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Biological explanations of links between childhood adversity and later self-harm: a focus on inflammation

Abigail Russell

Senior Research Associate, Centre for Academic Mental Health

@DrAbbyRussell @SASHBristol a.e.russell@bristol.ac.uk

bristol.ac.uk

Medical Research Foundation

MRC Medical Research Council

Abigail Russell, Jon Heron, David Gunnell, Tamsin Ford, Gibran Hemani, Carol Joinson, Paul Moran, Caroline Relton, Matthew Suderman and Becky Mars

Centre for Academic Mental Health, Population Health Sciences, University of Bristol Medical School

NIHR Biomedical Research Centre at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol.

University of Exeter College of Medicine and Health

MRC Integrative Epidemiology Unit, University of Bristol Medical School; Population Health Sciences, University of Bristol Medical School

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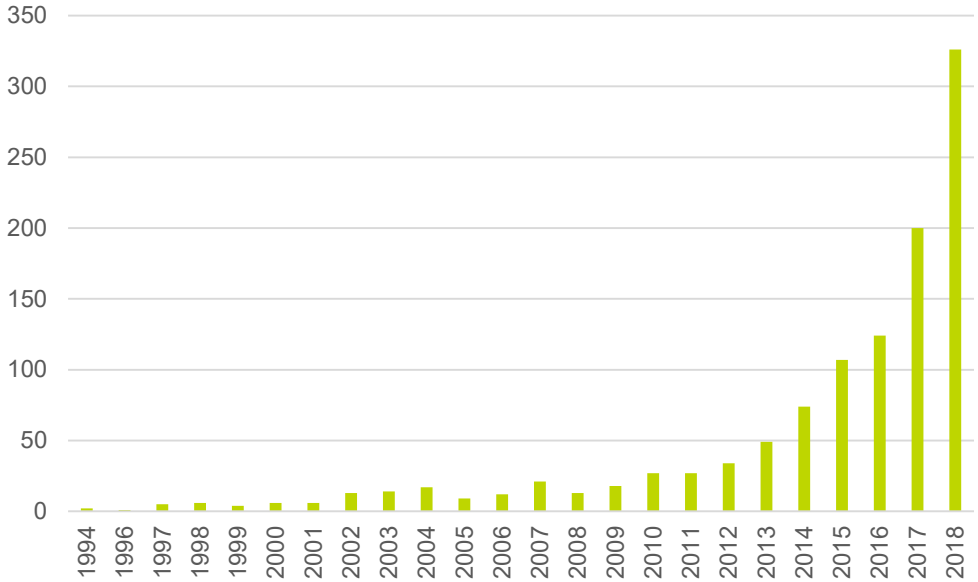
Childhood adversity

- Adverse childhood experiences “ACEs”
- Household dysfunction and child maltreatment



Number of publications with “adverse childhood experiences” in the title or abstract by year.

Source: https://www.ncbi.nlm.nih.gov/pubmed

The ‘original’ ACEs study

Felitti, V. J., et al. (1998). "Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study." American journal of preventive medicine **14(4): 245-258.**

Adversity, self-harm and suicide

International Journal of Epidemiology, 2016, 501–511
doi: 10.1093/ije/dyw012
Advance Access Publication Date: 31 March 2016
Original article

Health in Adolescence and Young Adulthood

Childhood household dysfunction and risk of self-harm: a cohort study of 107 518 young adults in Stockholm County

Emma Björkenstam[1,2]*, Kyriaki Kosidou[3,4] and Charlotte Björkenstam[5]

doi:10.1111/jcpp.12831

Suicide among youth – etiology, and treatment

Christine B. Cha,[1] Peter J. Franz,[2] Eleonora M. Guzmán,[1] Catherine R. Glenn,[3] Evan M. Kleiman,[2] and Matthew K. Nock[2]

Childhood maltreatment

There is strong evidence indicating that various forms of childhood maltreatment such as sexual, physical, and emotional abuse predict future suicidal ideation and suicide attempt among youth. Prospective cohort studies and twin studies have demonstrated the unique

