

Mental health disorders during childhood and adolescence: ALSPAC

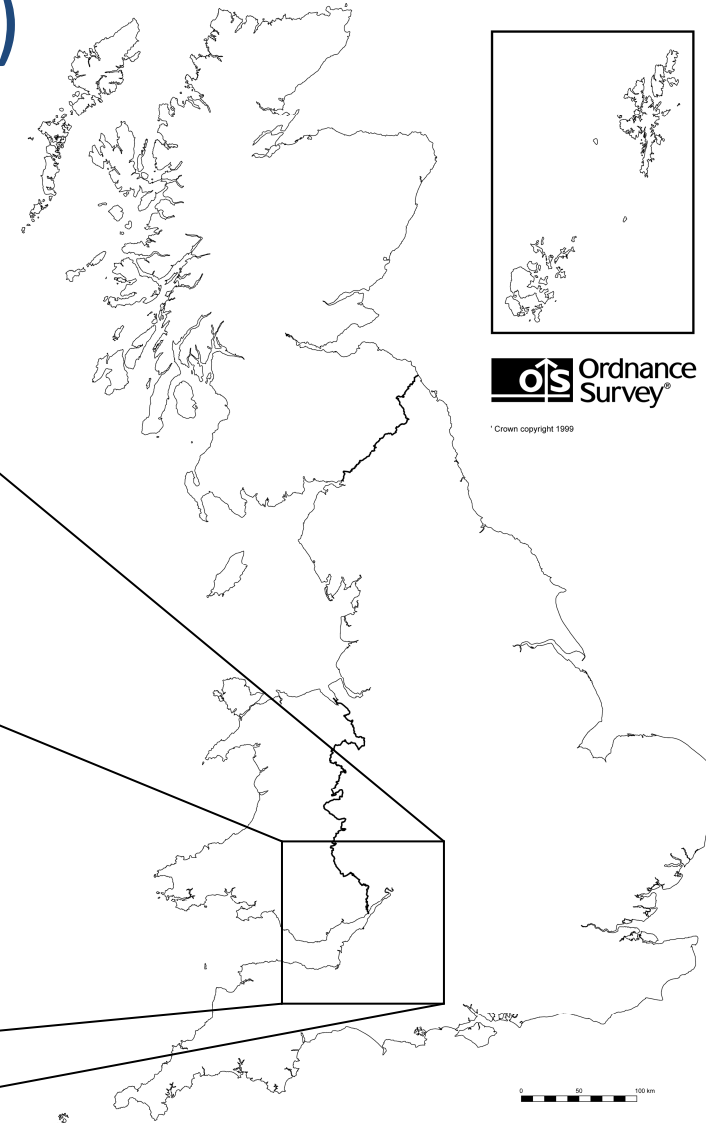
Stan Zammit

School of Social & Community Medicine, University of Bristol &
MRC Centre for Neuropsychiatric Genetics & Genomics, Cardiff University



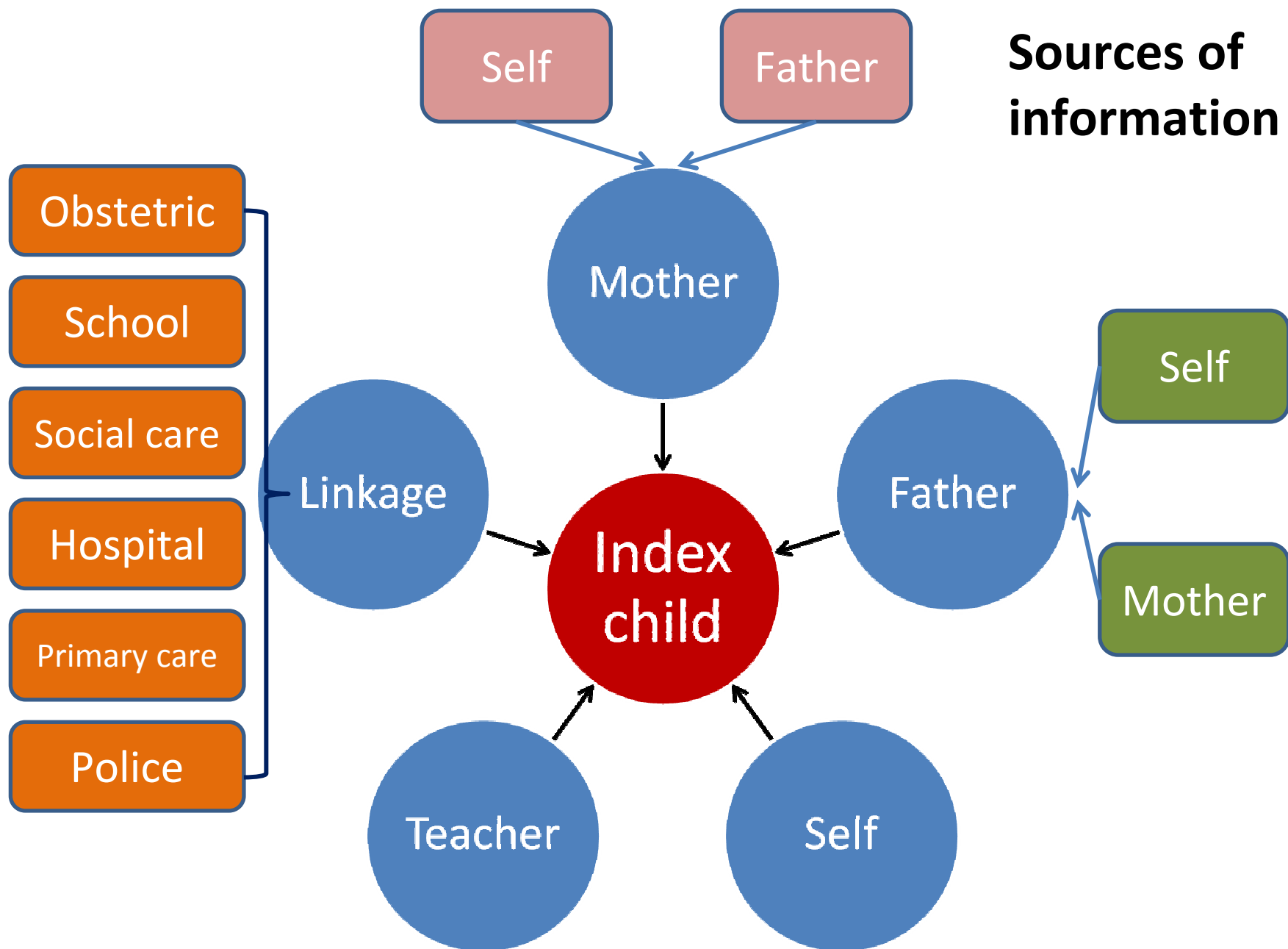


Avon Longitudinal Study of Parents & Children (ALSPAC)



Participants

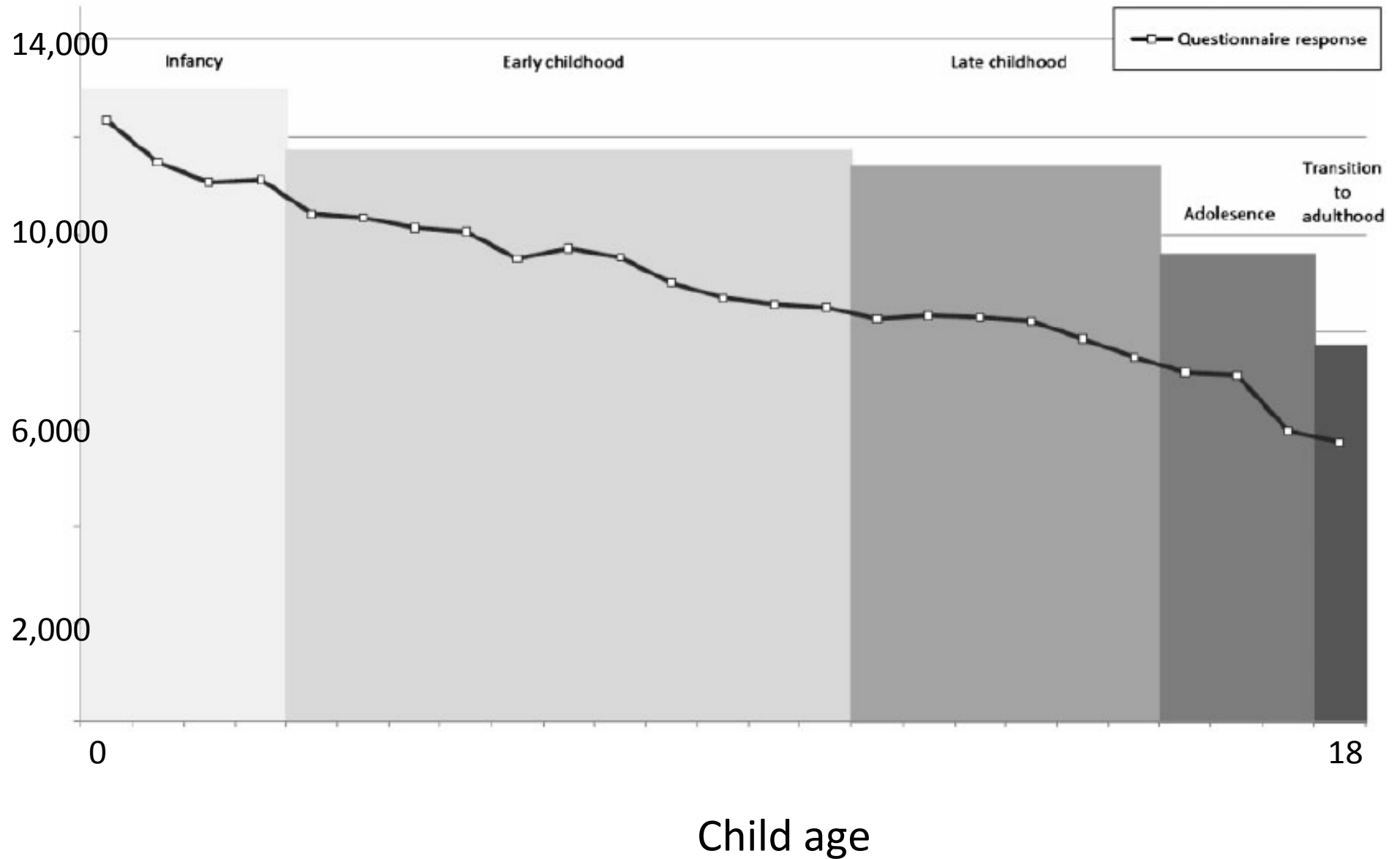
- Approximately 15,000 mothers enrolled during pregnancy 1991-1992
- Mothers & Fathers (1st Generation)
- Index children (2nd Generation) – currently age 22-23
- Their children (3rd Generation)



Data available

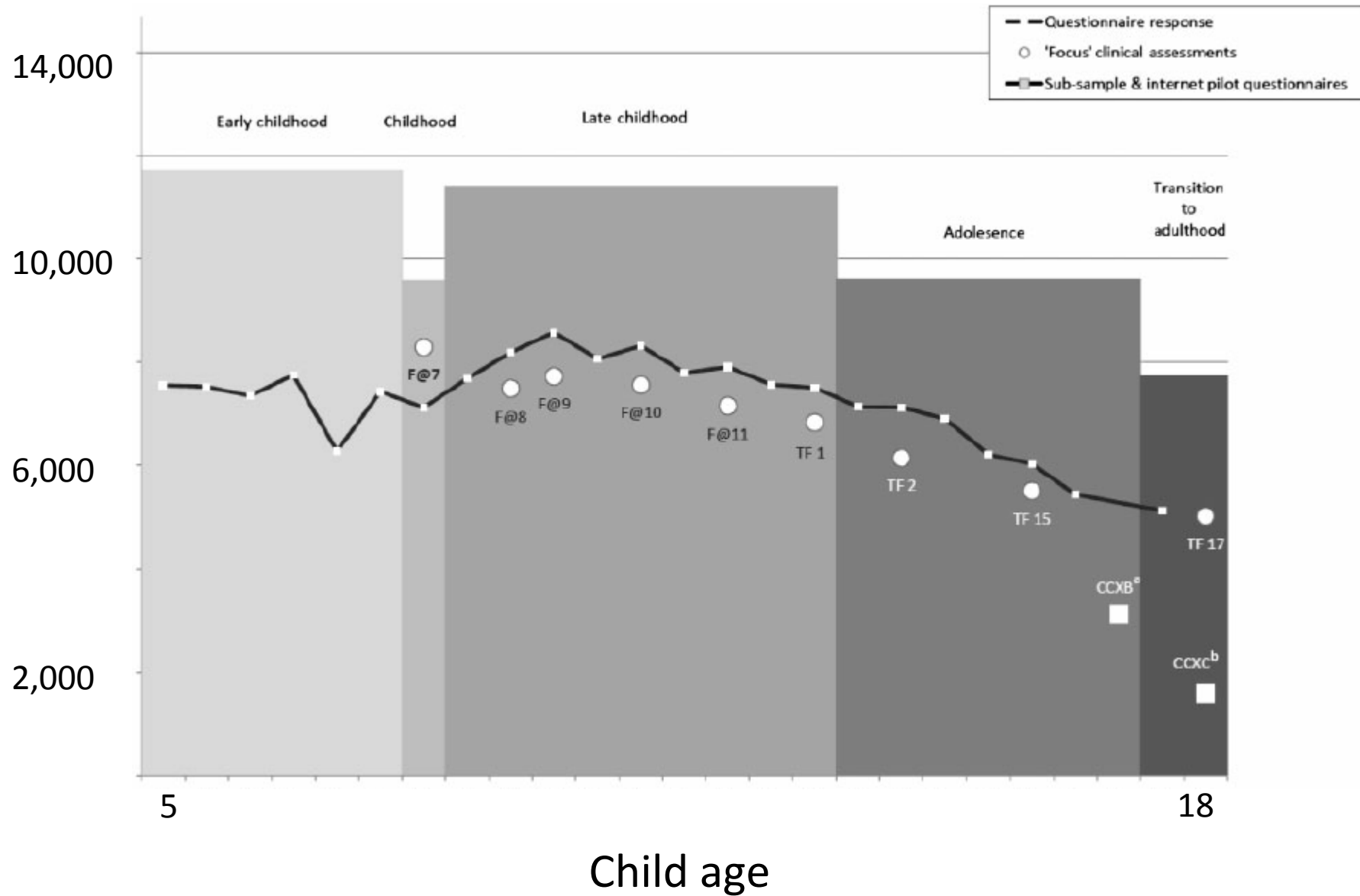
- Types of data:
 - Questionnaires
 - Interviews
 - Cognitive tests
 - Physical measures
 - Biological samples
 - Genomic / proteomic / metalobomic / epigenetic data
 - Neuroimaging
- No of assessments: 70+ data collection time points between birth and 22 years

25 Parent-completed Questionnaires about the child



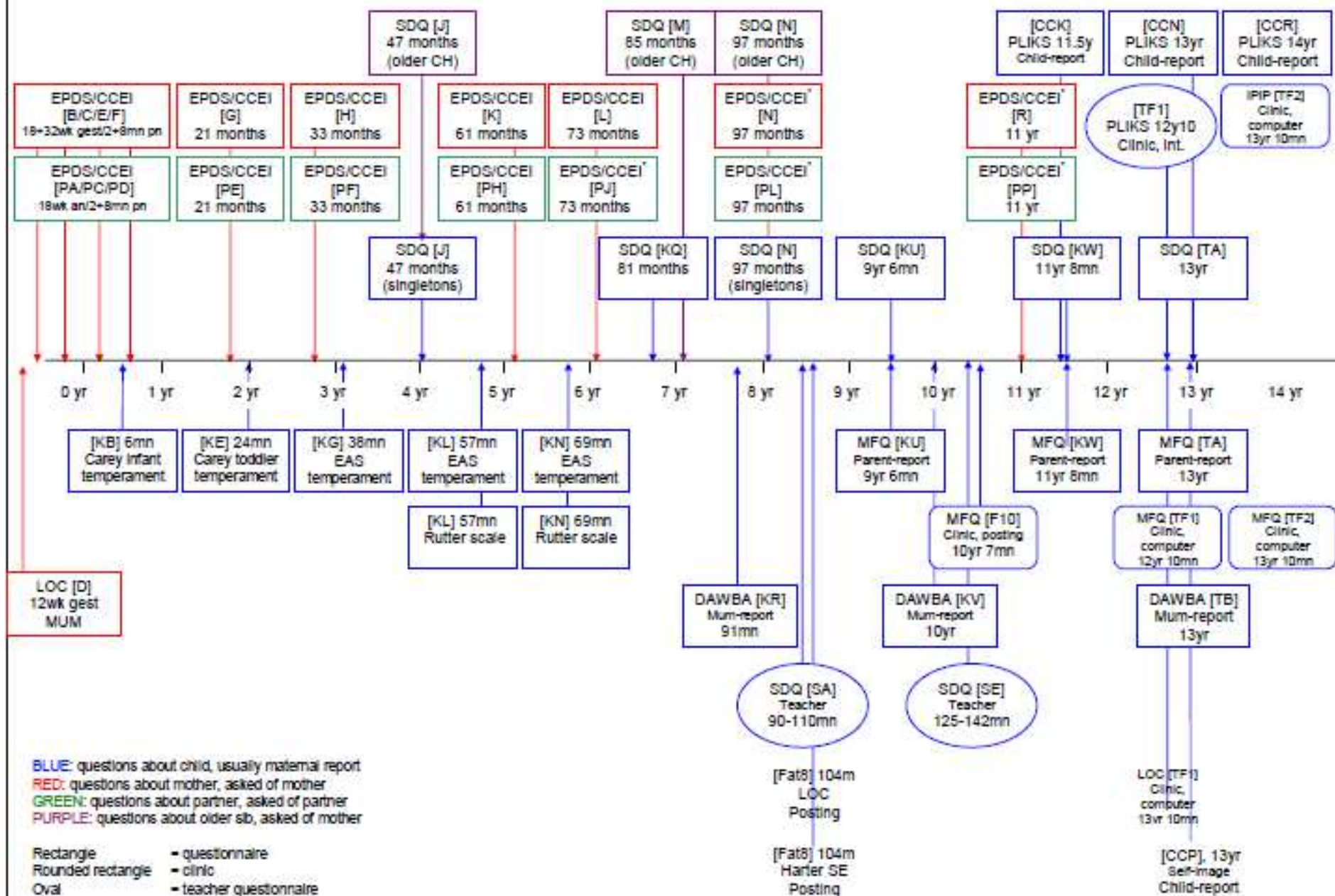
Boyd et al 2012

Child-completed (25 Questionnaires & 9 Clinic assessments)



Courtesy of Jon Heron

Timeline for ALSPAC psych measures



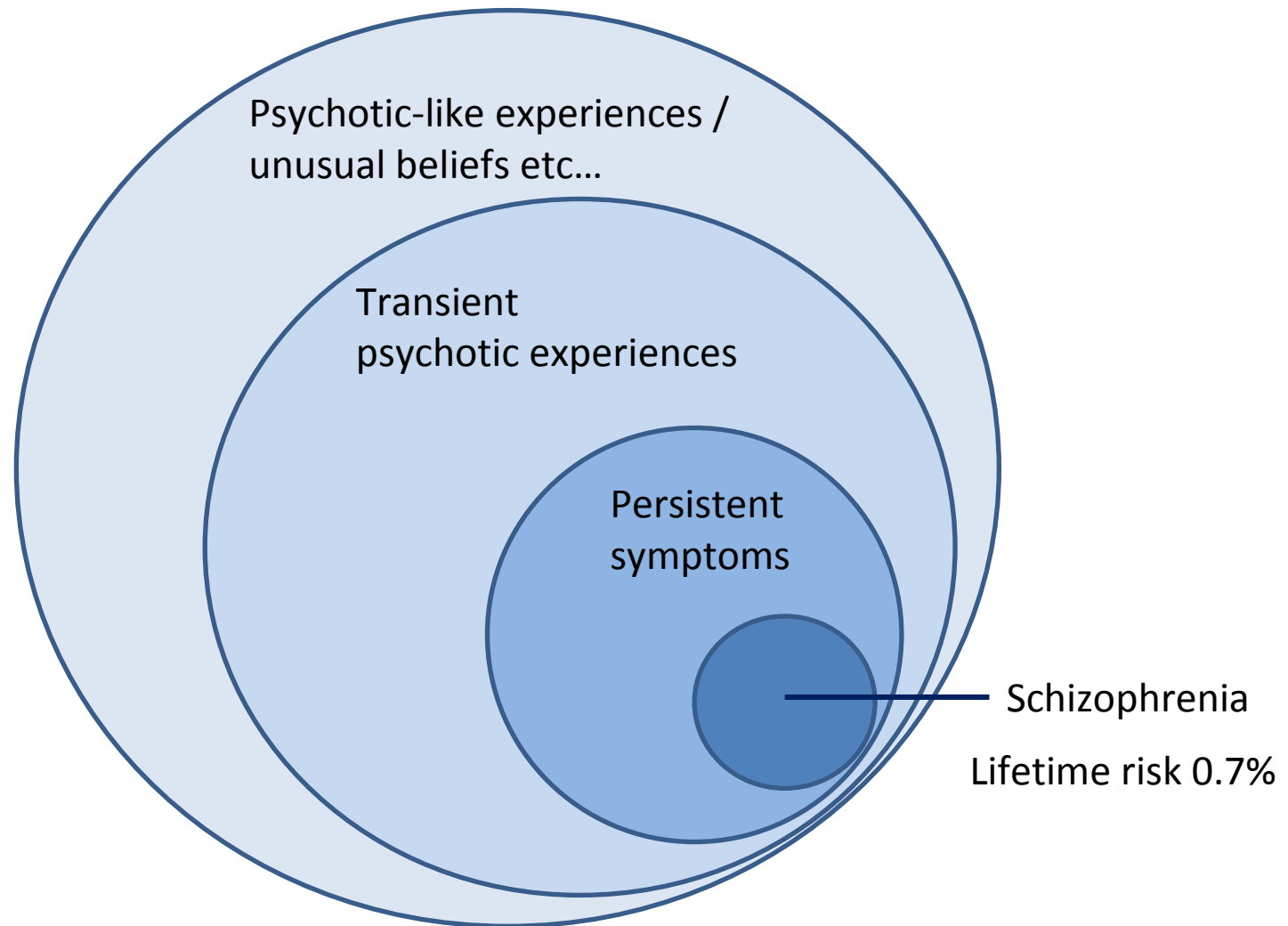
Advantages & disadvantages

- Large, population-based sample
- Repeated, detailed measures
- Longitudinal – can study mechanisms

