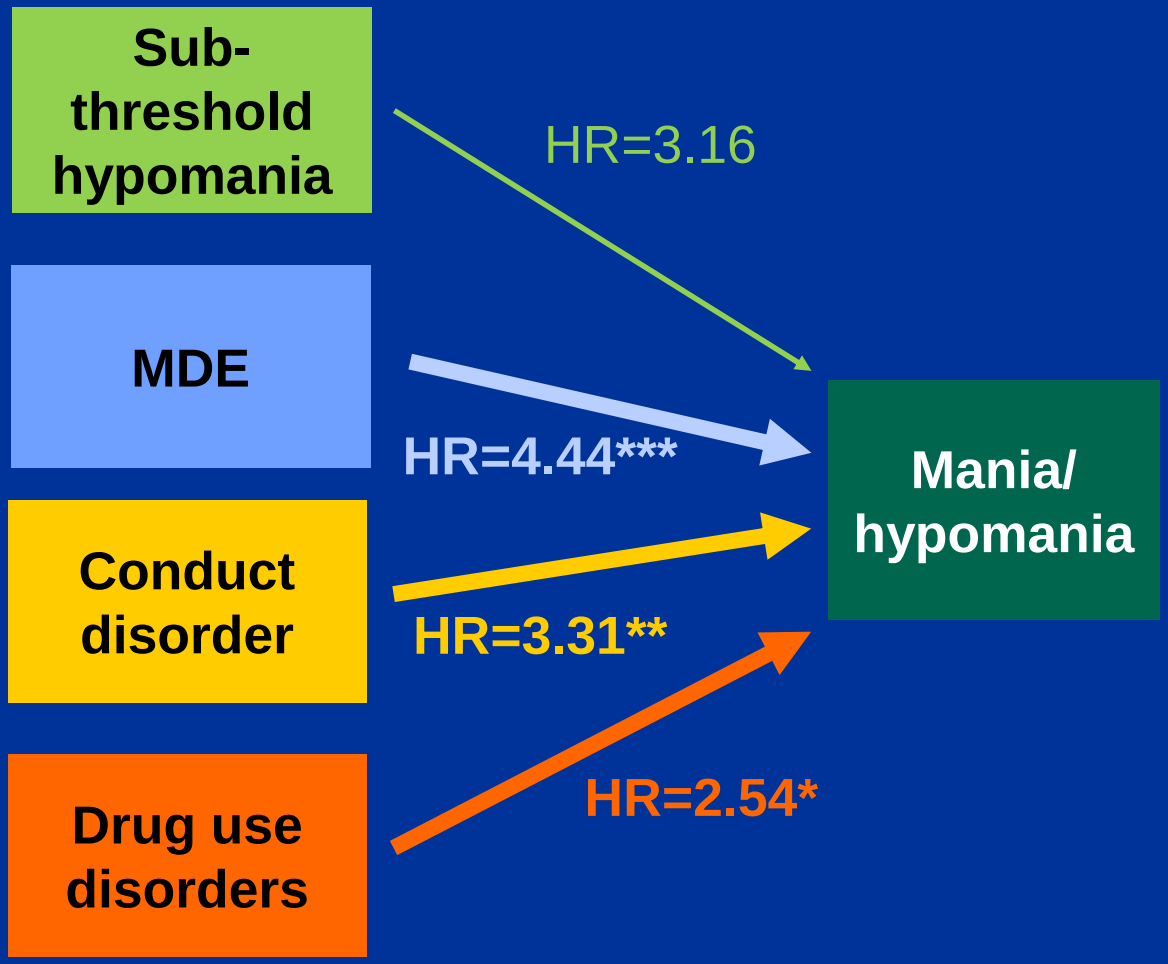
	(Hypo)mania (n=46)	MDD (n= 202)	Others (n= 201)
Girls (%)	**56.5**	**57.9*↑**	**42.8**
Age at first assessment (mean)	**11.5*↑**	**10.4**	**9.6**
SES of the family (1-5)	**3.2**	**3.2**	**3.1**
Duration of follow-up [yrs]	**14.0**	**13.9***↑**	**12.4**
# Assessments (mean)	**5.0**	**5.1**↑**	**4.6**
# Interviews (mean)	**3.9**	**4.2***↑**	**3.5**

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$

Clinical characteristics of offspring by diagnostic status (n=449)