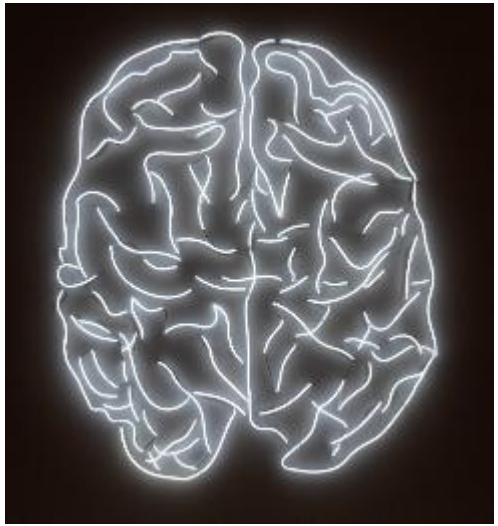
Biological embedding of early adversity

- Epigenetic changes
- Altered HPA axis reactivity
- Altered neural structure and function
- **Chronic inflammation**
  - The immune system and inflammatory response involve a host of cells, cytokines and other molecules that act to fight infection

Berens, A. E., et al. (2017). "Biological embedding of childhood adversity: from physiological mechanisms to clinical implications." BMC medicine **15(1): 135.**

"drawings 2004" by Marianna Ignataki

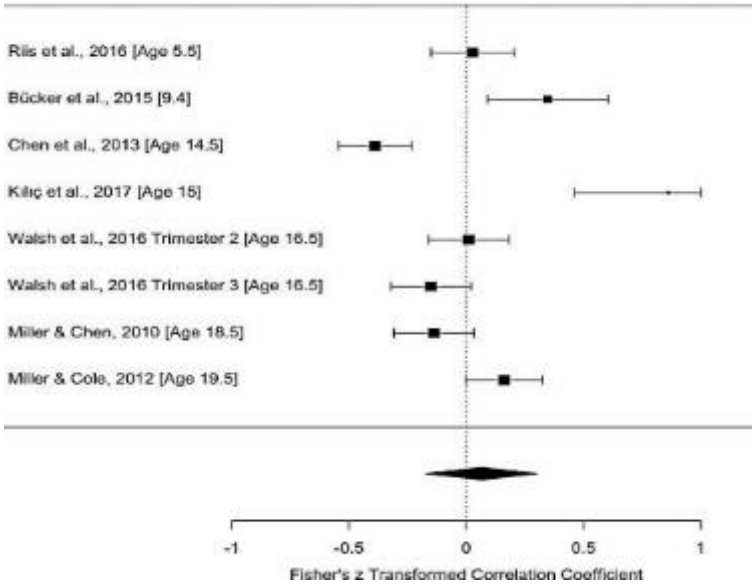
Linking inflammation and behaviour



- The brain recognises signals from the immune system
- This can lead to changes in mood and behaviour
- ‘Sickness behaviour’ triggered by pro-inflammatory molecules:
  - Fever
  - Decreased appetite
  - Depression
  - Suicidal behaviour

Childhood adversity and inflammation

- C-reactive protein
- Interleukin-6



Kuhlman, K. R., et al. (2019). "Early life adversity exposure and circulating markers of inflammation in children and adolescents: A systematic review and meta-analysis." Brain, behavior, and immunity.

Inflammation and suicidal behaviour

- Meta-analysis of inflammatory markers and suicidal ideation, suicidal behaviour or suicide (n=18)
- Blood levels of IL-6 and CRP were significantly increased in participants with suicidality compared to controls
- Small effect size estimates: IL-6 g=0.3, CRP g=0.45
- In children and adolescents (n=2)
- One study found no difference in IL-6, one found higher IL-6 IL-1β and TNFα

Black, C. and B. J. Miller (2015). "Meta-analysis of cytokines and chemokines in suicidality: distinguishing suicidal versus nonsuicidal patients." Biological psychiatry **78(1): 28-37.**

Kim, J.-W., et al. (2014). "Inflammatory markers and the pathogenesis of pediatric depression and suicide: a systematic review of the literature." The Journal of clinical psychiatry **75(11): 1242-1253.**

Do high levels of inflammatory markers mediate the association between ACEs and self-harm?