Advantages & disadvantages

- Large, population-based sample
- Repeated, detailed measures
- Longitudinal – can study mechanisms
- Attrition (but can use multiple imputation)
- Limited power if rare outcomes or exposures (but can study continuum)

Spectrum of psychotic phenomena



Psychotic experiences (PEs)

Structured interviews:

Dunedin – 15%

NEMESIS – 17%

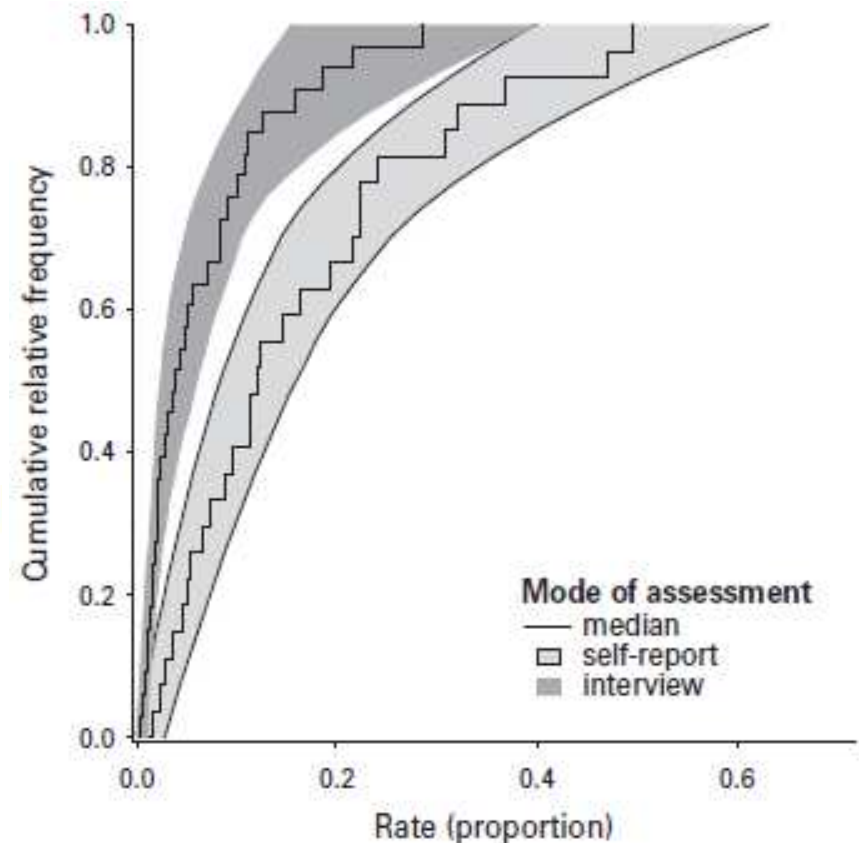
EDSP – 18%

As with questionnaires, likely to over-estimate

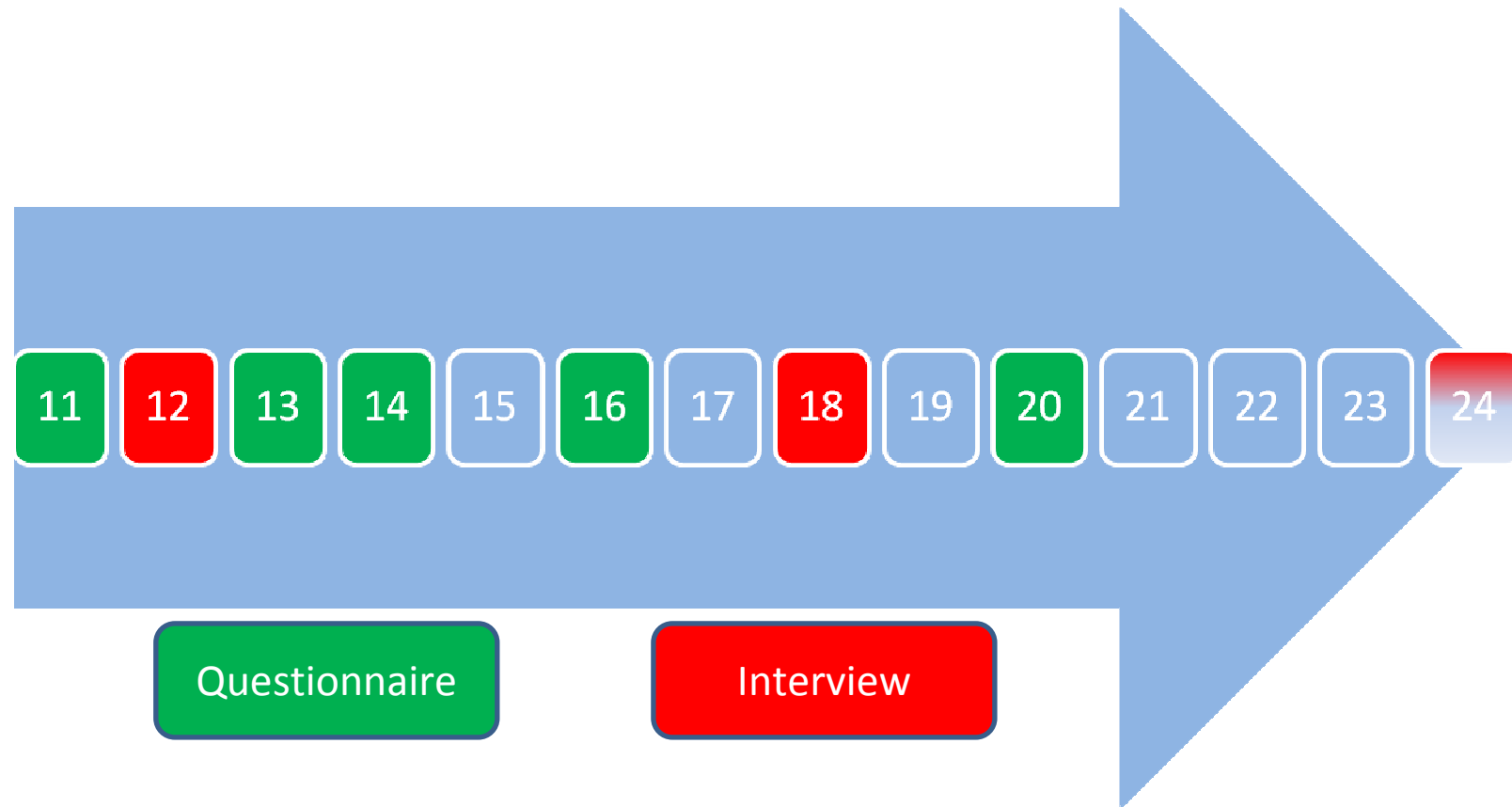
An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults:

R. J. Linscott^{1,2} and J. van Os^{2,3*}

Psychological Medicine (2013), **43**, 1133–1149.



ALSPAC: Psychotic experiences



Psychosis-Like Symptoms interview (PLIKSi)

- A semi-structured interview
- 11 core questions

Hallucinations (auditory & visual)

Delusions (persecution, reference, being spied on, grandiosity, thoughts being read, passivity, etc..)

PLIKSi

- Stem question example:

Have you heard voices that other people could not hear or when no one else was around?

– Yes, no, maybe

- Semi-structured interview:

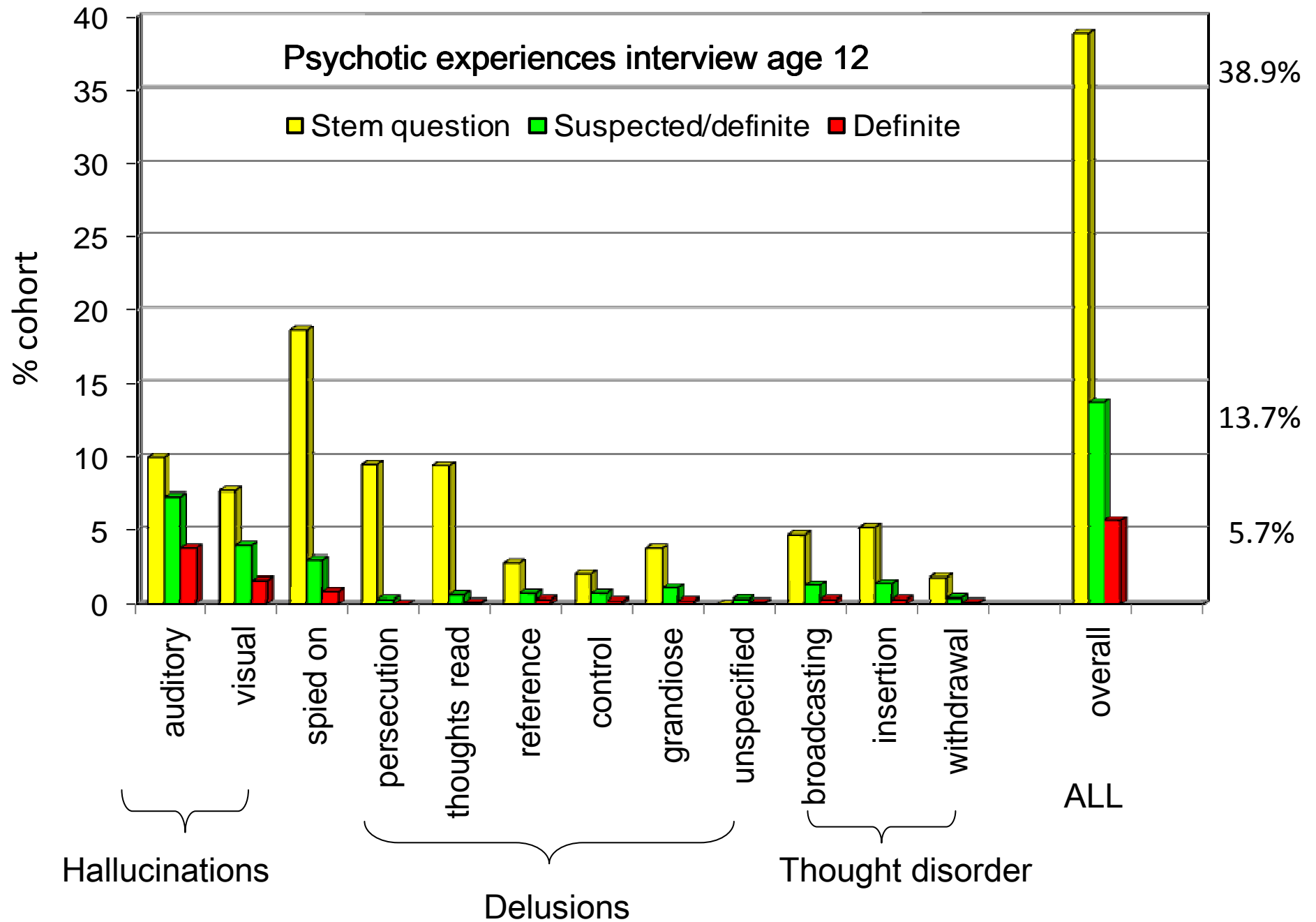
What do you mean by that? give an example etc.....

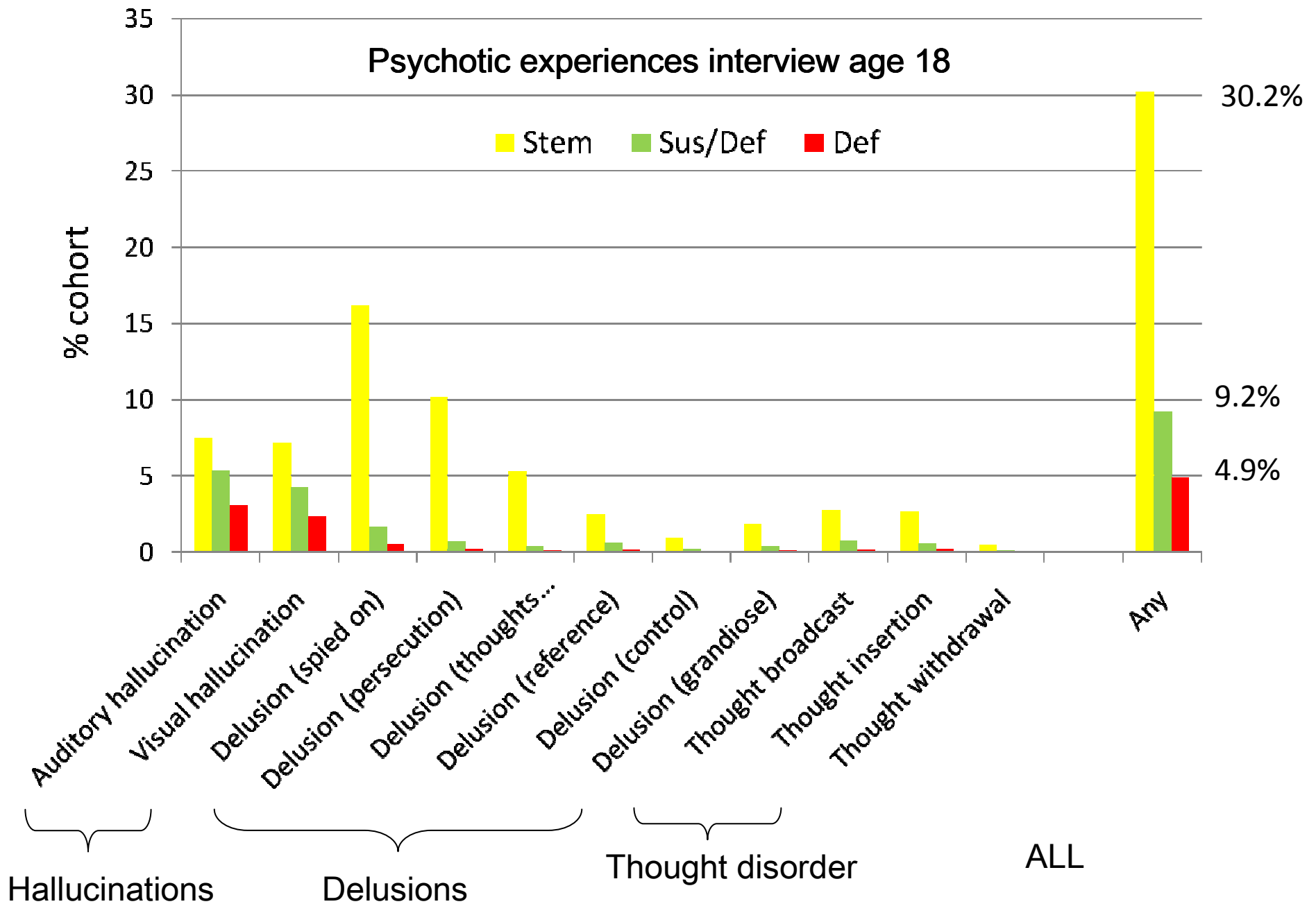
– Interviewer rates as:

Definitely present

Suspected

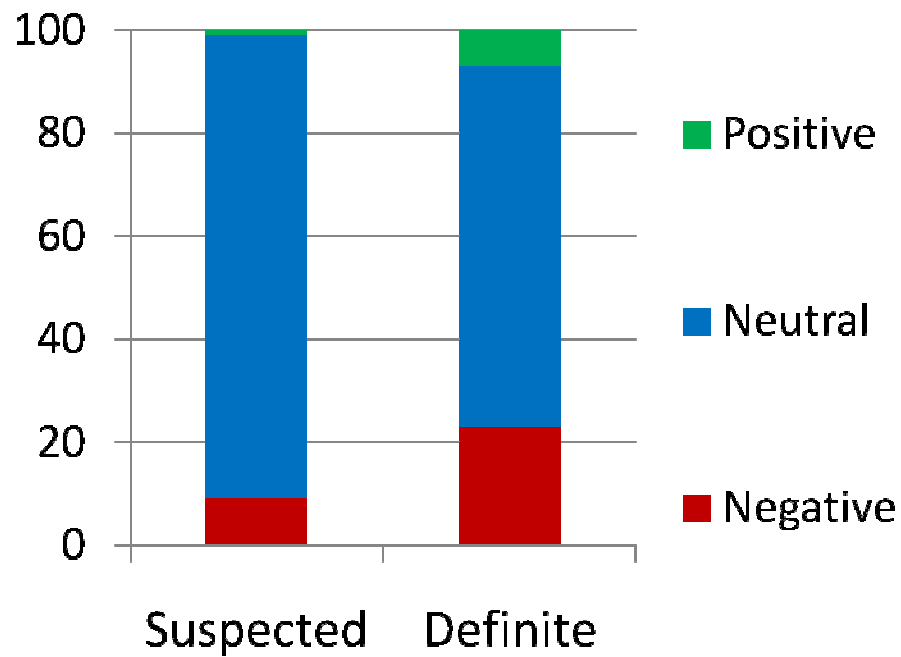
Not present



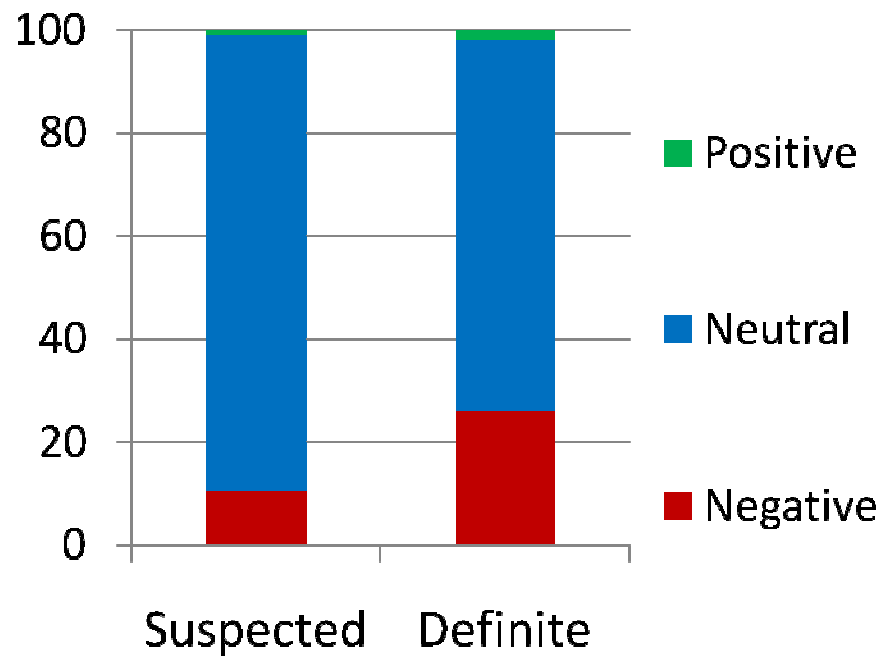


Psychotic experiences at age 18

Social function

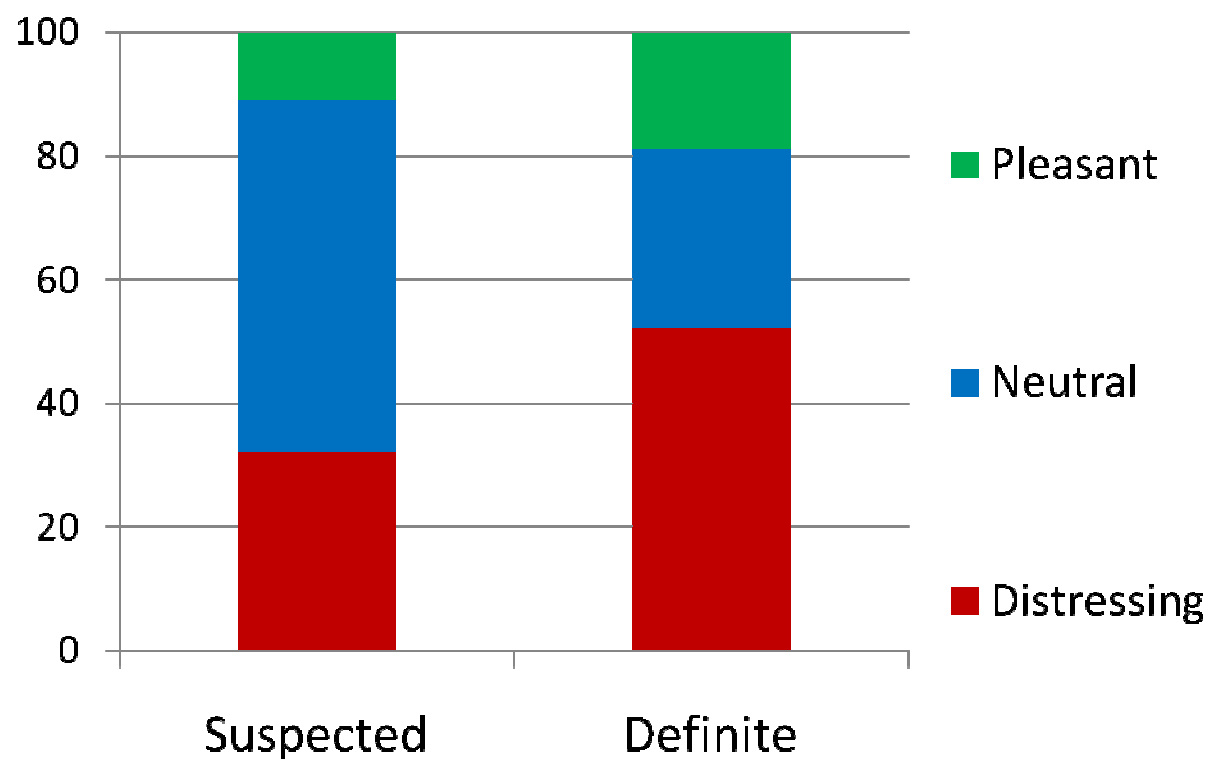


Occupational function



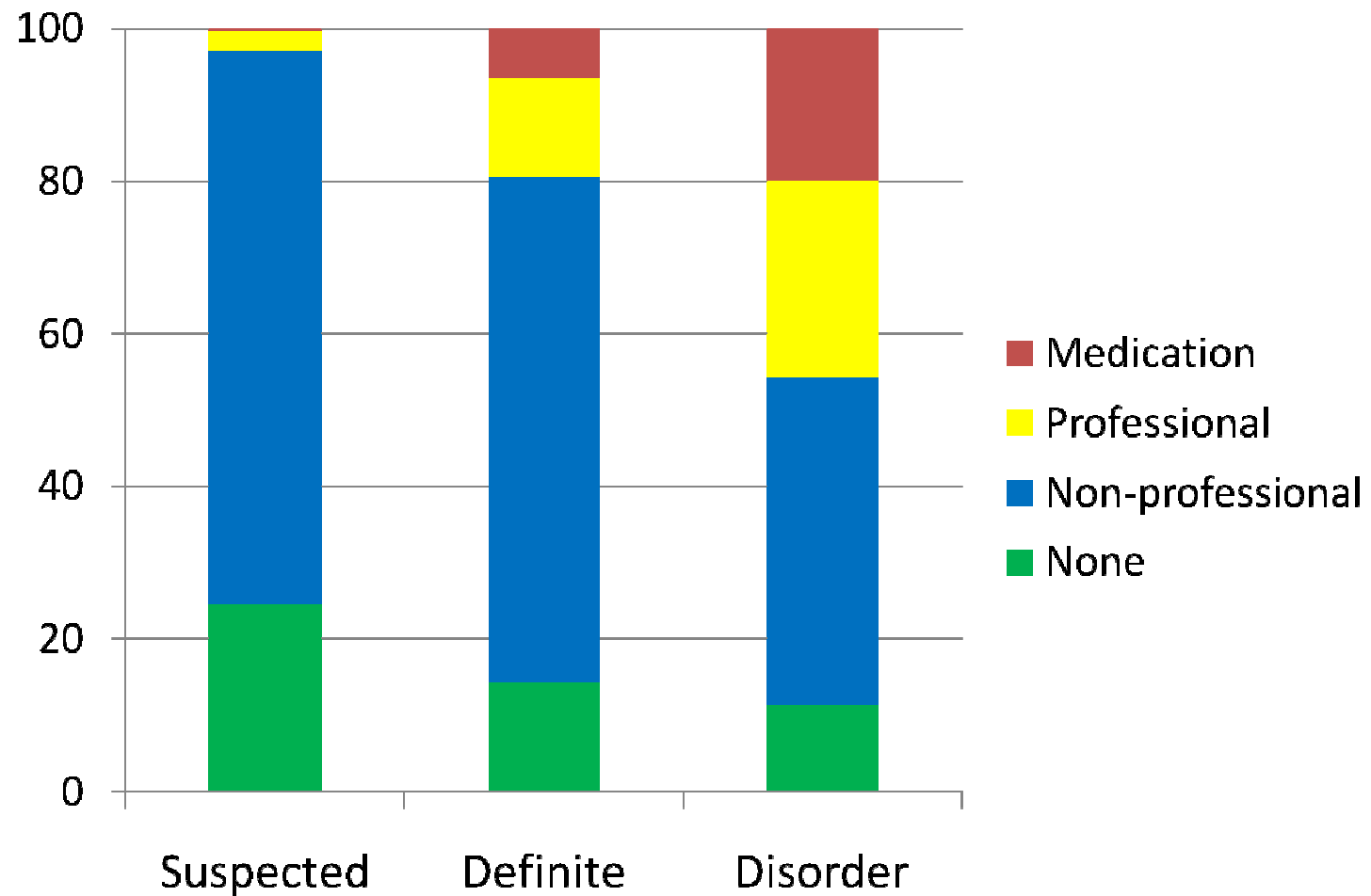
Psychotic experiences at age 18

Distress



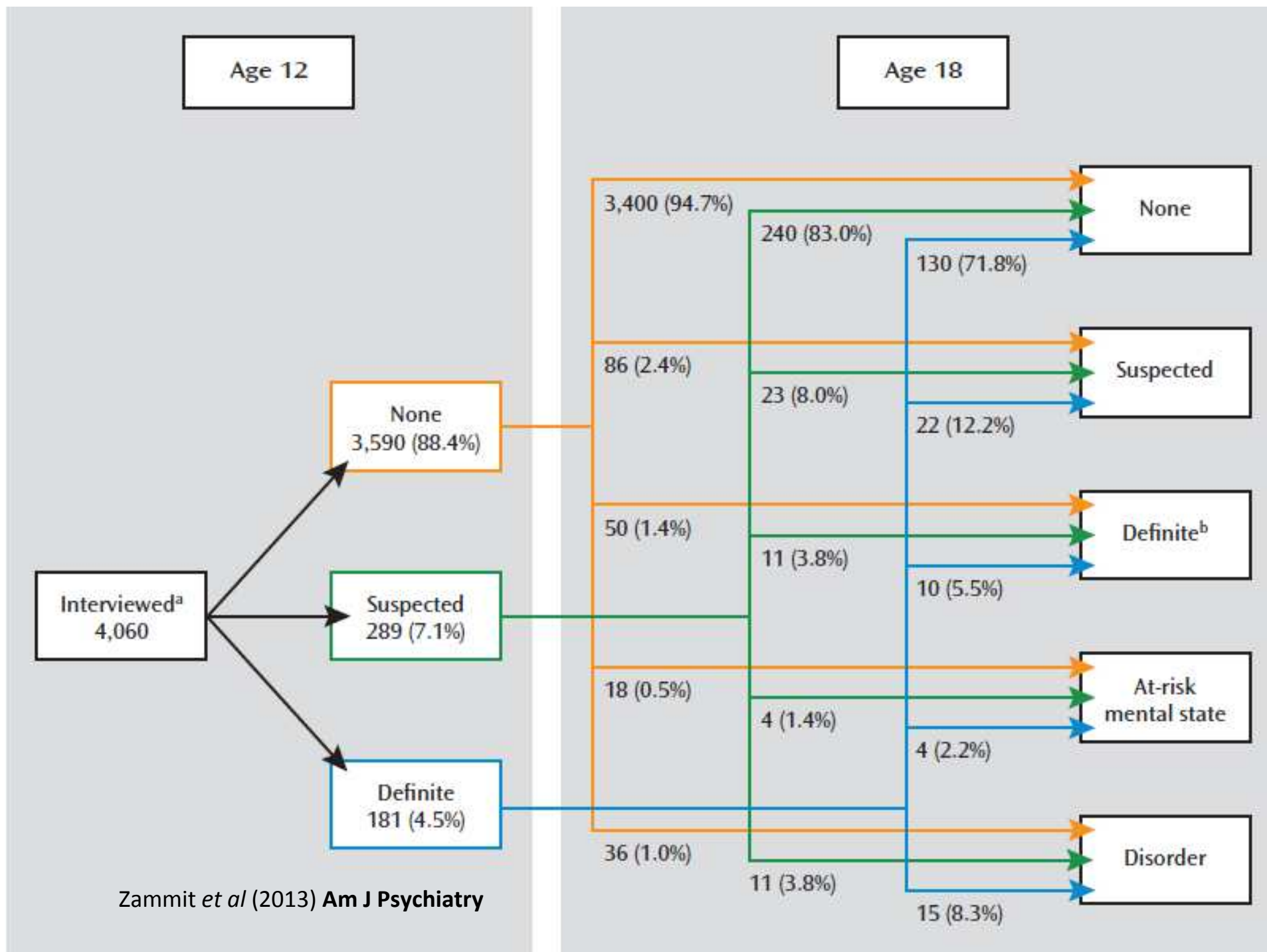
Psychotic outcomes at age 18

Help-seeking



Psychotic experiences

- Under-recognised public health burden



Psychotic experiences ages 12 & 18

	N (% sample)	Definite PE at age 18	Definite PE OR (95% CI)	
PLIKS 12				
None	2354 (60.9%)	42 (1.8%)	1	
Stem (self-report)	591 (15.3%)	25 (4.2%)	2.4 (1.5, 4.0)	
Unusual experience	400 (10.4%)	20 (5.0%)	2.9 (1.7, 5.0)	
PE due to sleep/fever	72 (1.9%)	8 (11.1%)	6.9 (3.1, 15.2)	
Suspected PE	271 (7.0%)	24 (8.9%)	5.3 (3.2, 9.0)	
Definite PE	176 (4.6%)	28 (15.9%)	10.4 (6.3, 17.3)	

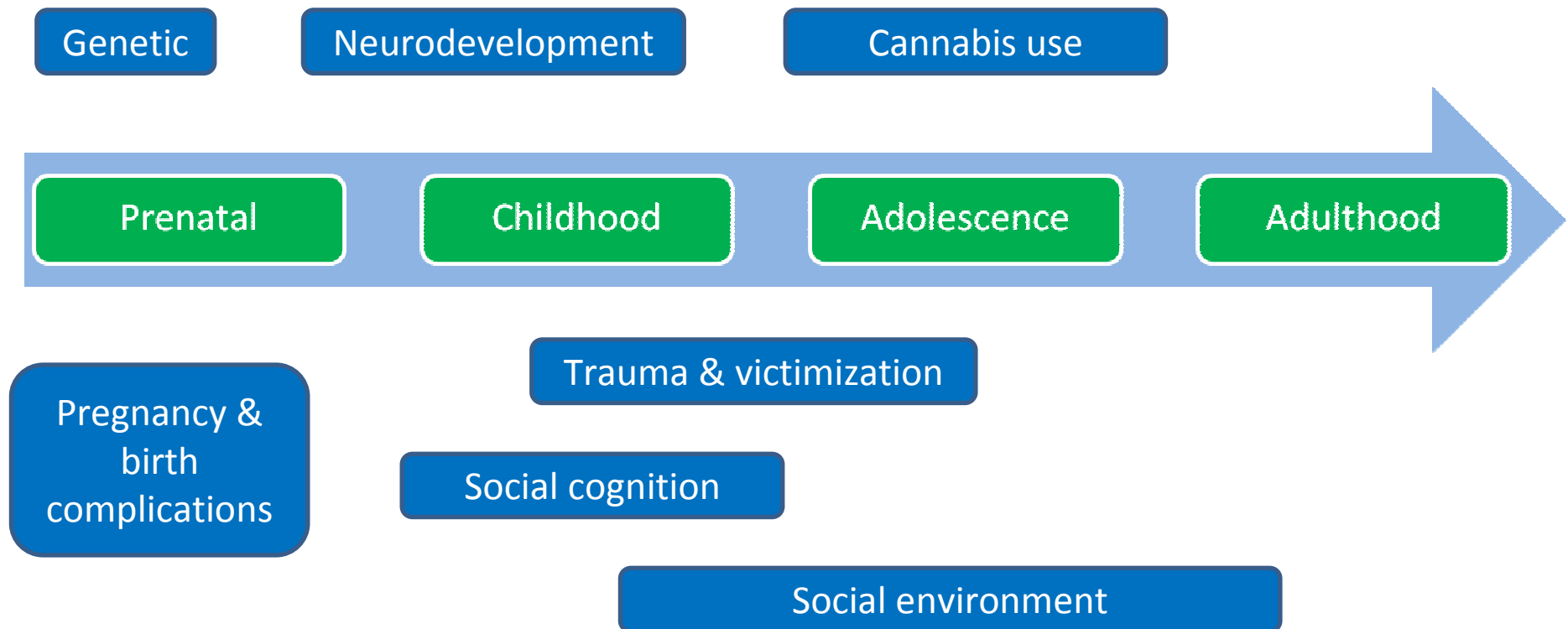
Psychotic experiences ages 12 & 18

	N (% sample)	Definite PE at age 18	Definite PE OR (95% CI)	Disorder OR (95% CI)
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Unusual experience	400 (10.4%)	20 (5.0%)	2.9 (1.7, 5.0)	4.3 (1.9, 9.7)
PE due to sleep/fever	72 (1.9%)	8 (11.1%)	6.9 (3.1, 15.2)	7.3 (2.0, 25.9)
Suspected PE	271 (7.0%)	24 (8.9%)	5.3 (3.2, 9.0)	6.4 (2.8, 14.6)
Definite PE	176 (4.6%)	28 (15.9%)	10.4 (6.3, 17.3)	15.6 (7.4, 32.8)

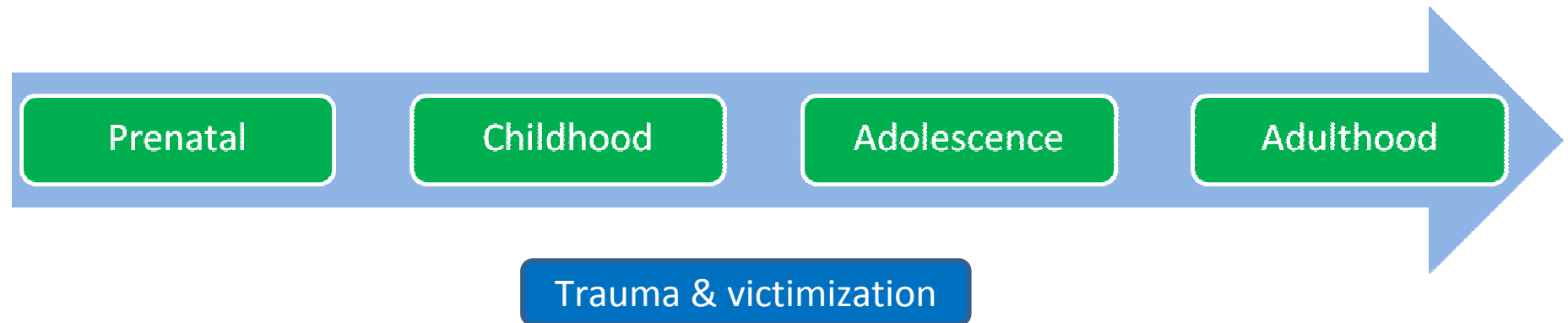
Psychotic experiences

- Under-recognised public health burden
- Strong association with clinical outcomes demonstrates potential utility for studying mechanisms

Most risk factors for schizophrenia show similar associations
with psychotic experiences



Most risk factors for schizophrenia show similar associations
with psychotic experiences



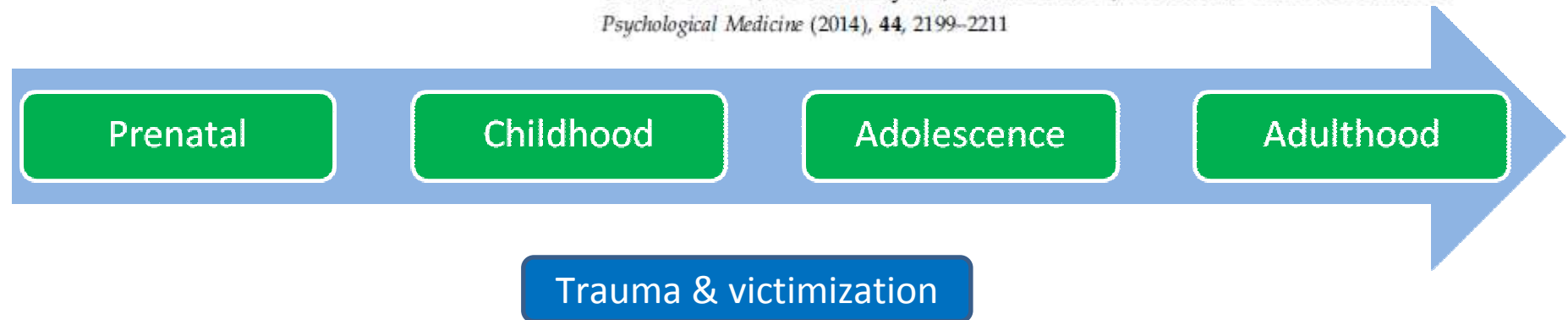
Prospective Study of Peer Victimization in Childhood and Psychotic Symptoms in a Nonclinical Population at Age 12 Years

Arch Gen Psychiatry. 2009;66(5):527-536

Bullying in elementary school and psychotic experiences at 18 years: a longitudinal, population-based cohort study

D. Wolke^{1*†}, S. T. Lereya^{1†}, H. L. Fisher², G. Lewis³ and S. Zammit^{3,4}

Psychological Medicine (2014), **44**, 2199–2211



Pathways Between Childhood Victimization and Psychosis-like Symptoms in the ALSPAC Birth Cohort

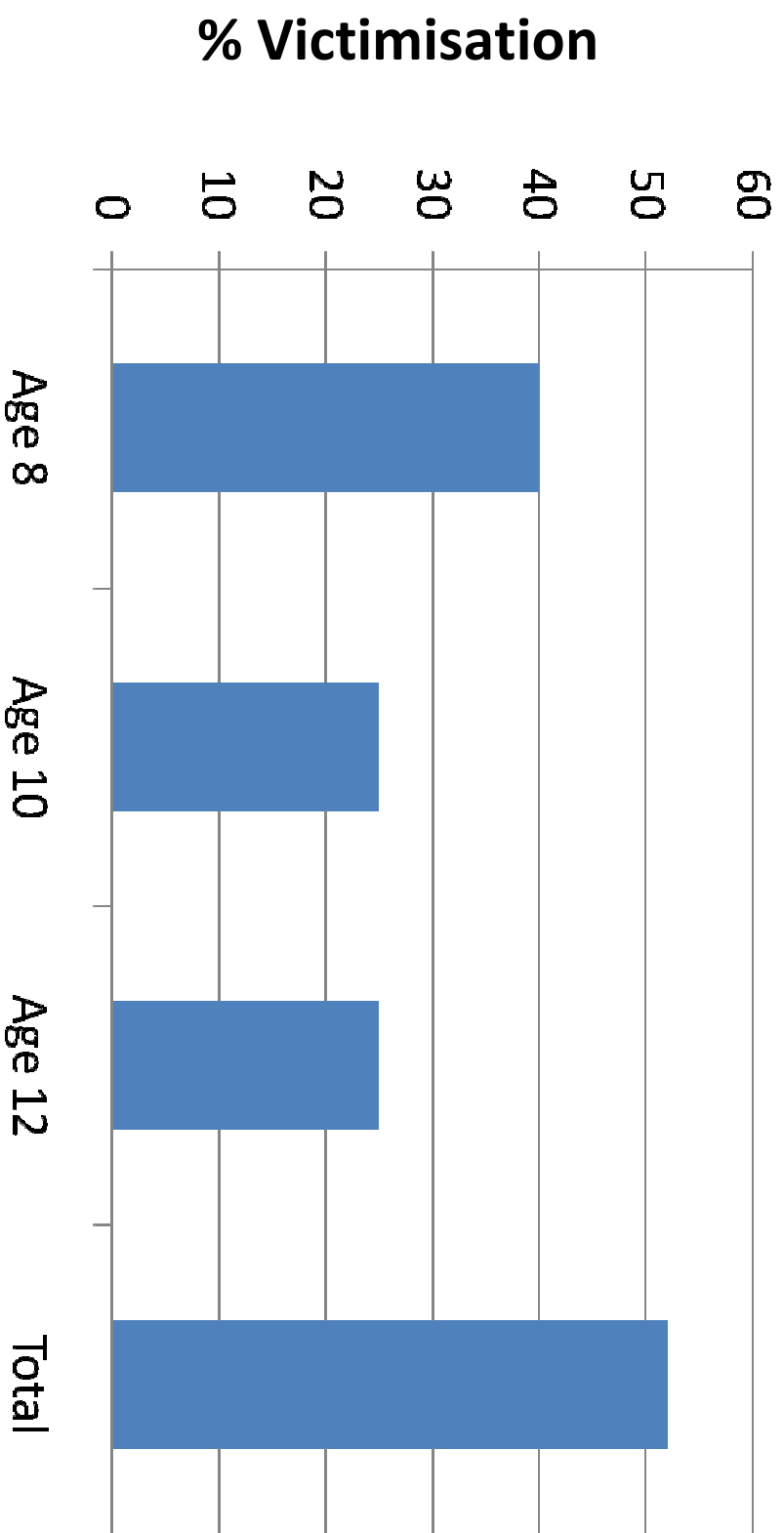
Schizophrenia Bulletin vol. 39 no. 5 pp. 1045–1055, 2013