	(Hypo)mania (n=46)	MDD (n= 202)
Age of onset of first (hypo)mania (mean)	**17.1**	**-**
Age of onset of first MDE (mean)	**13.8**	**14.5**
# **(Hypo)manic episodes** (mean)	**2.0**	**-**
# **MDE** (mean)	**2.9**	**2.6**

Antecedents of (hypo)mania



γ-frailty model with adjustment for offspring sex and SES of the family
***$p < 0.001$; **$p < 0.01$; *$p < 0.05$

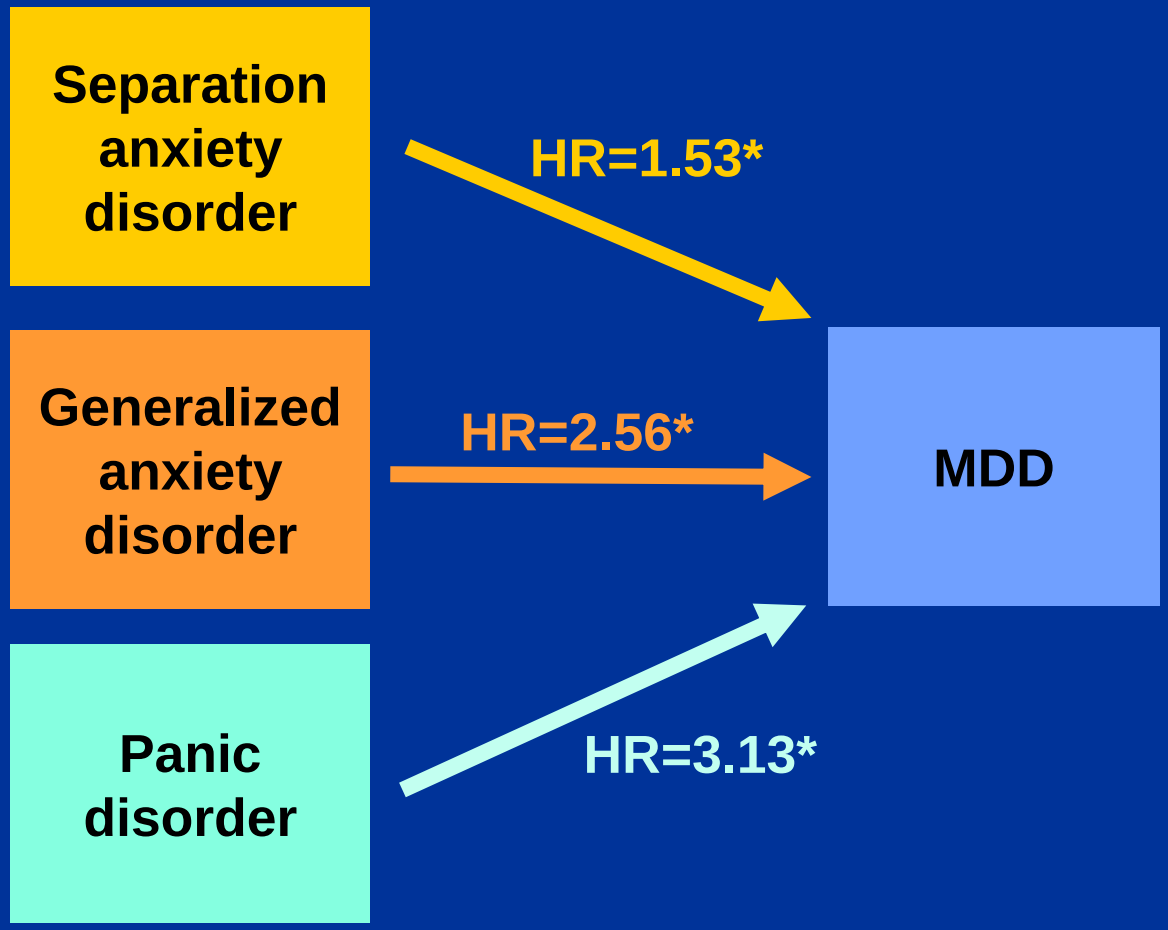
Predictive value of antecedents of (hypo)mania

All offspring	Sensitivity
MDE	0.70
Conduct disorder	0.25
Drug use disorder	0.27

Predictive value of antecedents of (hypo)mania

All offspring	Sensitivity	Specificity	Positive predictive value	Negative predictive value
MDE	0.70	0.50	0.13	0.94
Conduct disorder	0.25	0.90	0.21	0.92
Drug use disorder	0.27	0.82	0.13	0.91