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- The Avon Longitudinal Study of Parents and Children (ALSPAC)
- Born in Bristol and Avon 1991-1992
- Initially ~14,000 children

- Information from 4,308 young people used in the current study

Childhood adversities ages 0-9: reported by mother, partner, young person

Blood samples age 9 ½

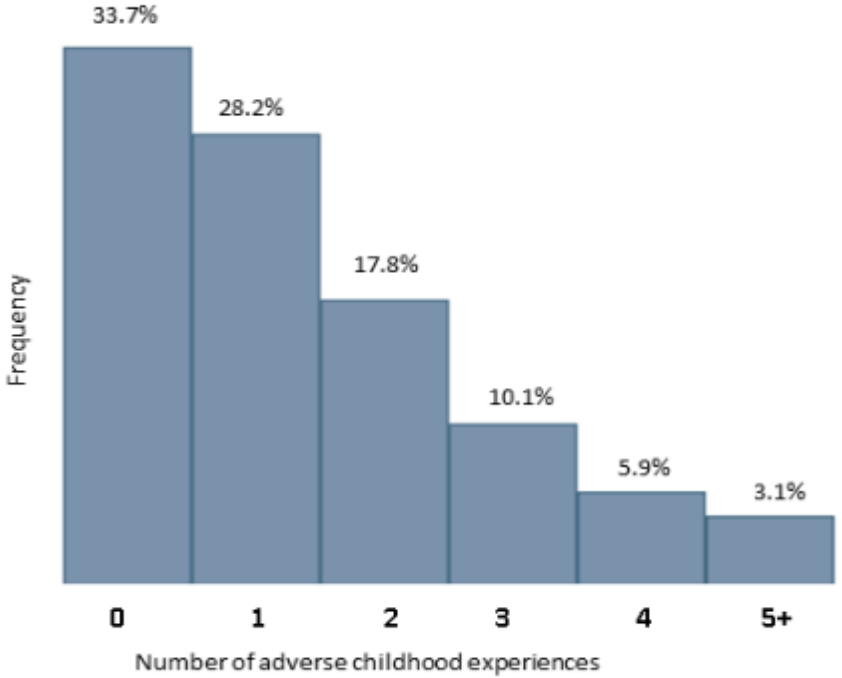
Self-harm reported by young person age 16

Covariates and intermediate confounders

Sensitivity analyses: self-harm with suicidal intent at 16, self-harm at 21, multiple self-harm in past year at 16, excluding those with psychiatric disorder, excluding those with high CRP indicating acute infection, using the mdNLR as an alternate measure of inflammation