Childhood Parasomnias and Psychotic Experiences at Age 12 Years

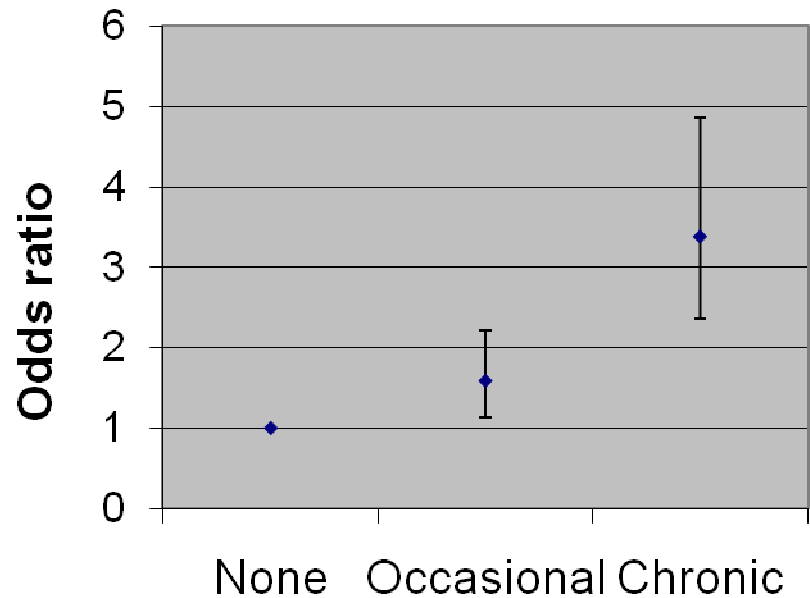
Helen L. Fisher, PhD¹; Suzet Tanya Lereya, PhD²; Andrew Thompson, MD³; Glyn Lewis, PhD⁴; Stanley Zammit, PhD^{4,5}; Dieter Wolke, PhD²

SLEEP, Vol. 37, No. 3, 2014

Victimisation



Victimisation & risk of psychotic experiences



Population attributable fraction $\approx 30\%$

Schreier et al 2009; Wolke et al 2014

- Impact of childhood trauma very under-recognised in clinical practice
- ALSPAC: 33% fewer help-seeking for psychotic experiences if victimised

Implications

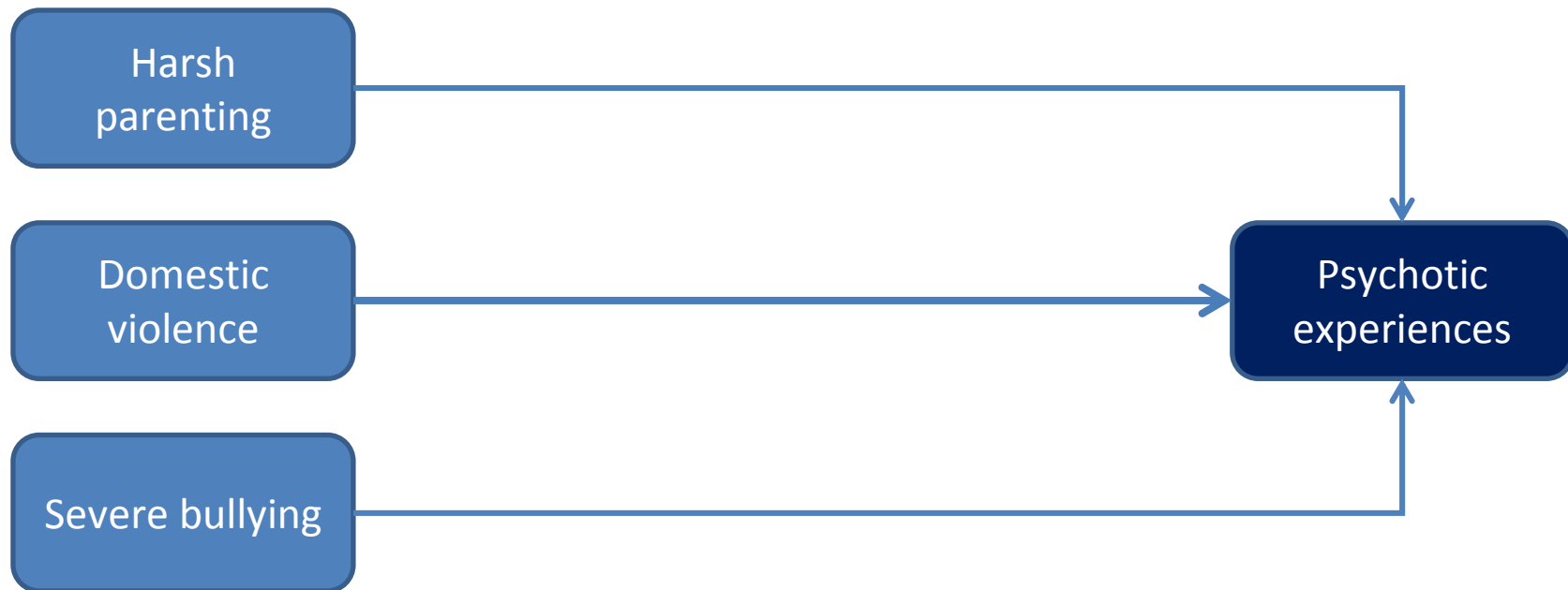
Trauma and victimisation are important contributors to mental health disorders

Requirement to improve training to enquire about and know how to manage disclosure of traumatic experiences

Pathways Between Childhood Victimization and Psychosis-like Symptoms in the ALSPAC Birth Cohort

Helen L. Fisher^{*,1}, Andrea Schreier², Stanley Zammit^{3,4}, Barbara Maughan¹, Marcus R. Munafò⁵, Glyn Lewis³, and Dieter Wolke²

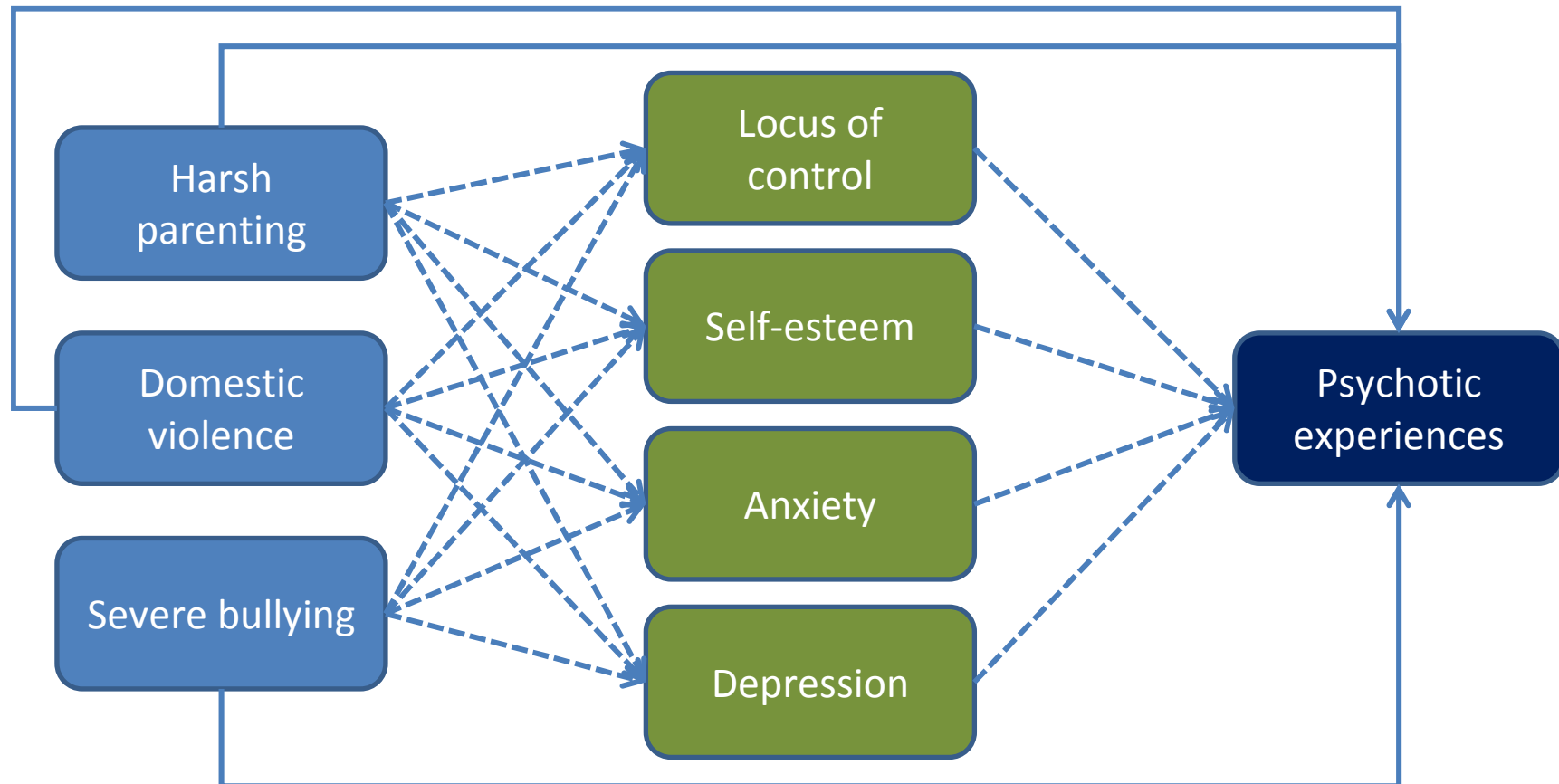
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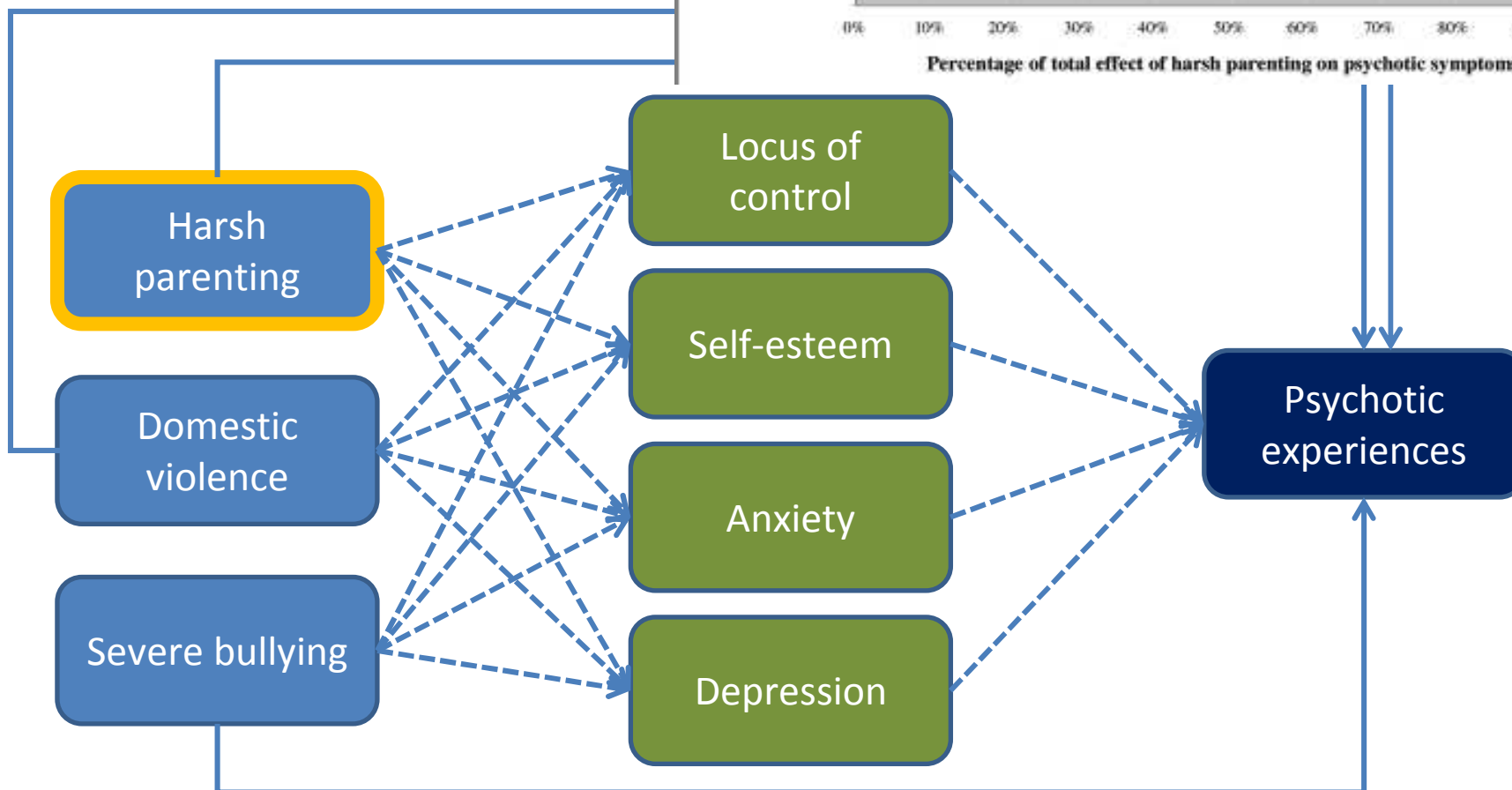
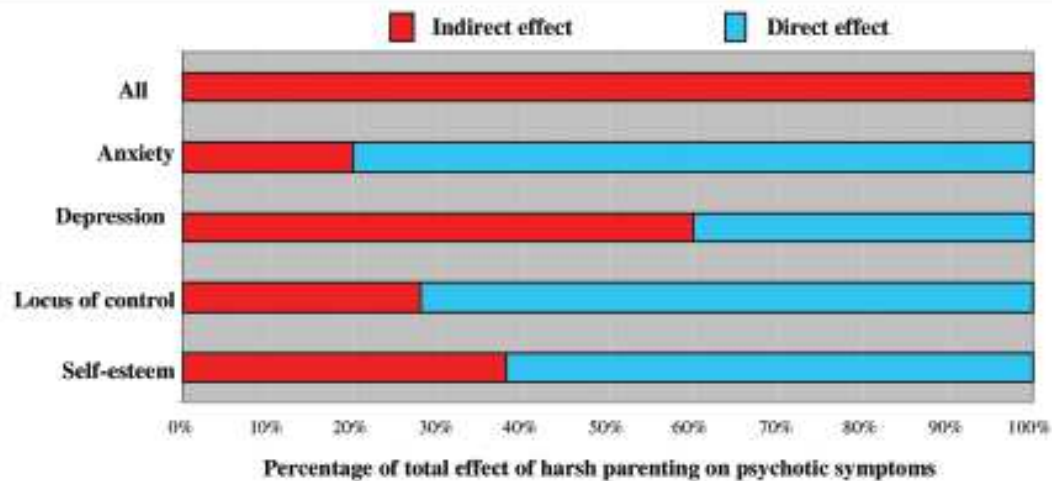


Pathways Between Childhood Victimization and Psychotic Experiences in the ALSPAC Birth Cohort

Helen L. Fisher^{a,1}, Andrea Schreier², Stanley Zammit^{3,4}, Barbara Maughan⁵ and Dieter Wolke²

Schizophrenia Bulletin vol. 39 no. 5 pp. 1045–1055, 2013

Panel A: Mediation of the effect of harsh parenting on definite psychotic symptoms

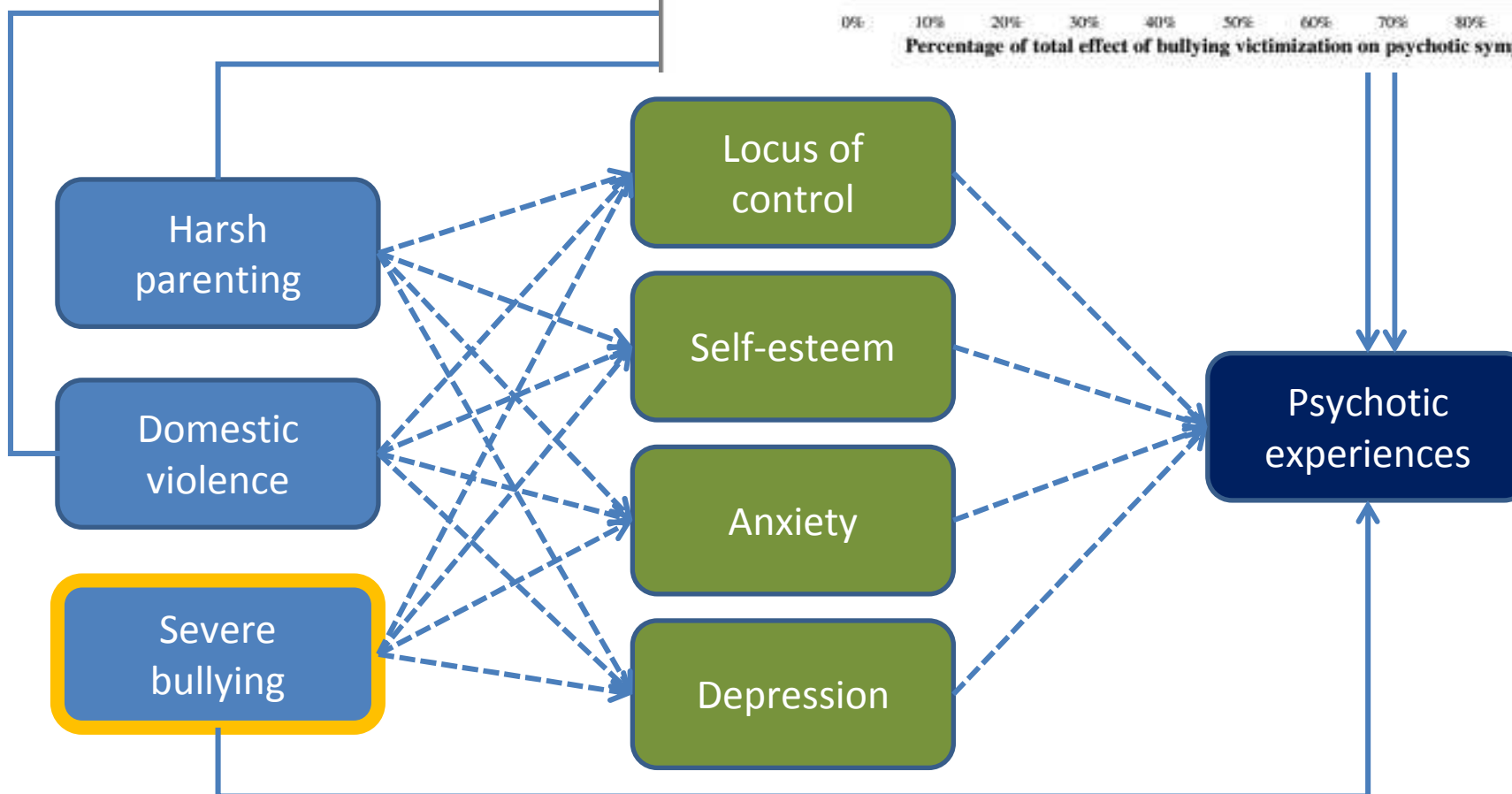
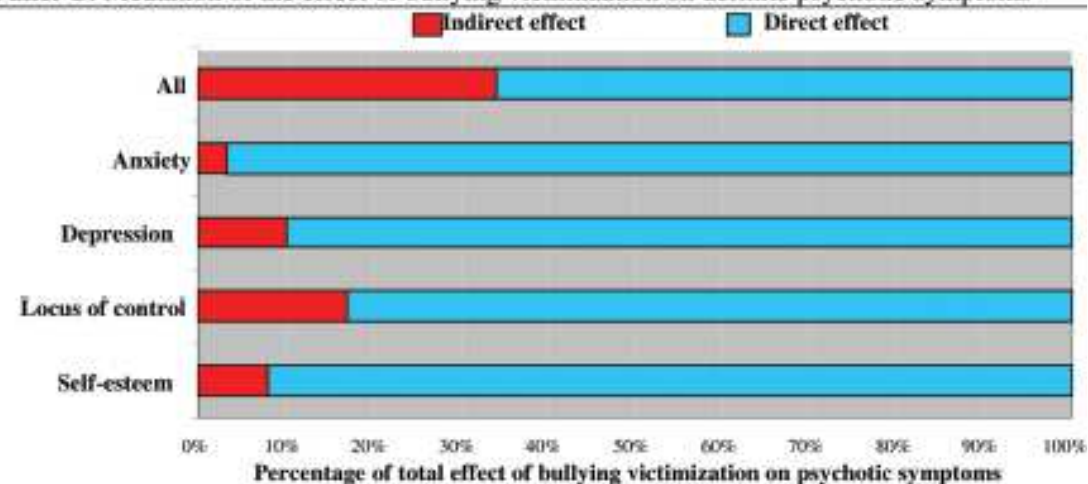


Pathways Between Childhood Victimization and in the ALSPAC Birth Cohort

Helen L. Fisher^{*,1}, Andrea Schreier², Stanley Zammit^{3,4}, Barbara Ma
and Dieter Wolke²