Antecedents of MDD



γ-frailty model with adjustment for offspring sex and SES of the family
***$p < 0.001$; **$p < 0.01$; *$p < 0.05$

Predictive value of antecedents of MDD

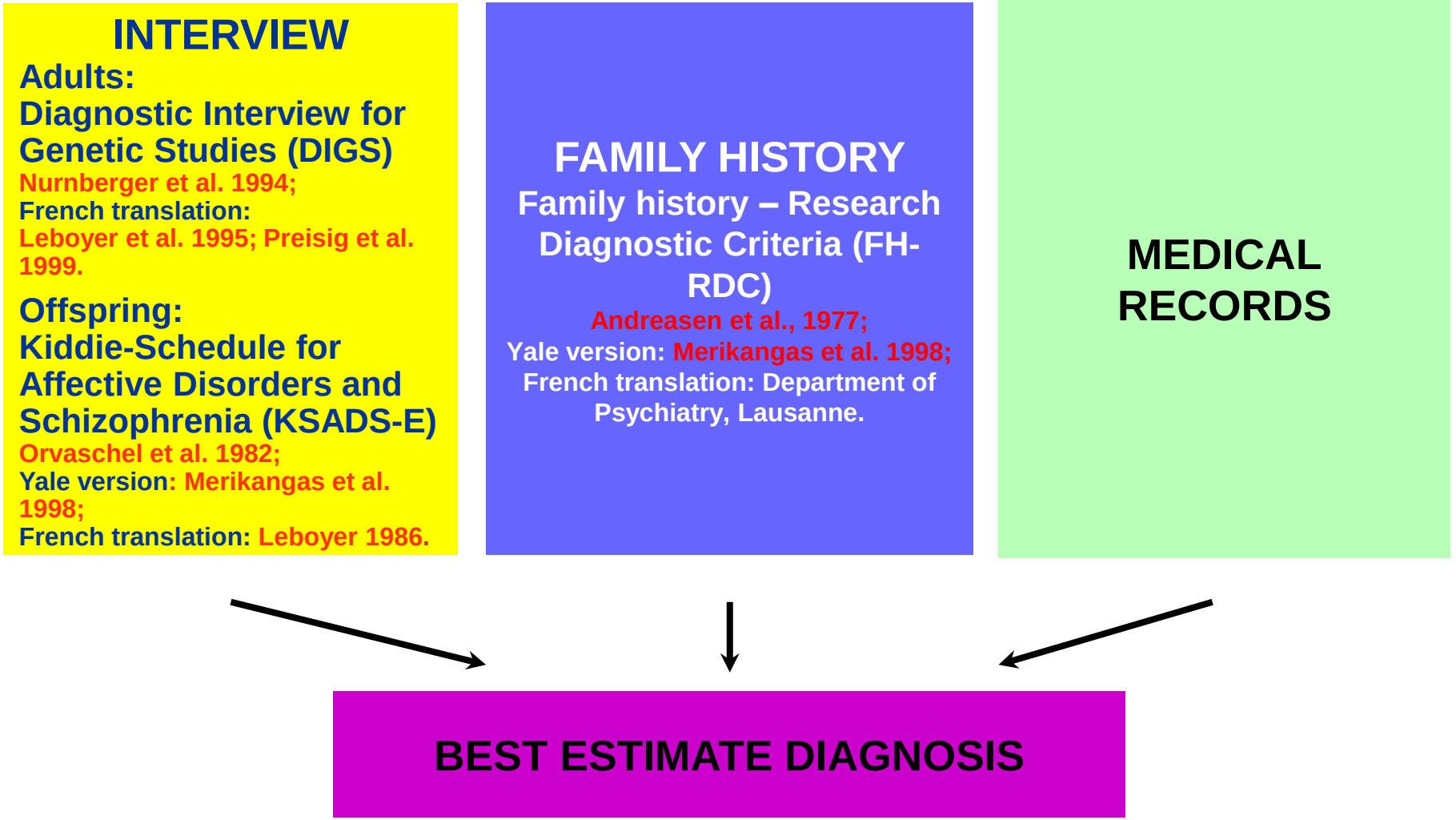
All offspring	Sensitivity
Separation anxiety	0.37
GAD	0.04
Panic disorder	0.03