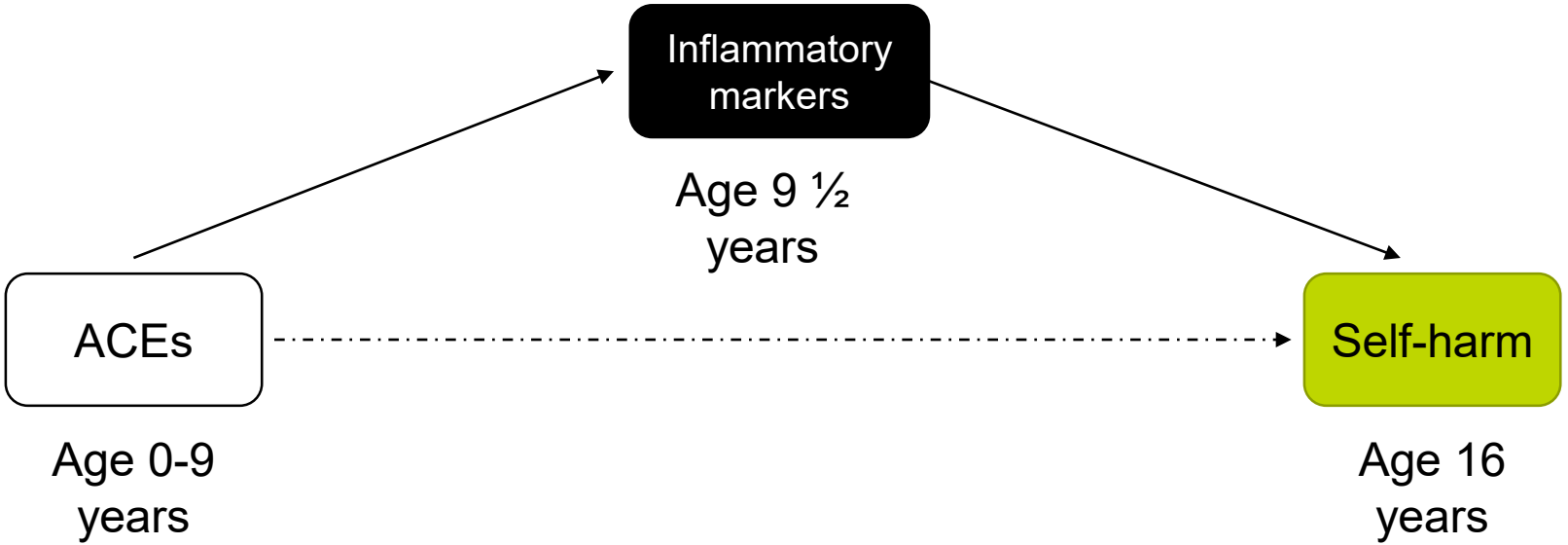
Childhood adversity

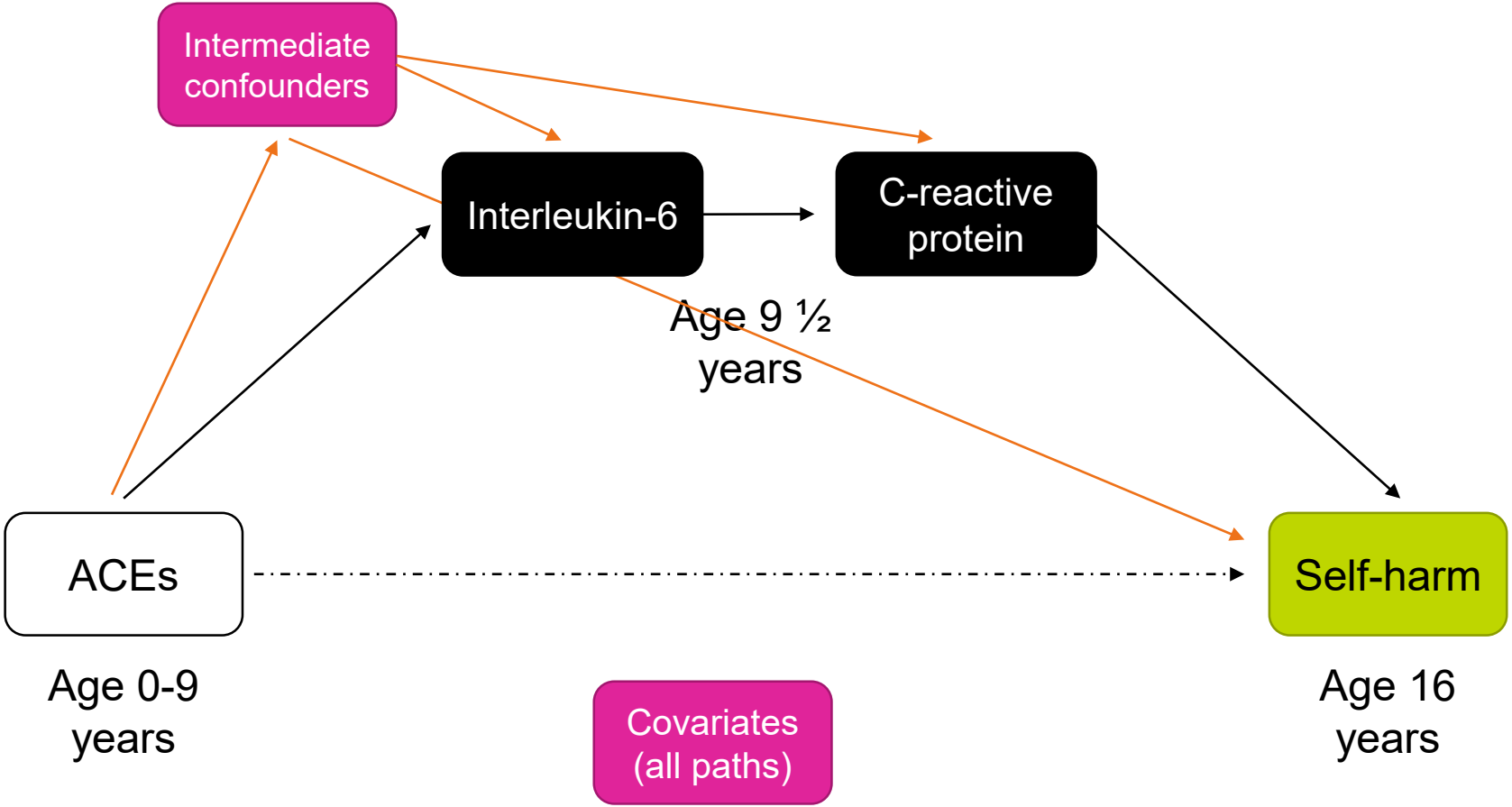
Adverse childhood experience	Percent
Sexual abuse	0.8
Physical abuse	7.6
Emotional abuse	19.1
Parent substance use	11.7
Parent mental health problems or suicide attempt	39.3
Violence between parents	21.7
Parental separation	21.6
Child experiences bullying	12.7
Parent criminal conviction	6.6