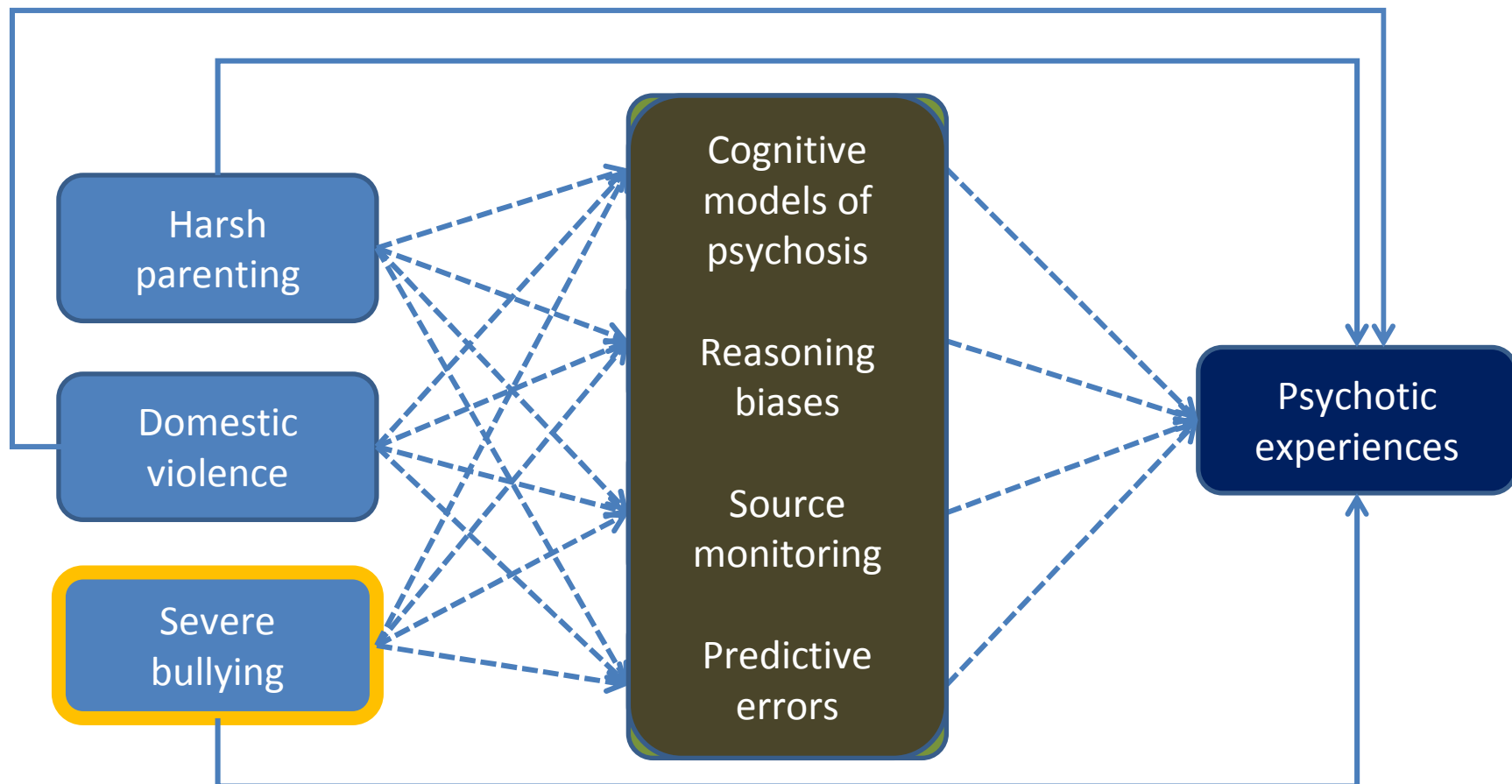
Schizophrenia Bulletin vol. 39 no. 5 pp. 1045–1055, 2013

Panel C: Mediation of the effect of bullying victimization on definite psychotic symptoms

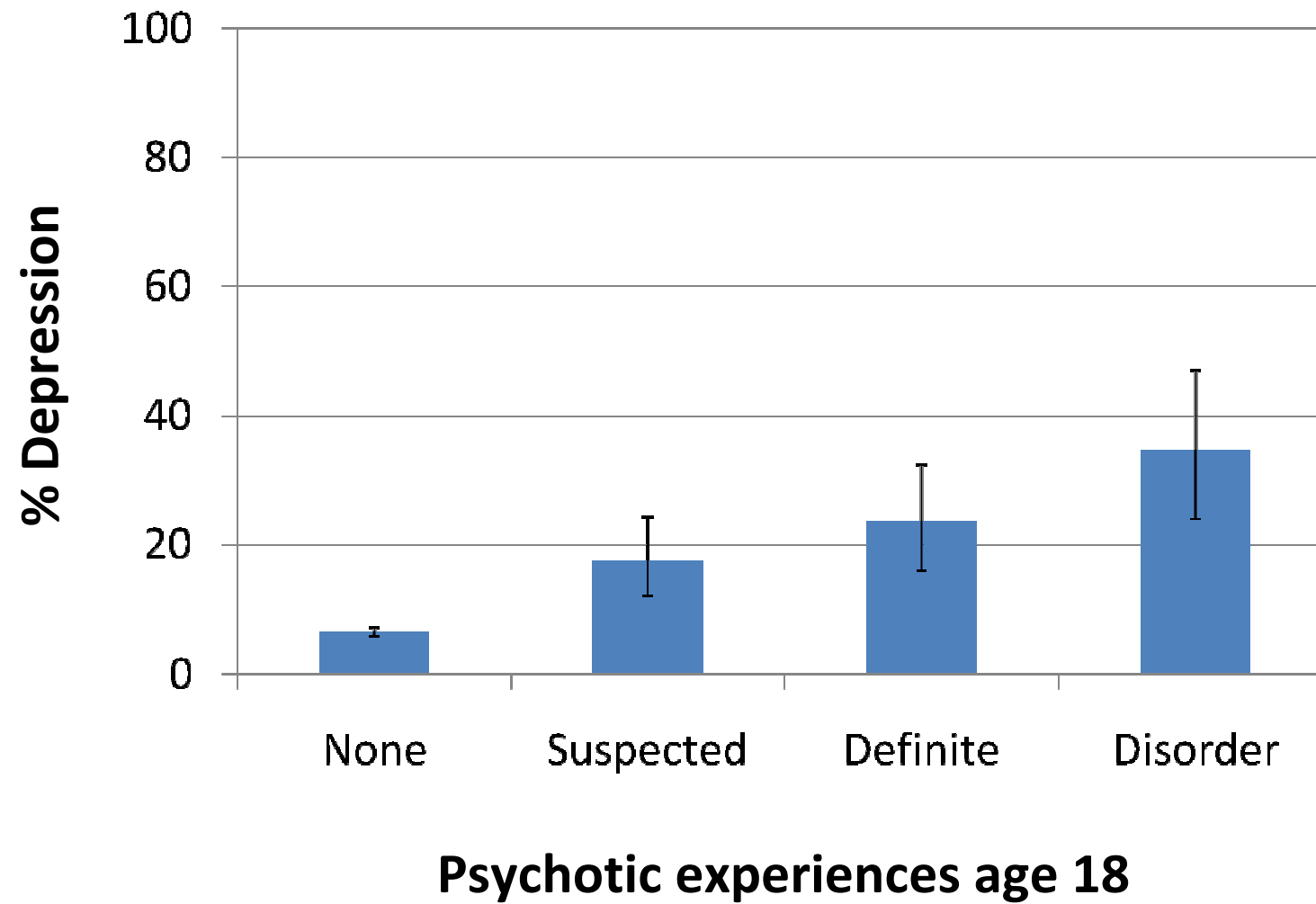


MRC Grant 2015-2019

“Pathways to Psychosis”

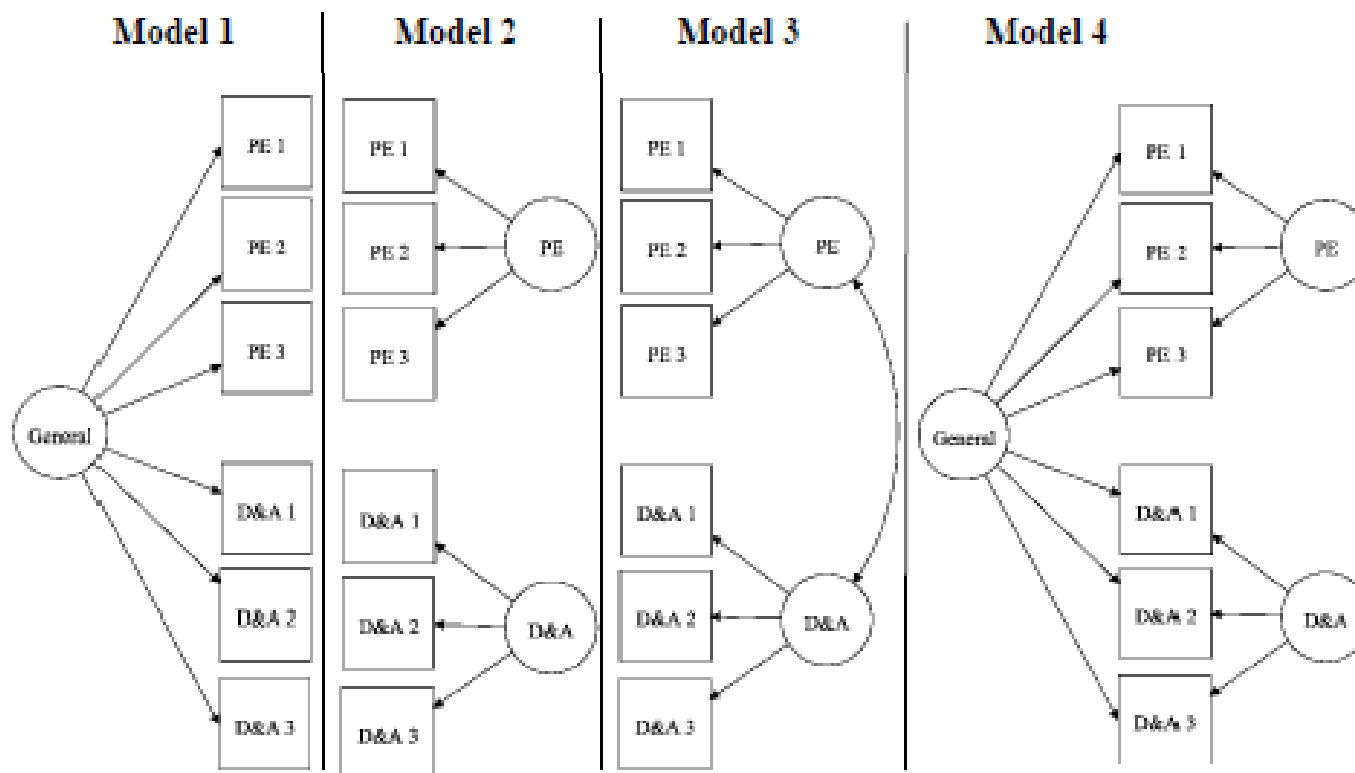


Psychotic experiences & depression



Mood, anxiety and psychotic phenomena measure a common psychopathological factor

Psychological Medicine, Page 1 of 11
doi:10.1017/S003329171400261X

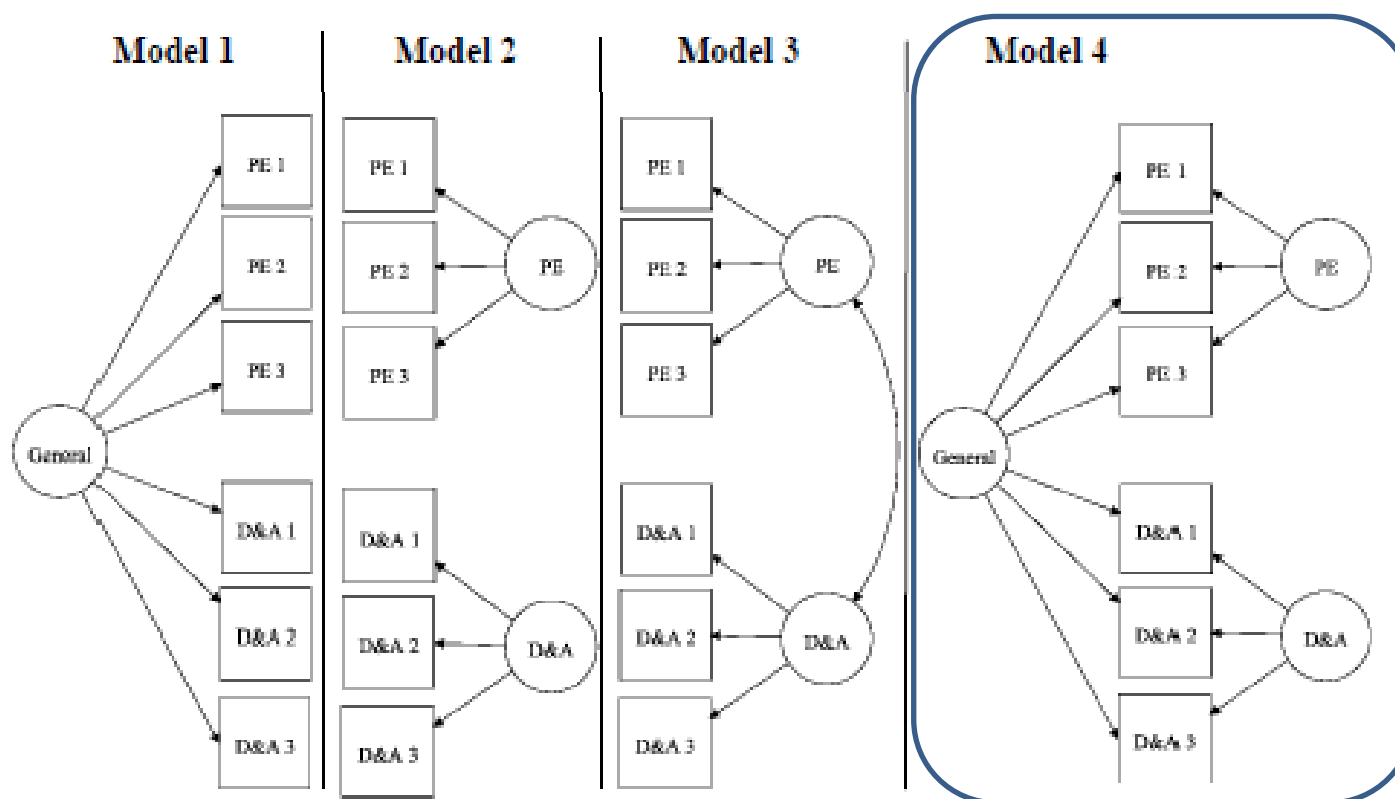


PE = Psychotic experience, D&A = Depressive and anxiety symptoms

Figure 1: Conceptual models of the alternative relationships between psychotic experiences, and depressive and anxiety symptoms

Mood, anxiety and psychotic phenomena measure a common psychopathological factor

Psychological Medicine, Page 1 of 11
doi:10.1017/S003329171400261X

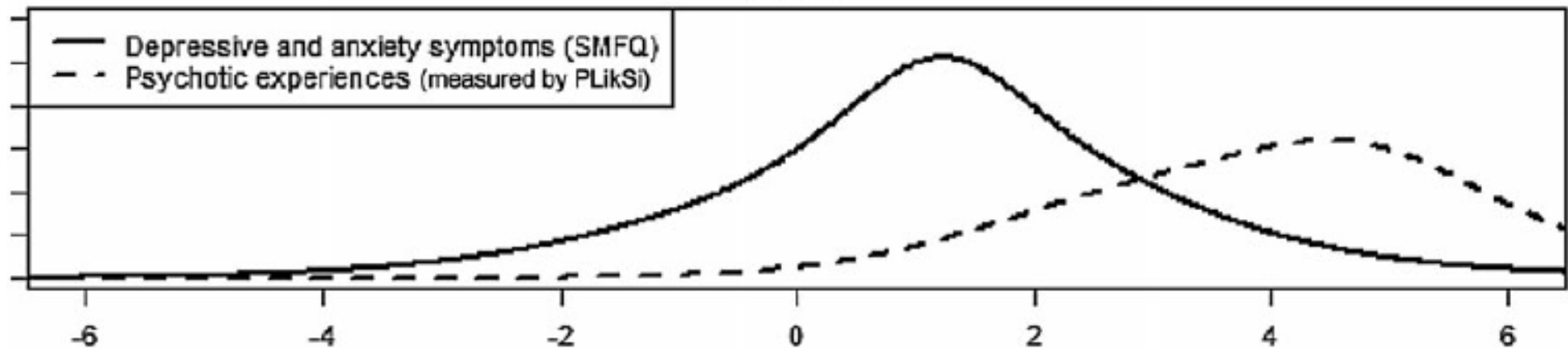


PE = Psychotic experience, D&A = Depressive and anxiety symptoms

Figure 1: Conceptual models of the alternative relationships between psychotic experiences, and depressive and anxiety symptoms

Location of items measuring Psychotic experiences and depression

ALSPAC



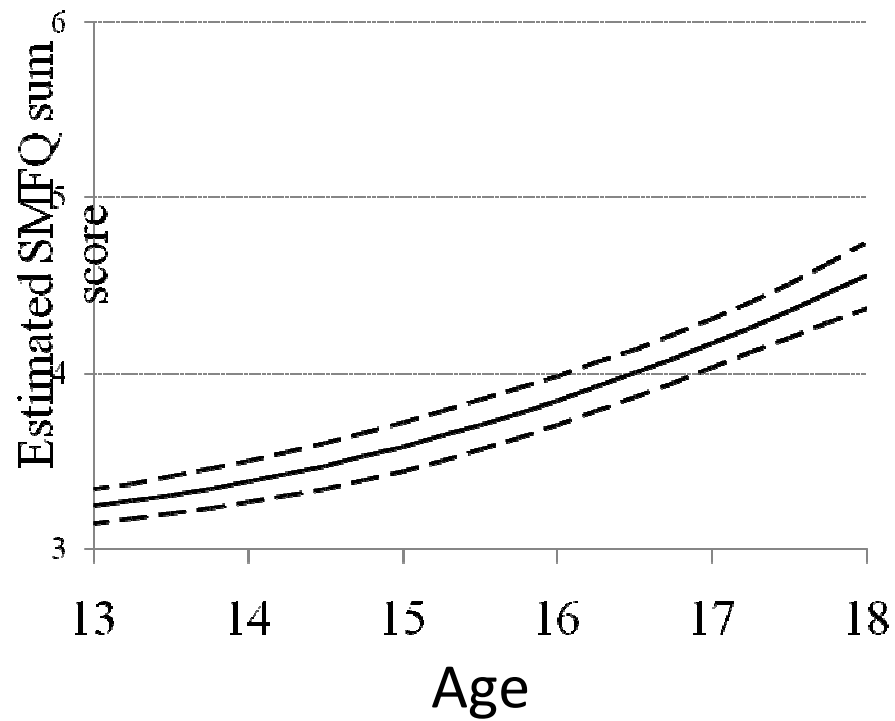
Latent continuum of common mental distress

Psychotic experiences

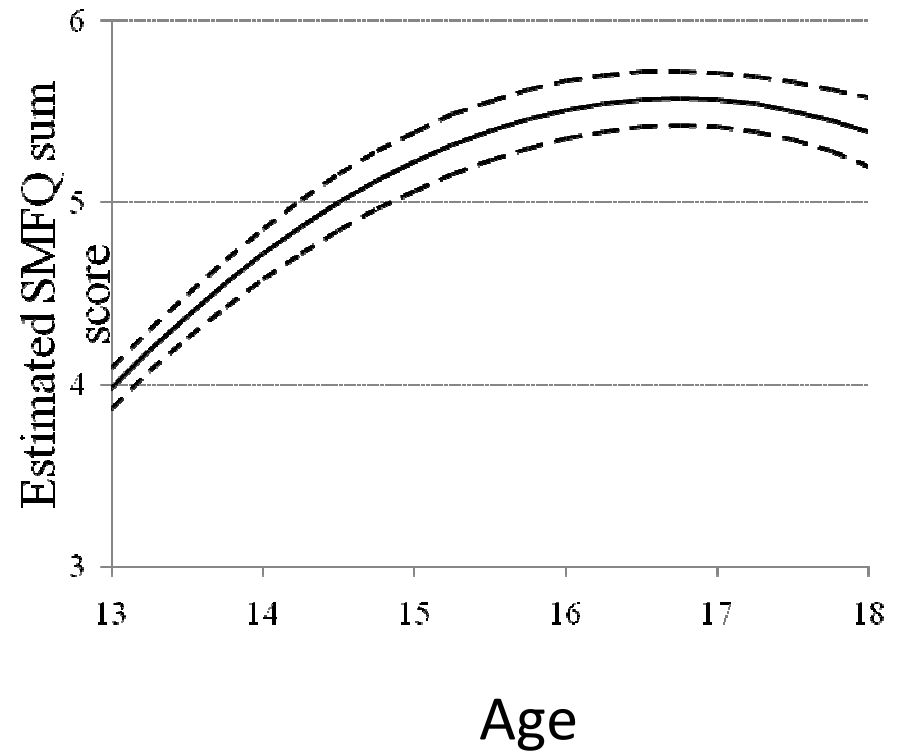
- Under-recognised public health burden
- Strong association with clinical outcomes demonstrates potential utility for studying mechanisms
- Represent more severe end of common mental disorders