Predictive value of antecedents of MDD

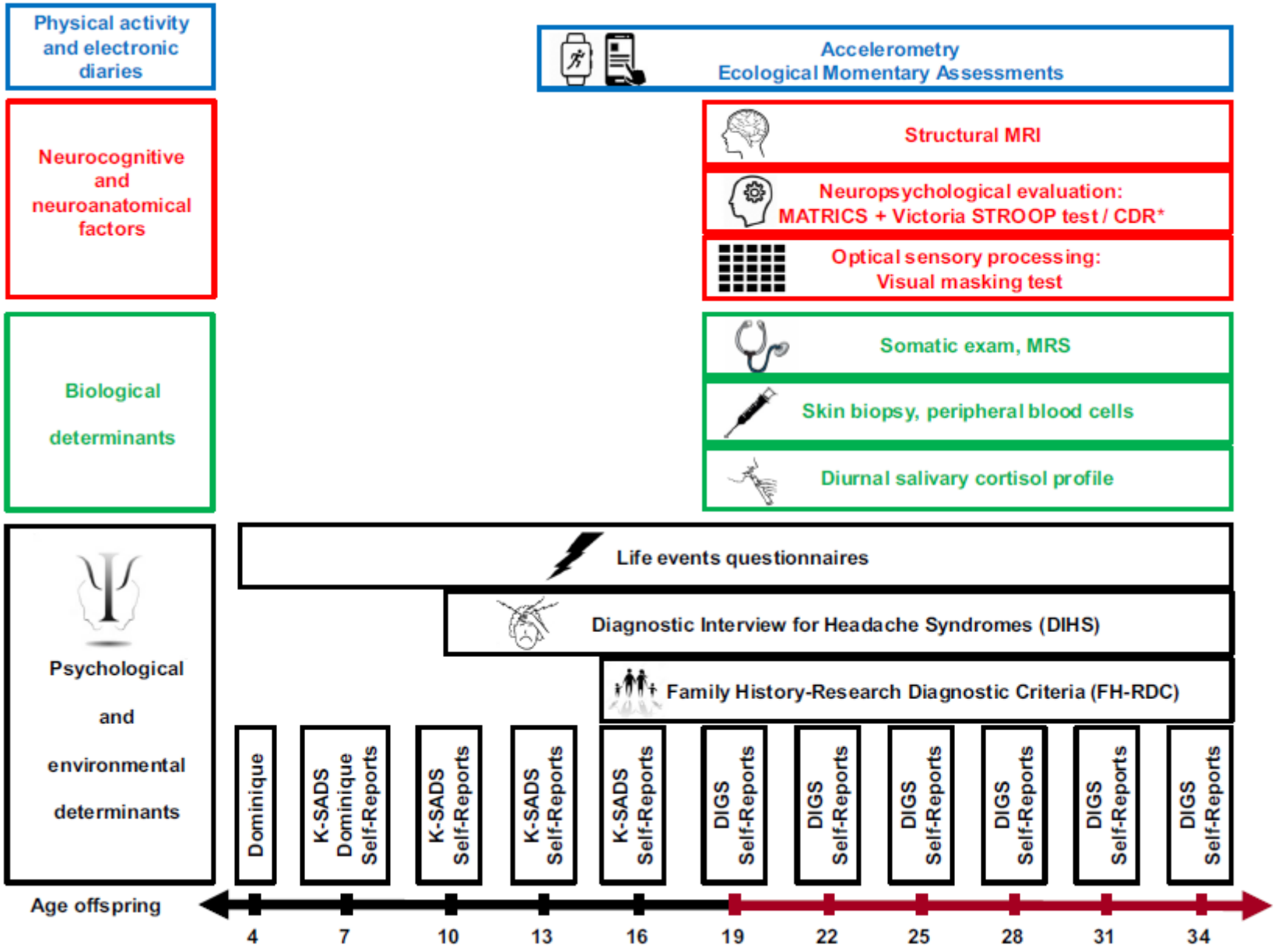
All offspring	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Separation anxiety	0.37	0.70	0.45	0.63
GAD	0.04	0.98	0.60	0.61
Panic disorder	0.03	0.99	0.63	0.61

End of the first part

Best estimate procedure



Assessments



Vandeleur et al. Soc Psychiatry Psychiatr Epidemiol. 2017; 52:1041-1058.