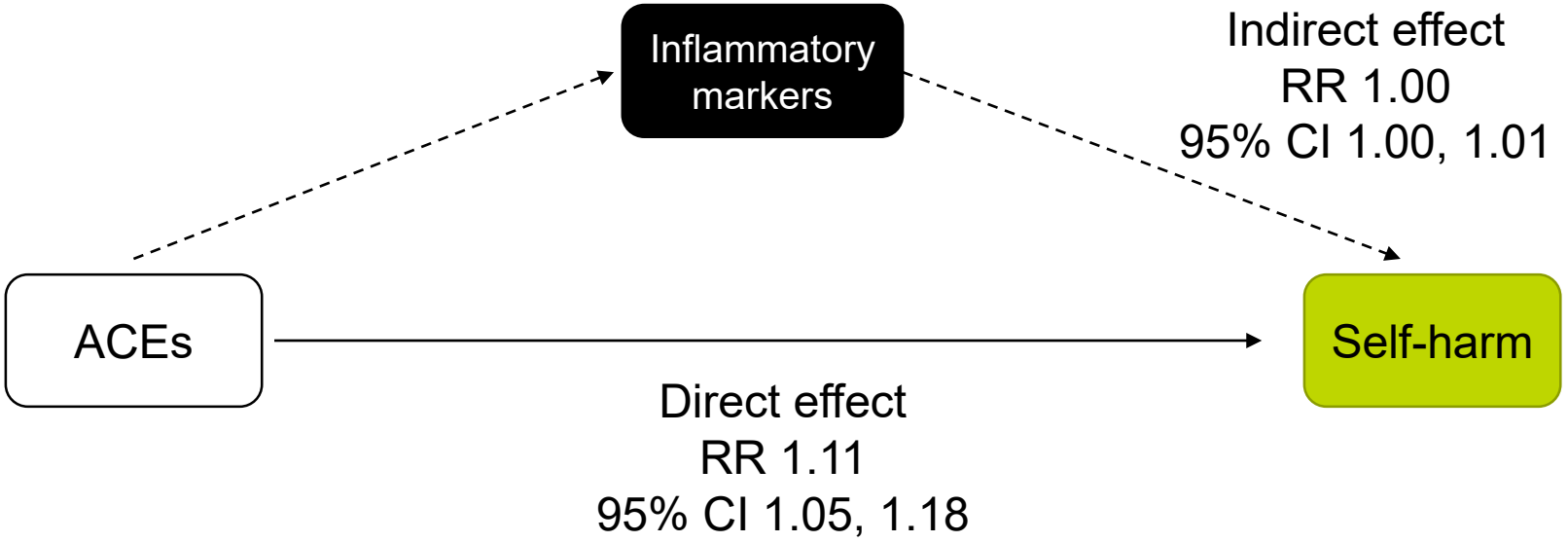
ACE	Definition	Number of questions
Sexual abuse	Was the child sexually abused	7
Physical abuse	Whether physically cruel to child	31
Emotional abuse	Whether or not mum/partner had been emotionally cruel to the child	32
Parent substance use	Daily use of cannabis or any use of other drugs. Or, alcohol problem by self-reported problematic use, and saw a doctor because of it	62
Parent mental health problems or suicide attempt	Depression scores (EPDS>12) and medication, presence of schizophrenia, bulimia, anorexia or attempted suicide.	57
Violence between parents	Parent experienced physical cruelty from partner, or displayed (specific types) of violence towards partner	43
Parental separation	Parents divorced or separated. Degree to which this impacted on the child.	32
Bullying	Child bullied	6
Parent convicted	Parent convicted of offence	18