Depression

Males

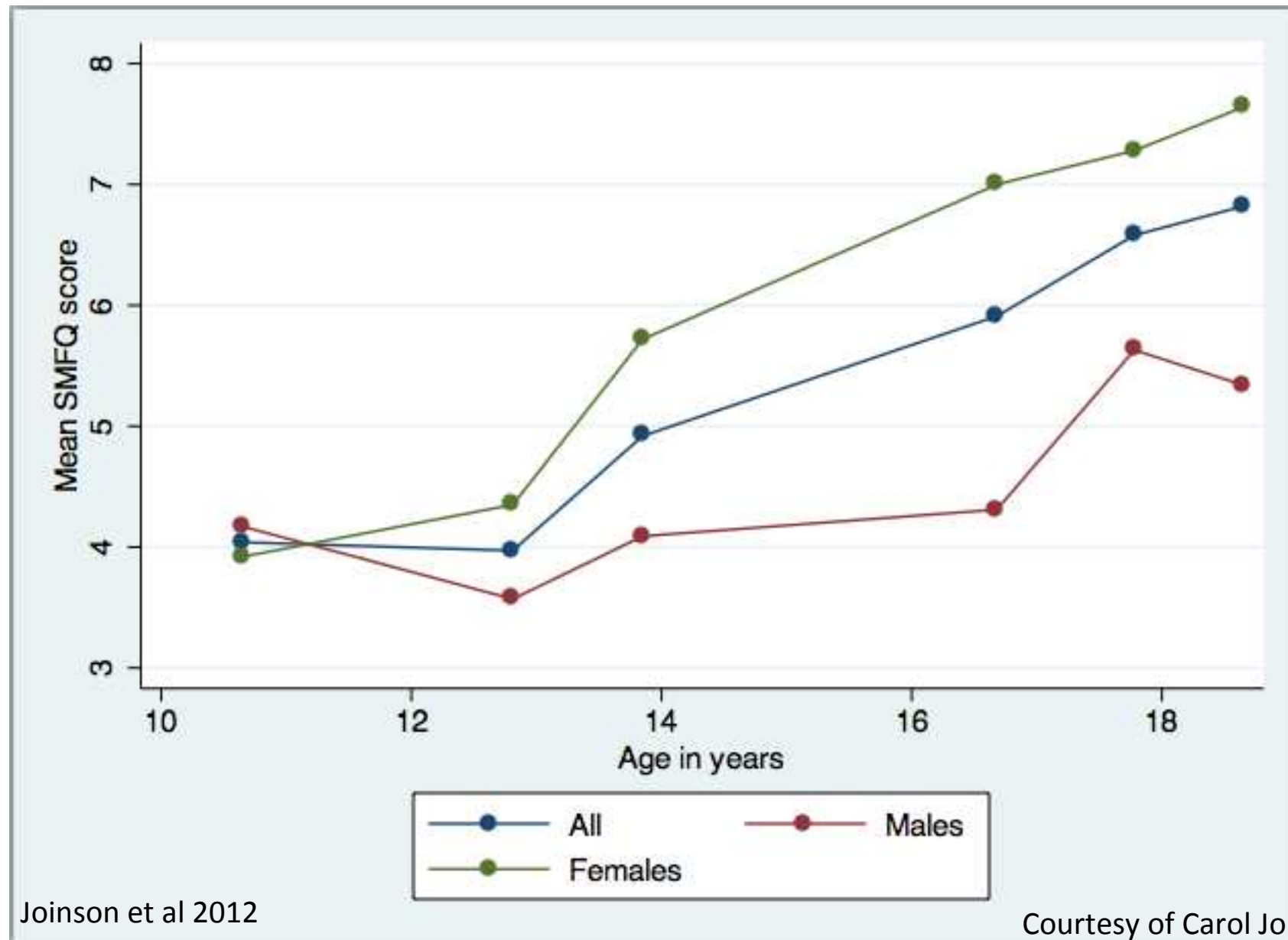


Females

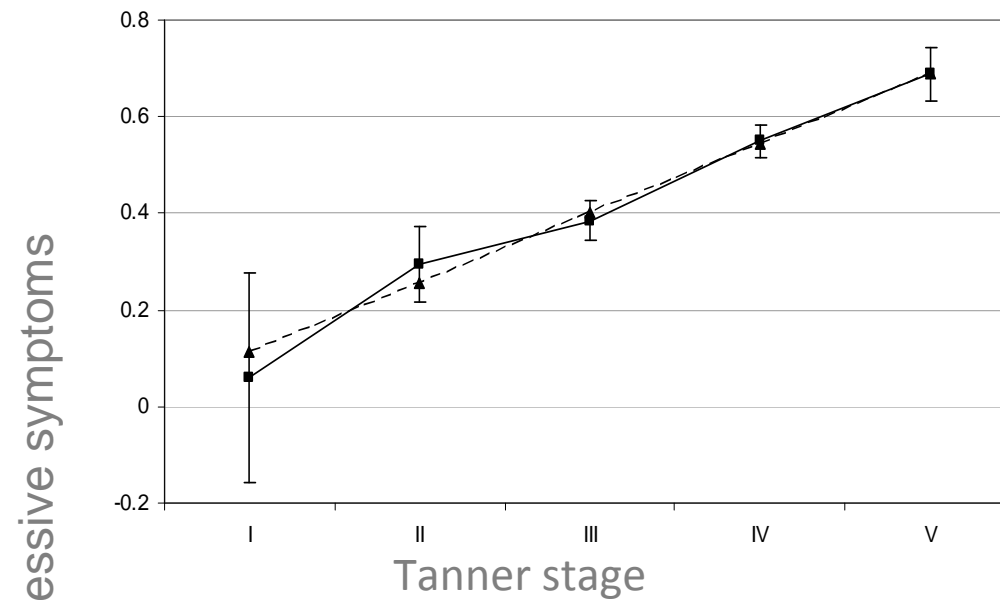


Courtesy of Matt Hickman

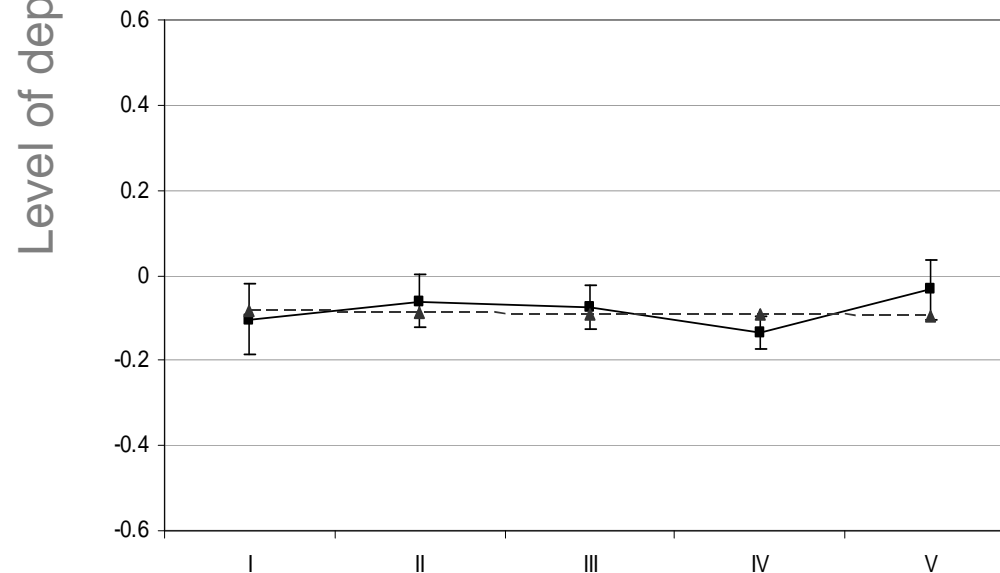
Gender differences in *mean level* of depressive symptoms at each time point



Association between depressive symptoms and pubertal status in mid-adolescence (14 years).



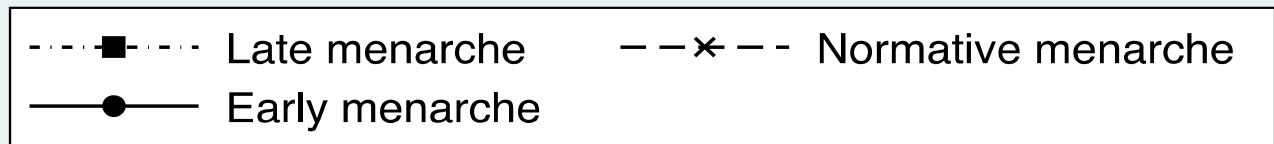
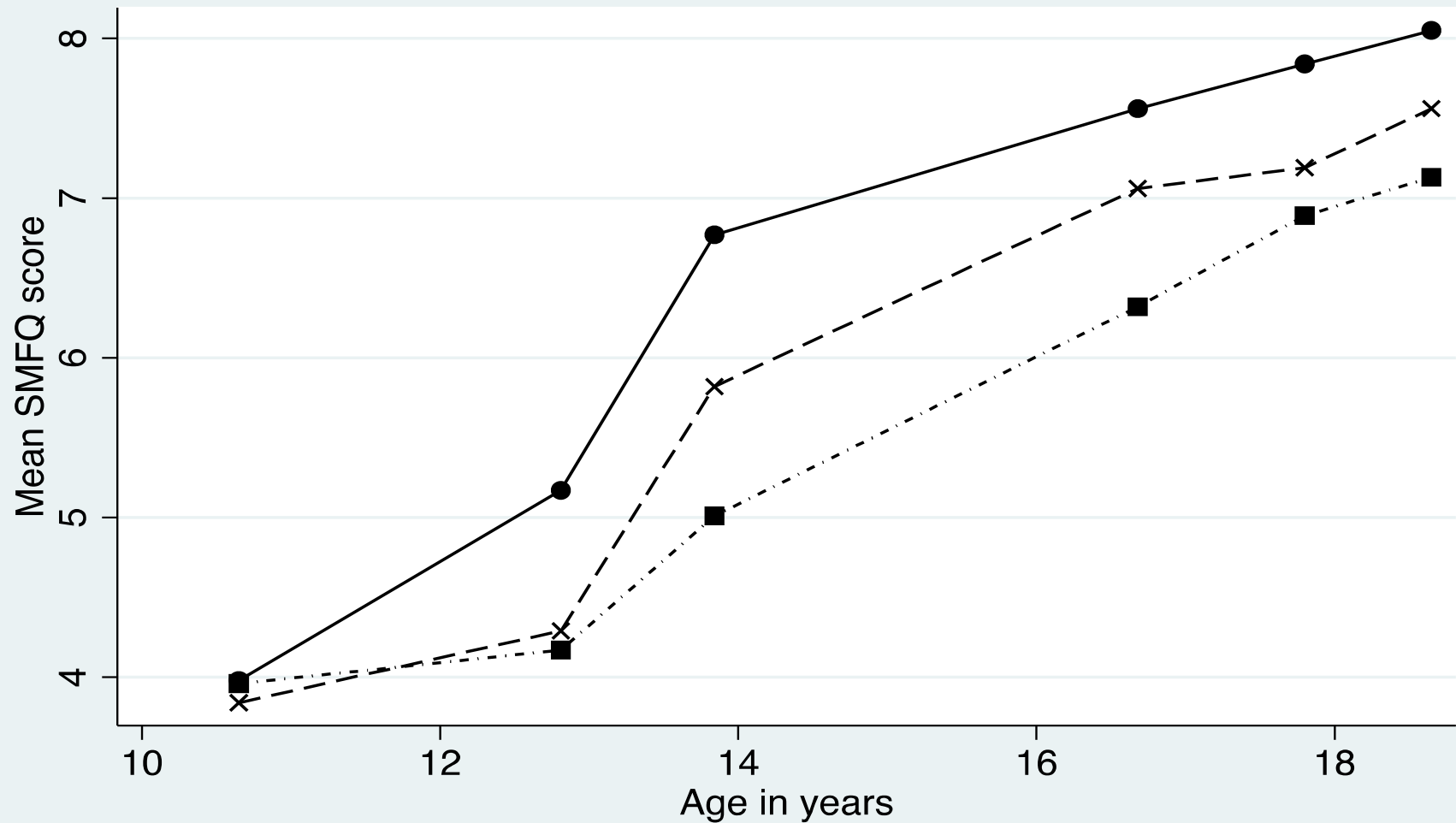
Females
Tanner breast development



Males
Tanner pubic hair development

Courtesy of Carol Joinson

Level of depressive symptoms by timing of menarche



Courtesy of Carol Joinson

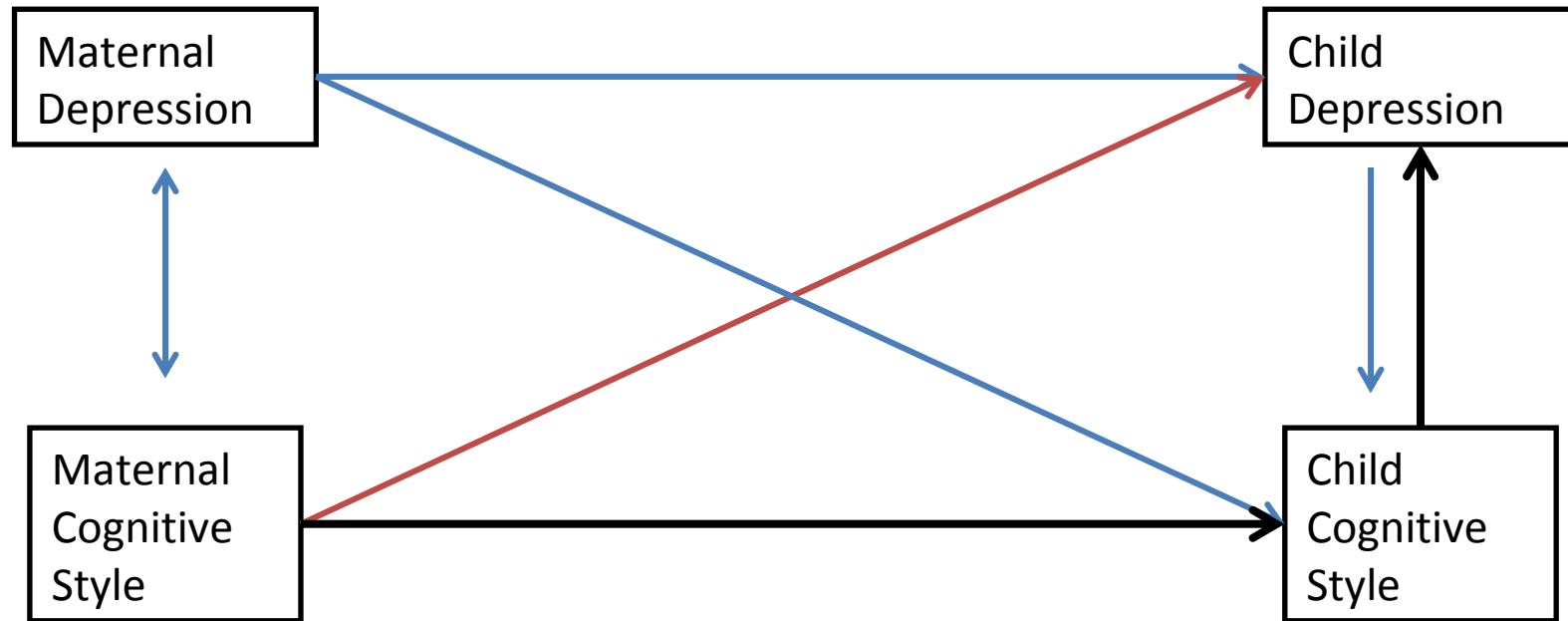
Implications

- Stronger association with pubertal status than with timing of puberty in co-adjusted models – indicative of biological effect as well as social impact
- Adolescence key period for determining longer-term risk of depression

Impact of maternal depression on child psychopathology

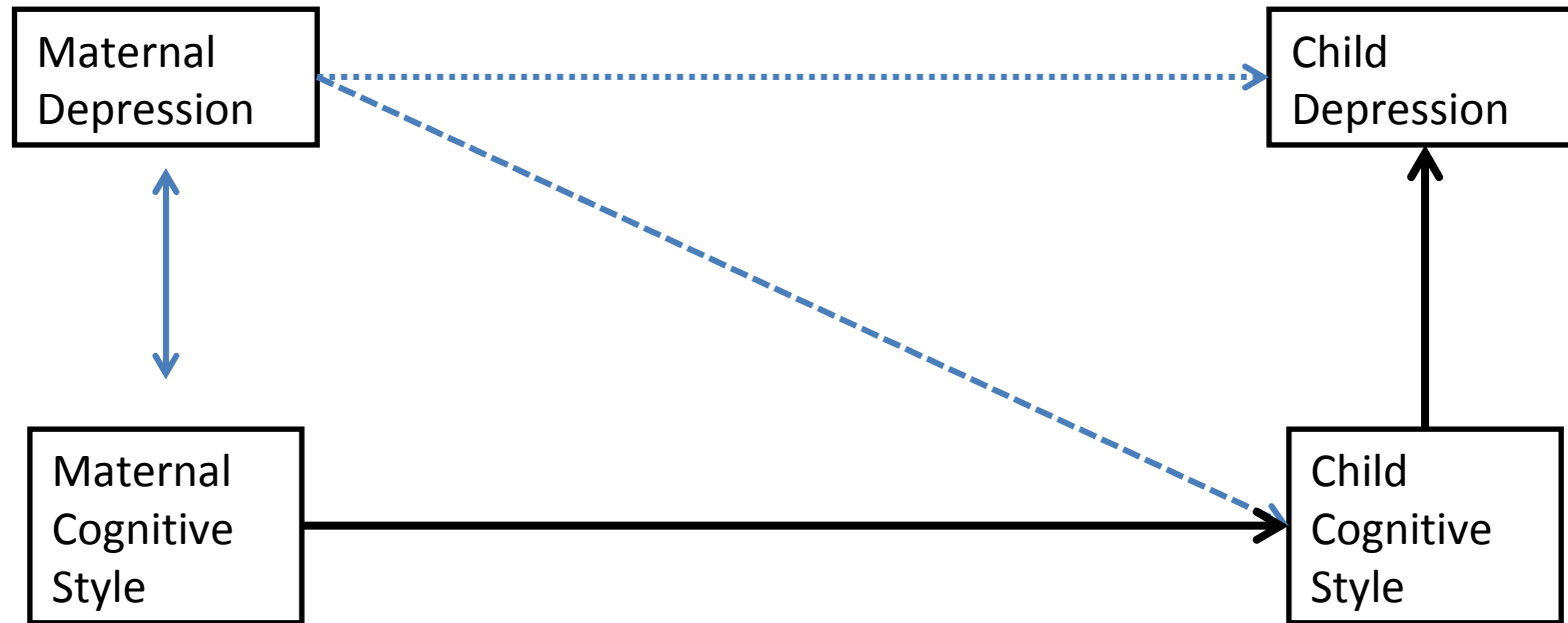


Impact of maternal depression on child psychopathology



Courtesy of Rebecca Pearson

Impact of maternal depression on child psychopathology



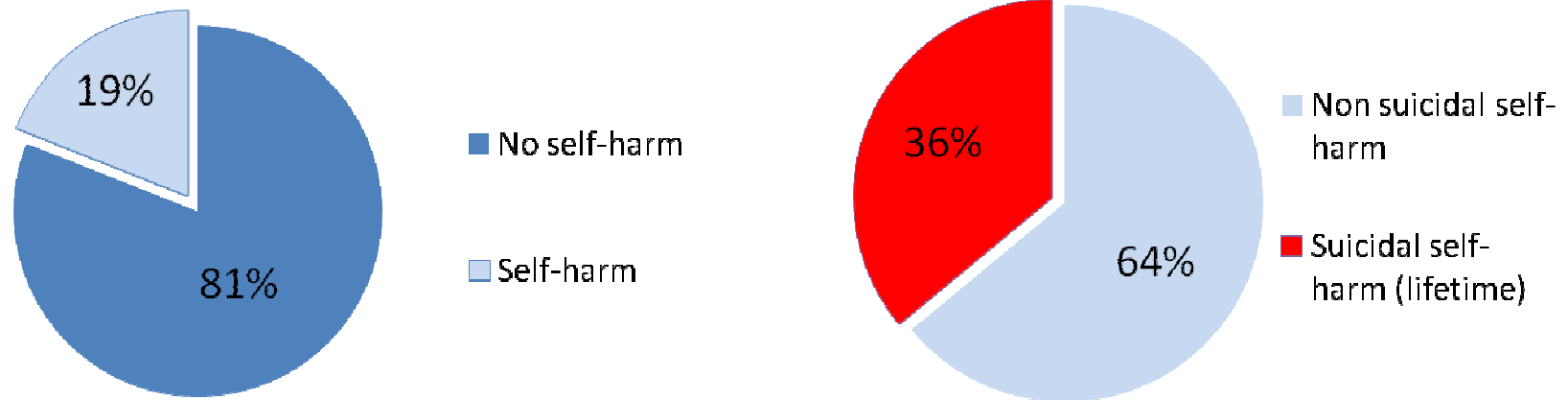
Mother's cognitive style (irrespective of her depression status) influences that of her child - explained 21% of the intergeneration transmission of depression

Implications

Interventions to improve a mother's cognitive style could help prevent her offspring from developing depression during adulthood

Self-harm in ALSPAC

4799 adolescents with data on self-harm with and without suicidal intent at age 16 years



Courtesy of Becky Mars

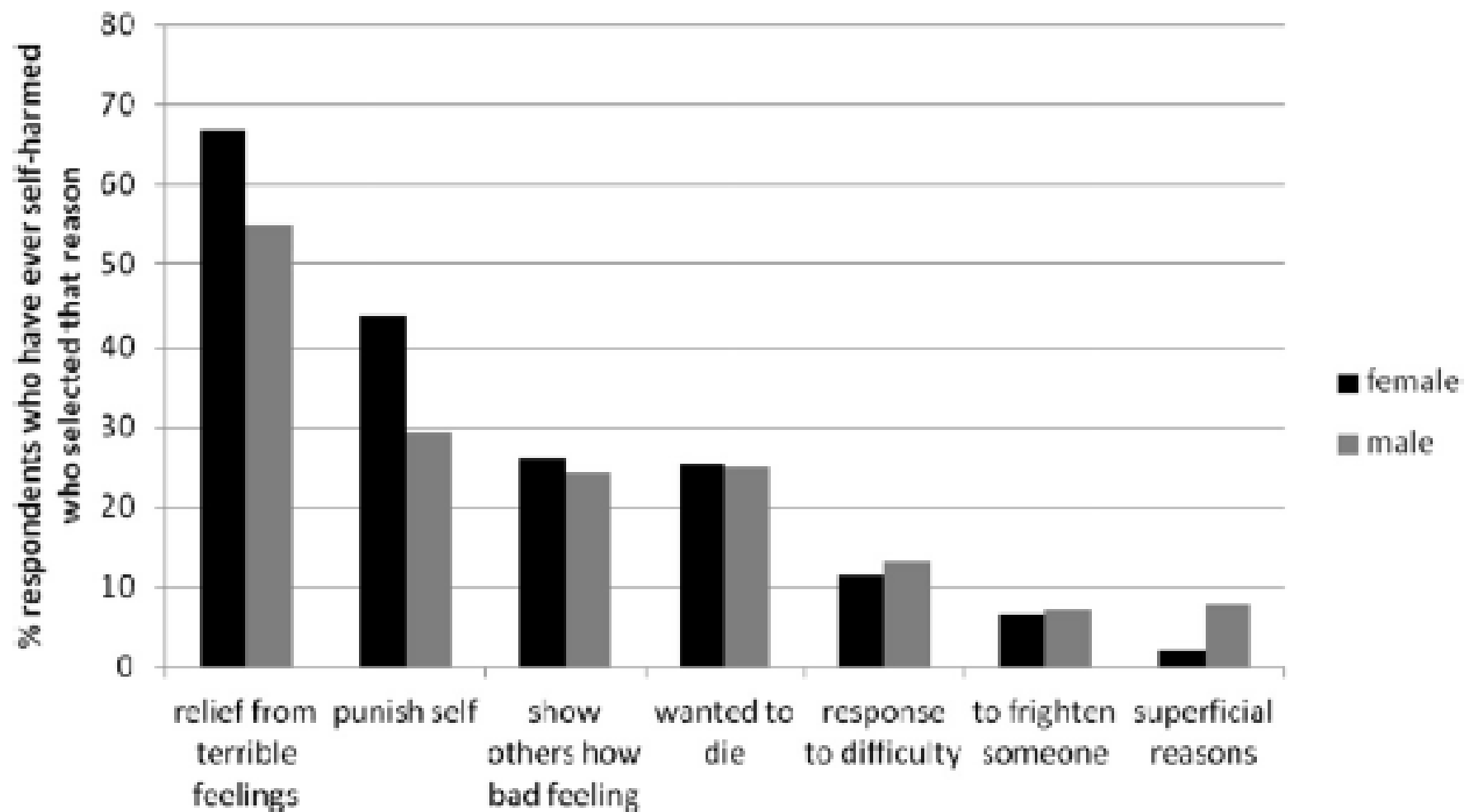
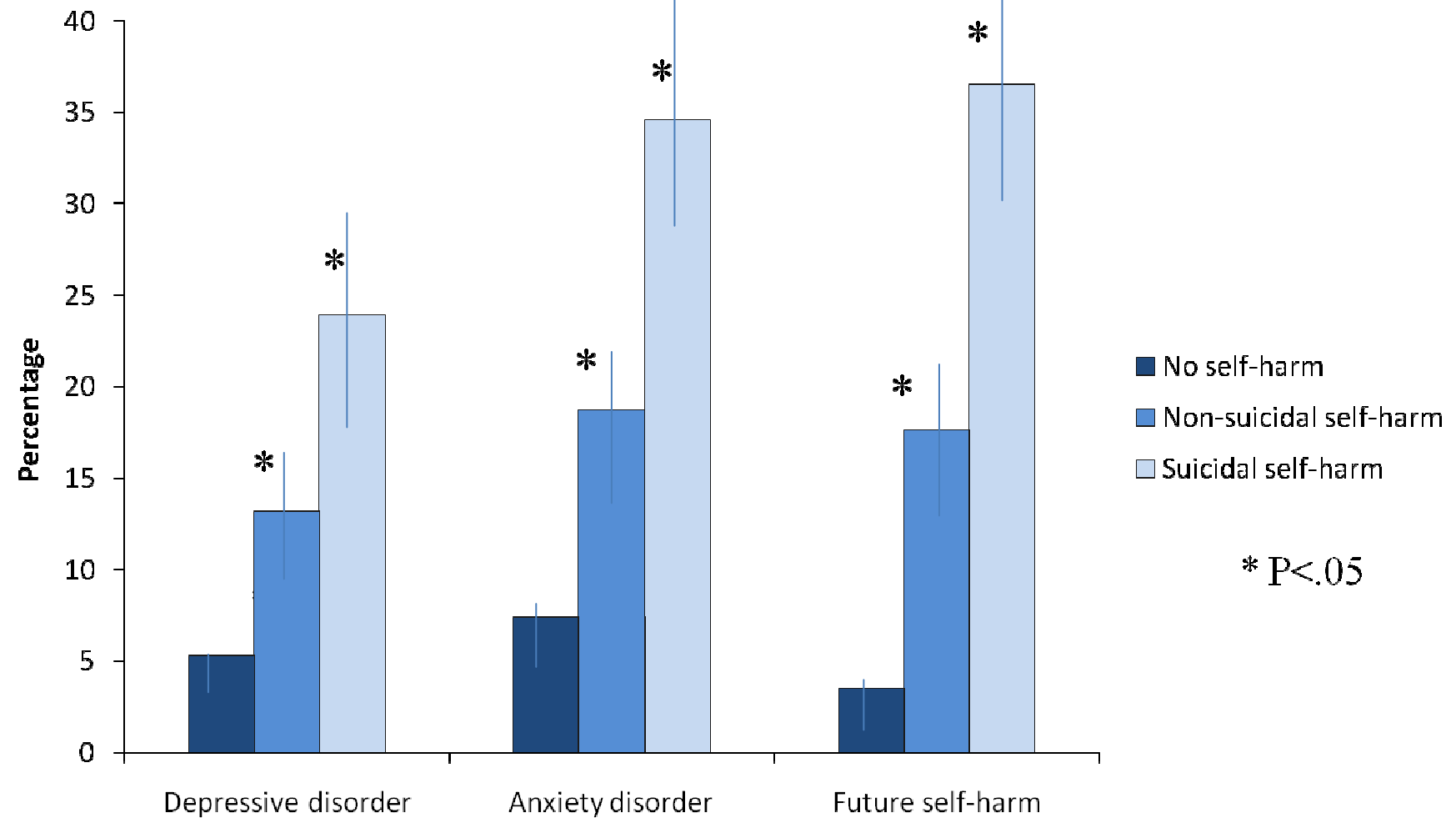


Figure 2 Reasons given for the most recent time participants self-harmed.

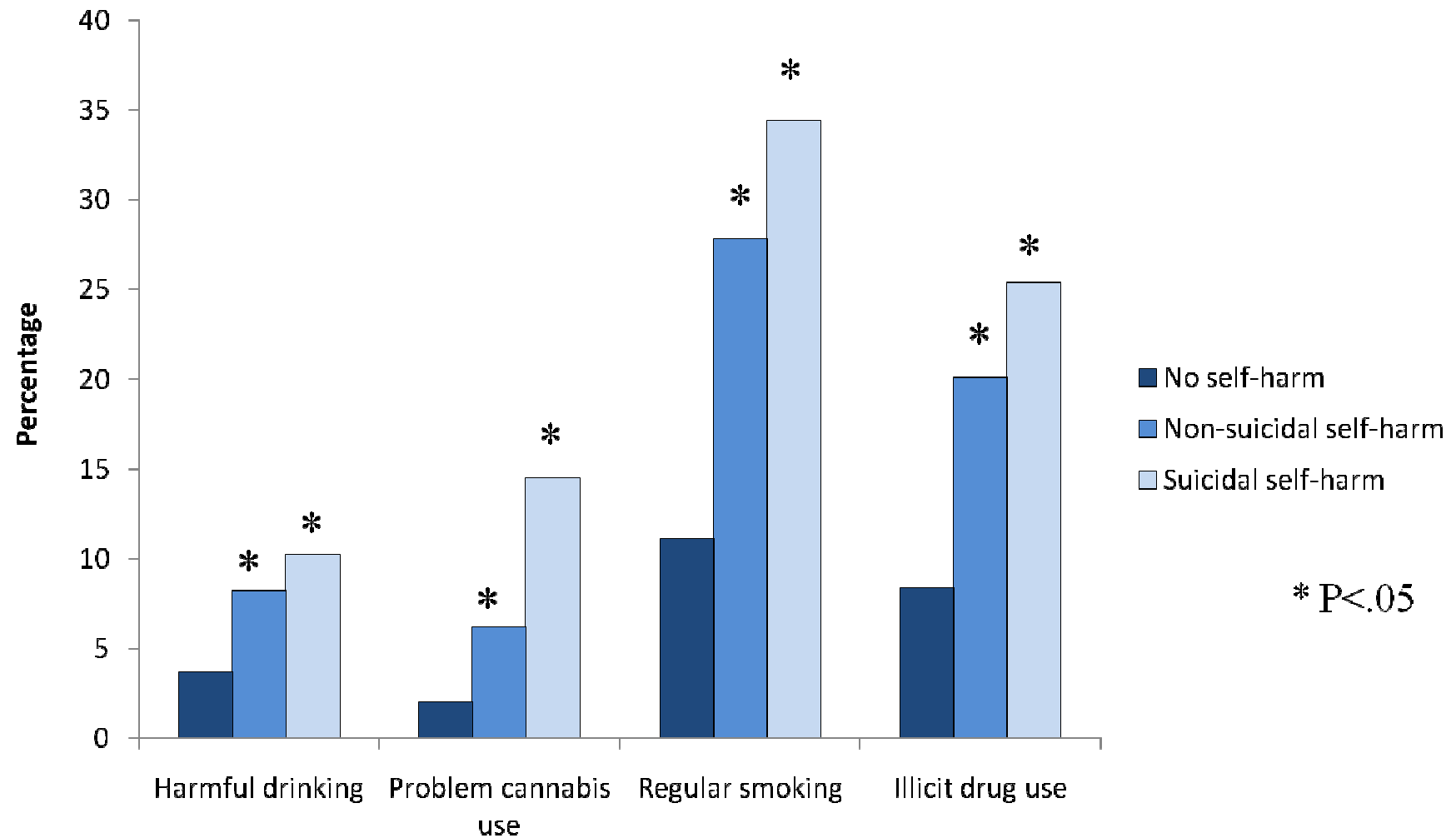
Future mental health problems



* P<.05

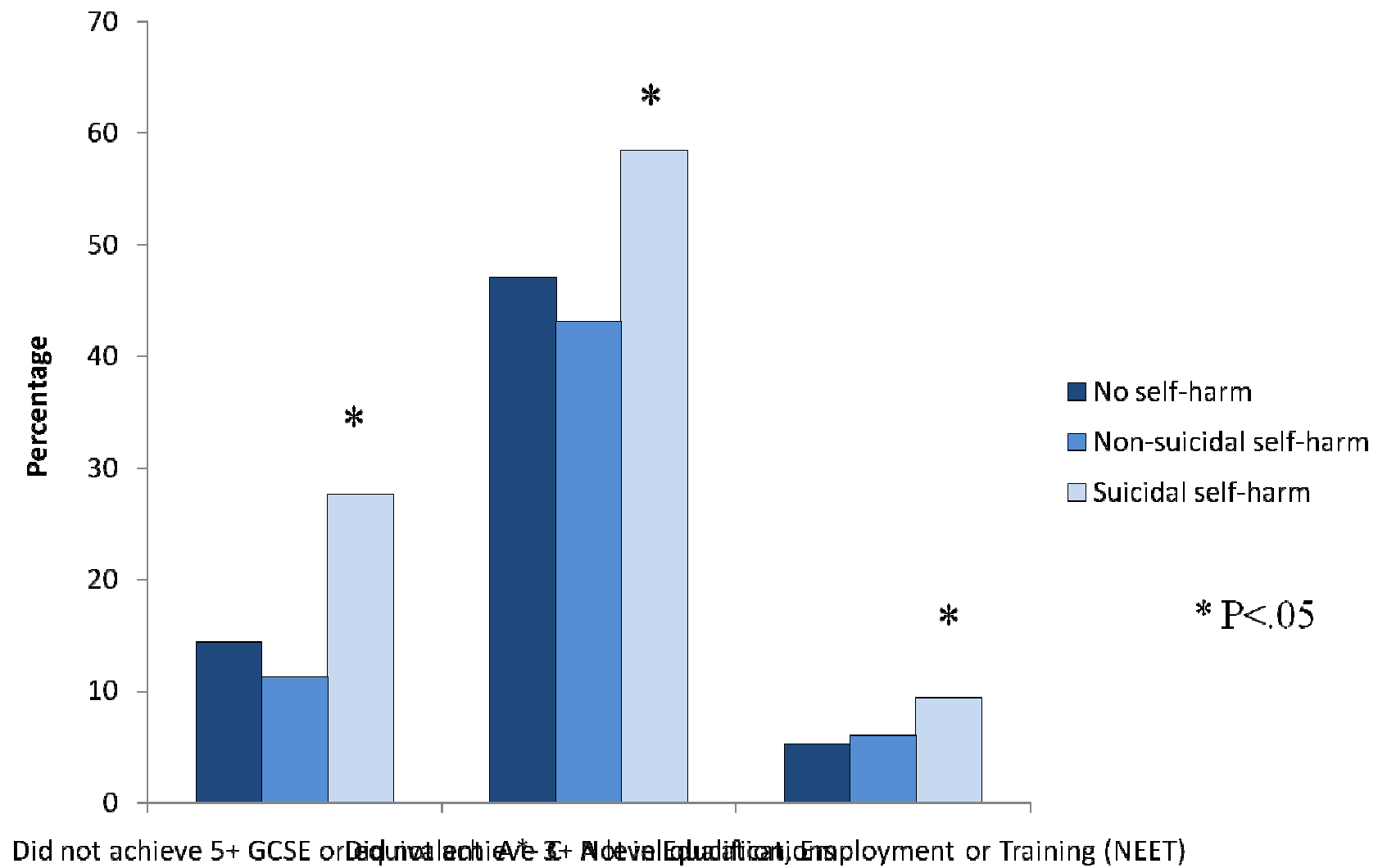
Courtesy of Becky Mars

Substance use problems



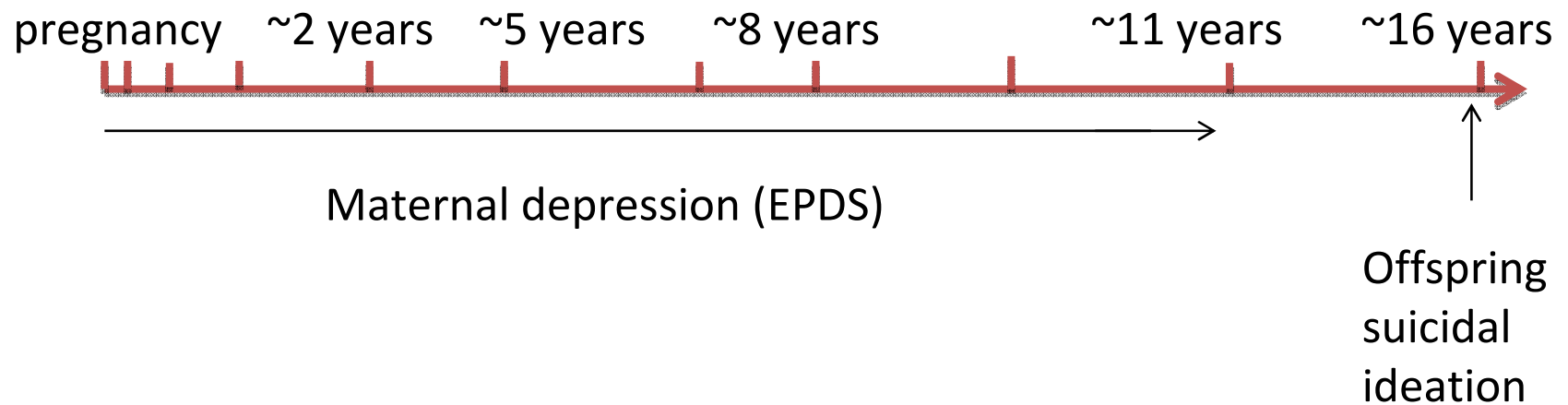
Courtesy of Becky Mars

Educational/occupational difficulties



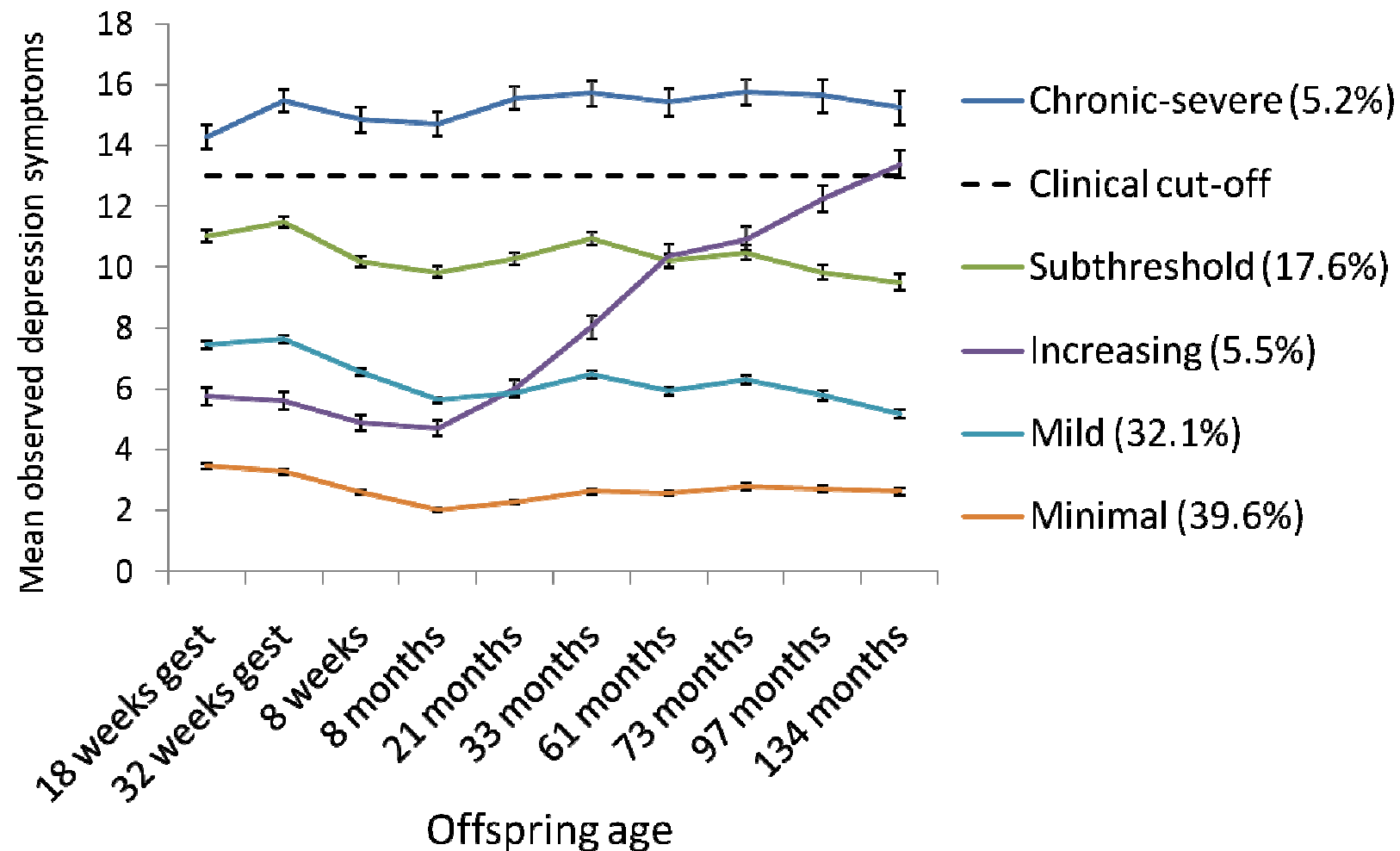
Courtesy of Becky Mars

Maternal depression and child suicidal ideation



Courtesy of Gemma Hammerton

Trajectories of maternal depression symptoms from pregnancy to child age 11 years

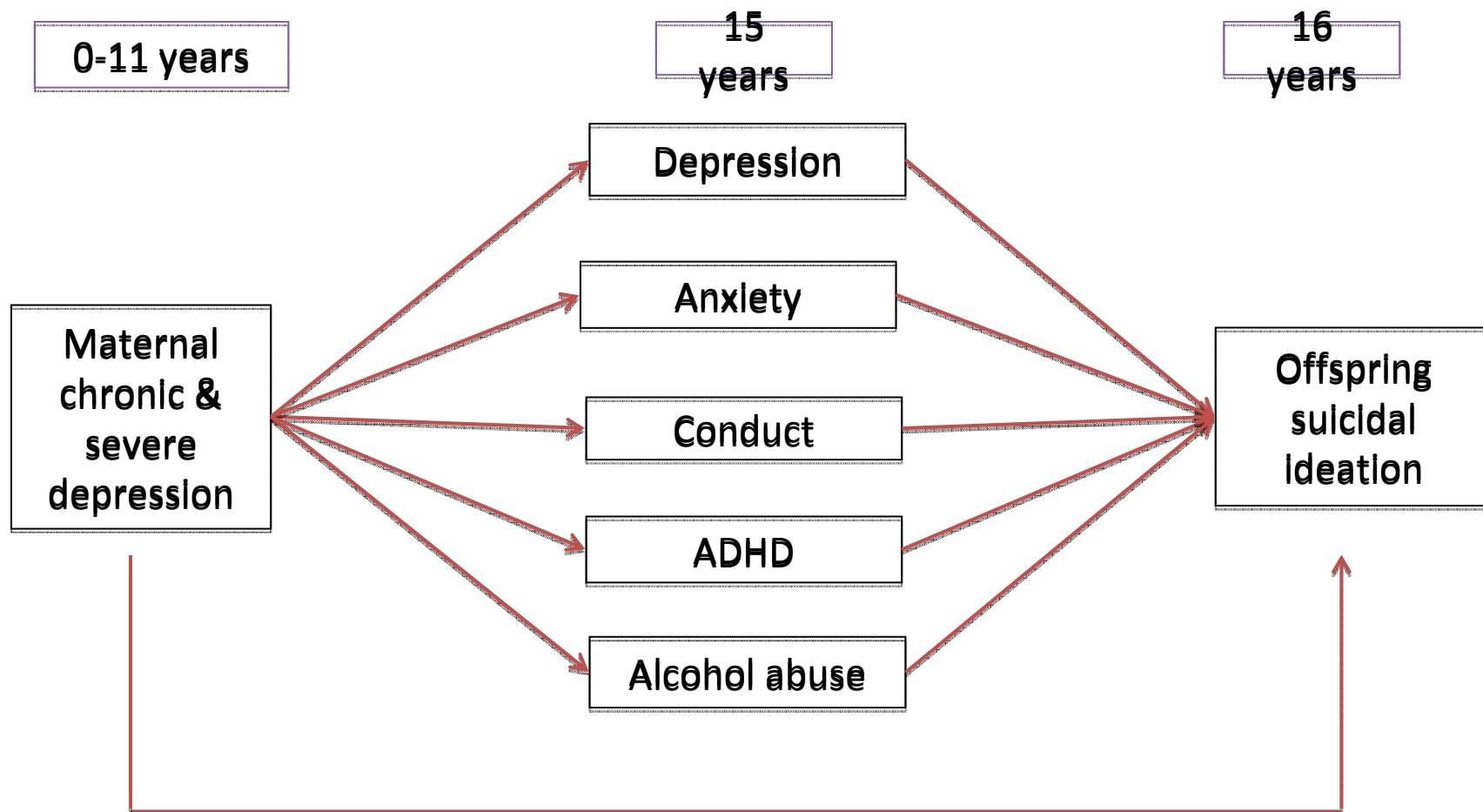


Hammerton et al (under review)

Courtesy of Gemma Hammerton

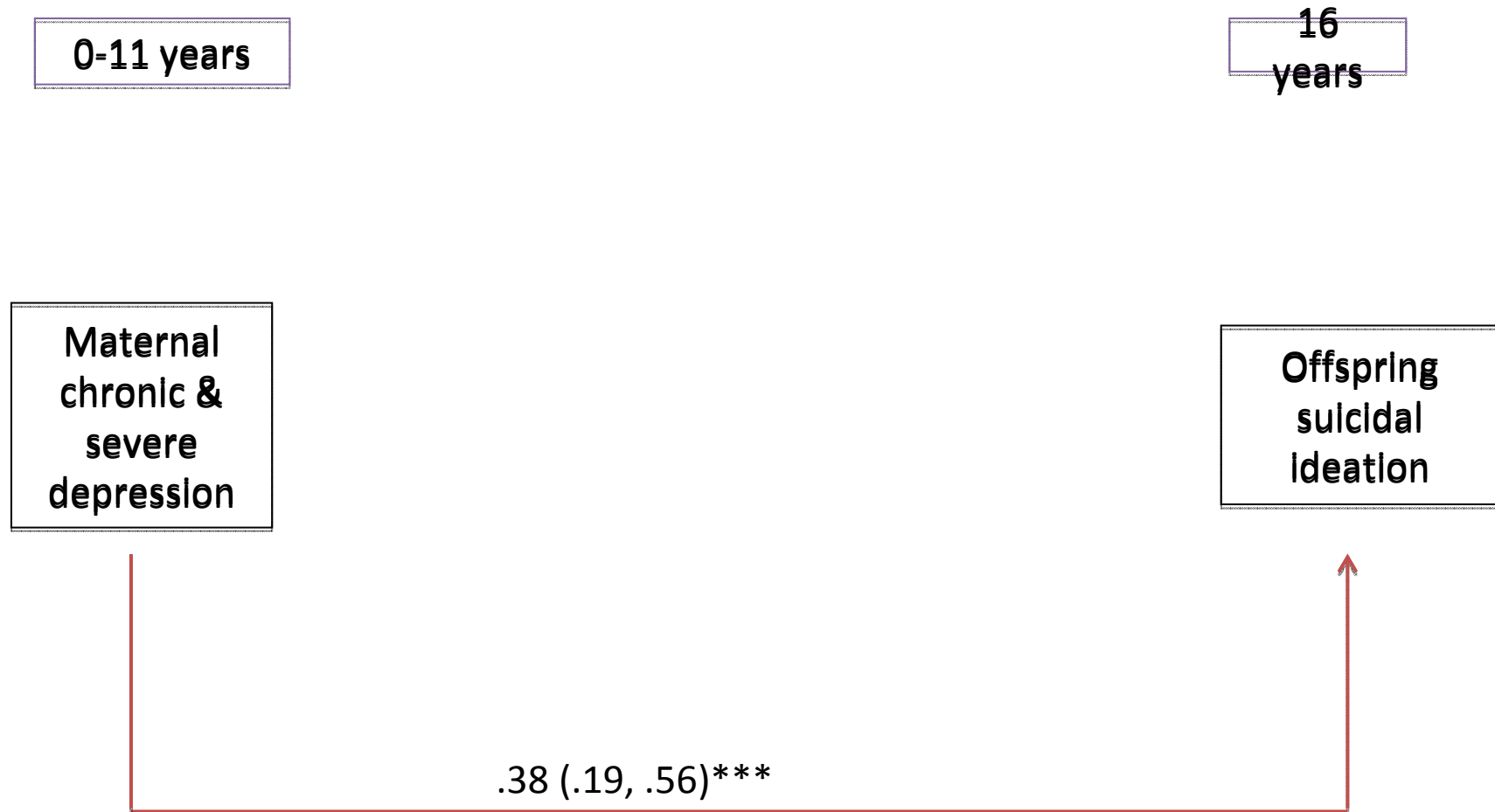
AIM: Investigate the unique contribution of offspring proximal symptoms

- Analyses were performed using structural equation modelling in Mplus

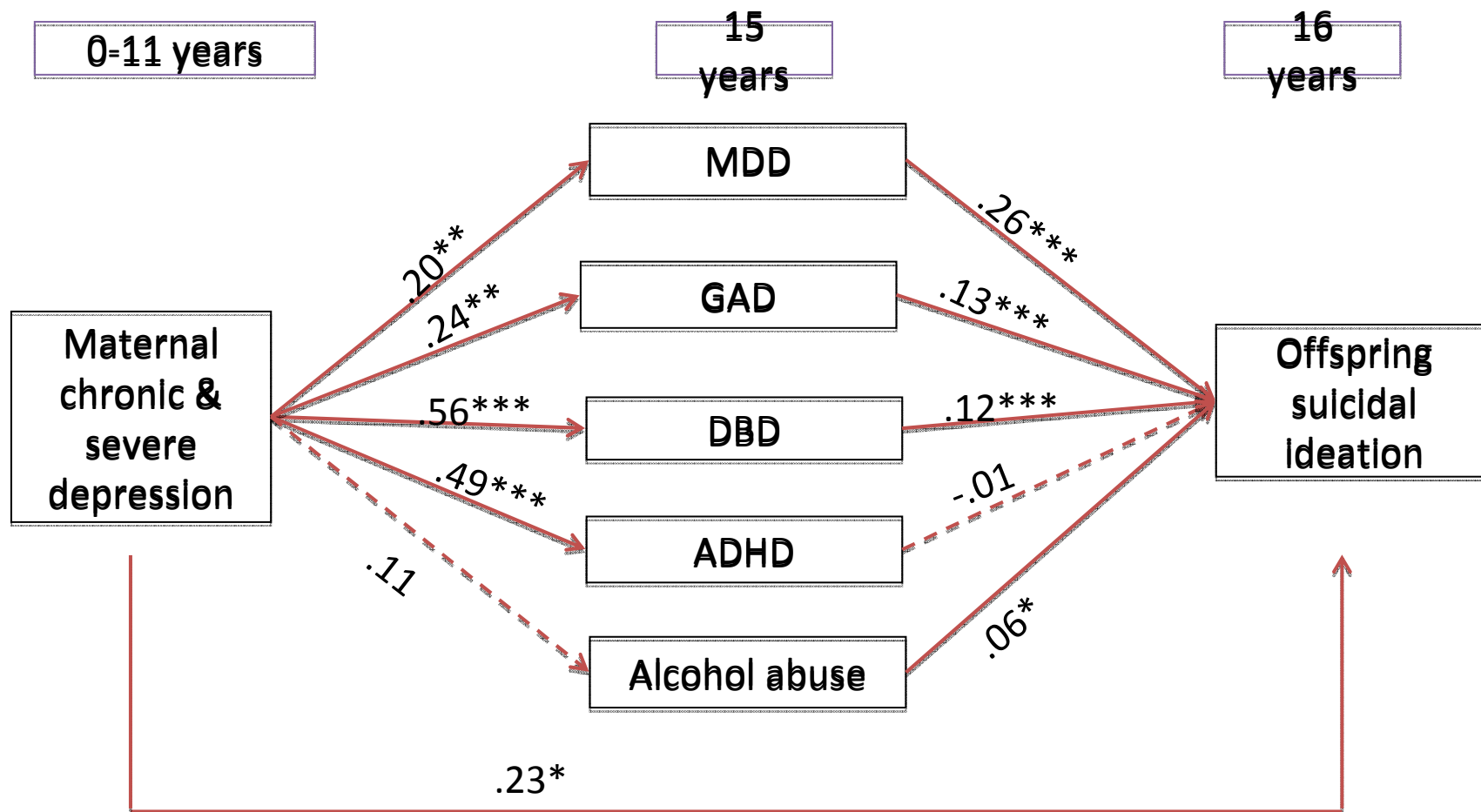


AIM: Investigate the unique contribution of offspring proximal symptoms

- Total effect of maternal *chronic-severe* depression on offspring suicidal ideation



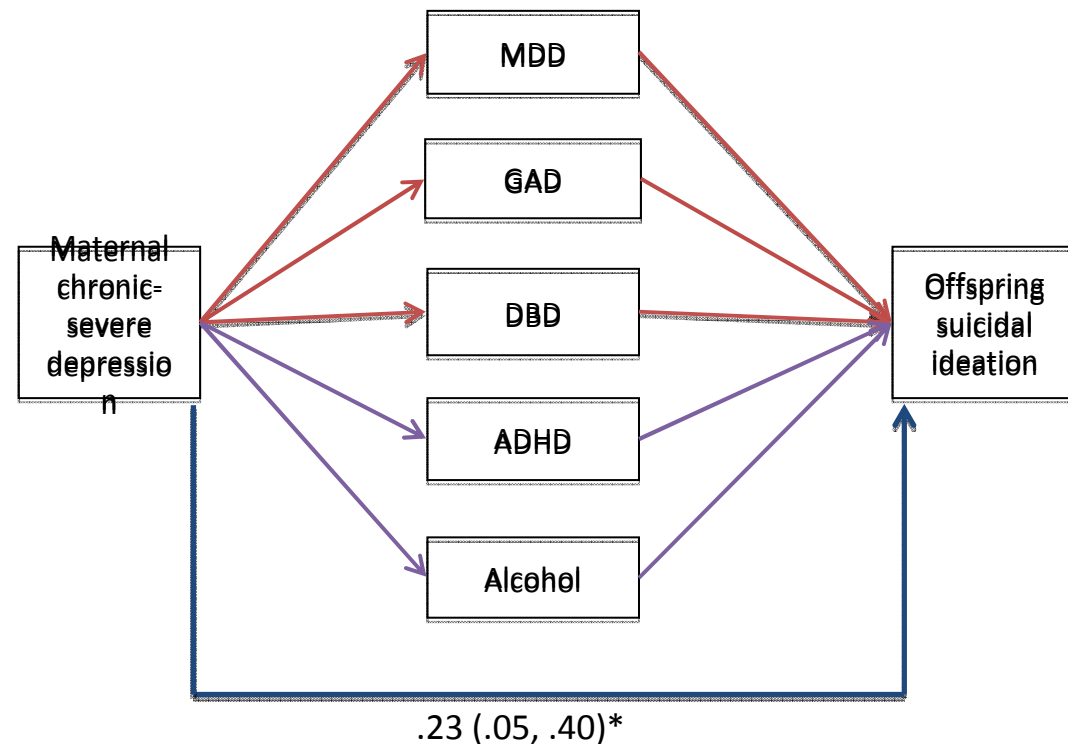
AIM: Investigate the unique contribution of offspring proximal symptoms



AIM: Investigate how much of the association is left unexplained

Offspring symptoms at age 15 years	Indirect effects ¹
MDD	.05 (.01, .09)*
GAD	.03 (.01, .05)**
DBD	.07 (.03, .10)***
ADHD	-.01 (-.03, .02)
Alcohol abuse	.01 (-.004, .02)

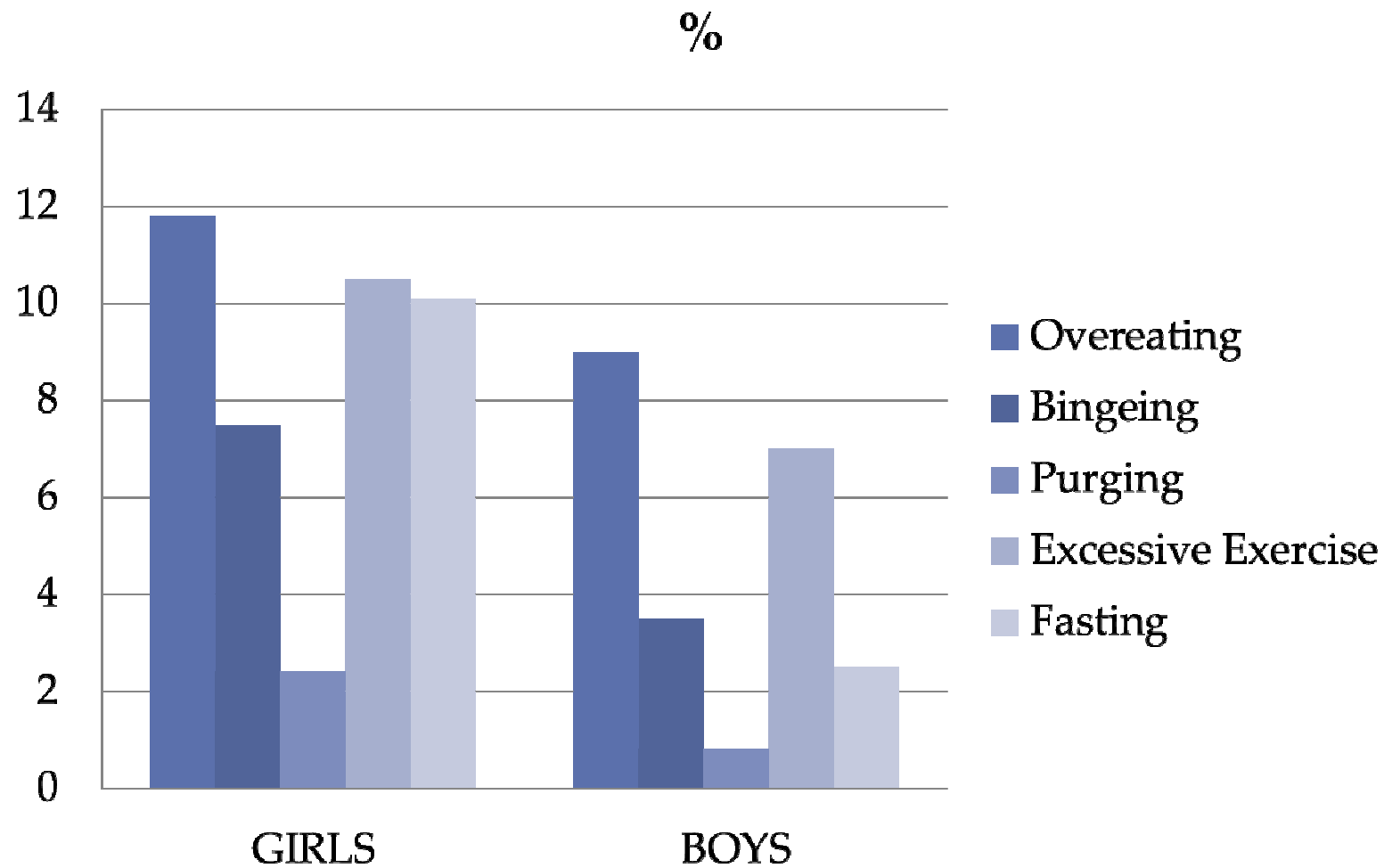
¹Adjusting for demographic & familial confounders



Implications

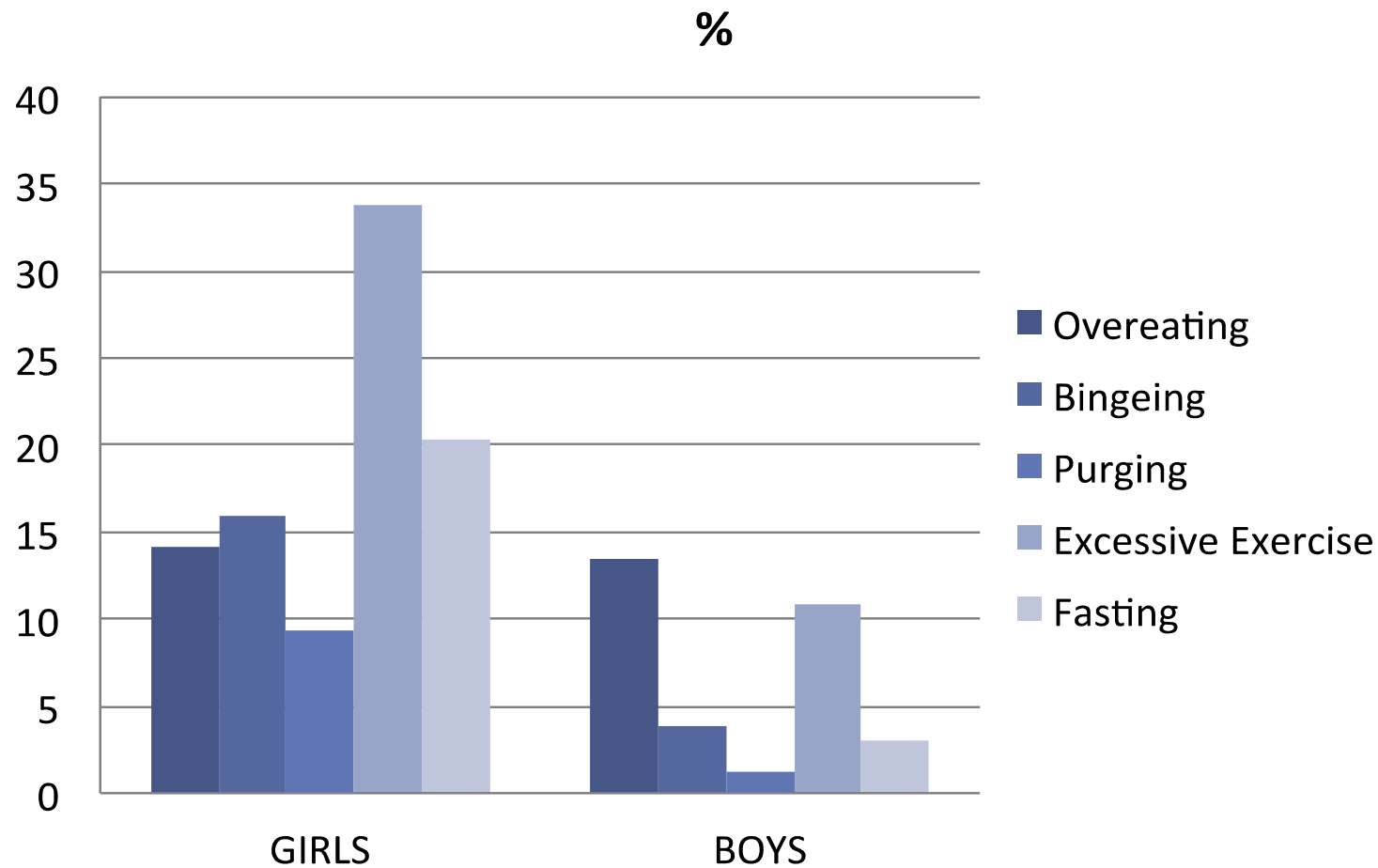
Need to develop useful predictors of future suicidal behaviour in high-risk children – presence of mental health disorders is not enough

Eating disorder behaviours at 14



Courtesy of Nadia Micali

Eating disorder behaviours at 16



Courtesy of Nadia Micali

Final summary

Birth cohorts have an important role for:

- 1) Measuring occurrence, impact on function, and likely population health burden
- 2) Understanding development of mental health disorders over time, and underlying aetiological mechanisms
- 3) Identifying potentially modifiable targets for early intervention

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Nadia Micali

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Matt Hickman

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