Mediation analysis

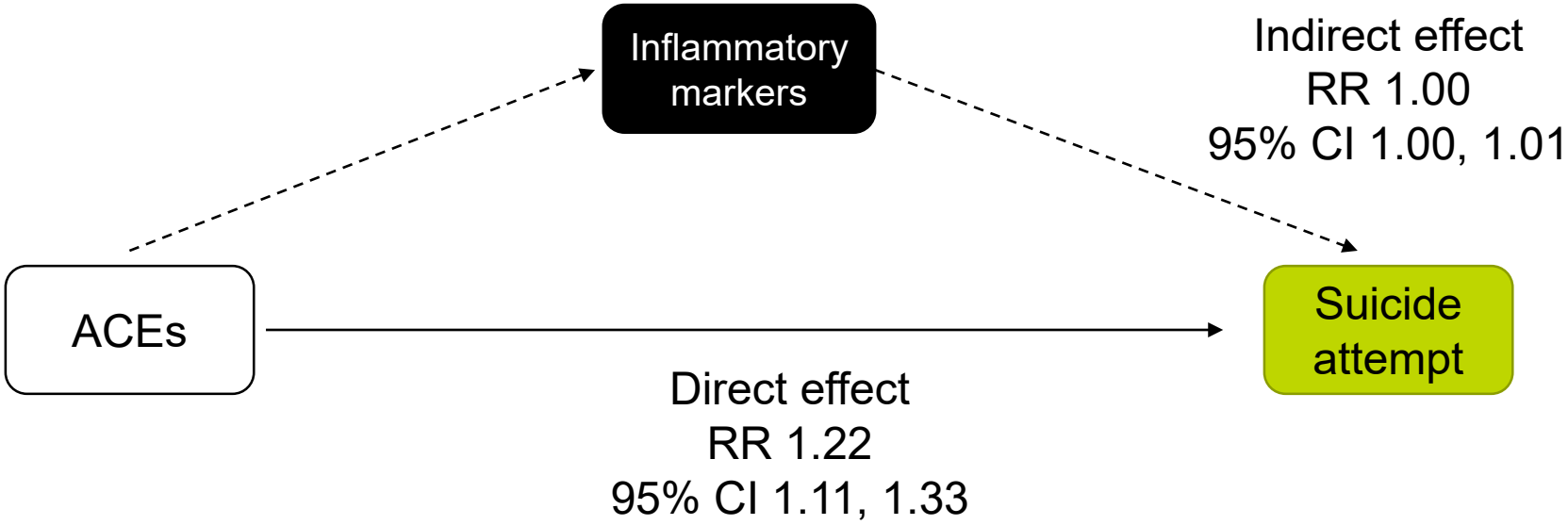


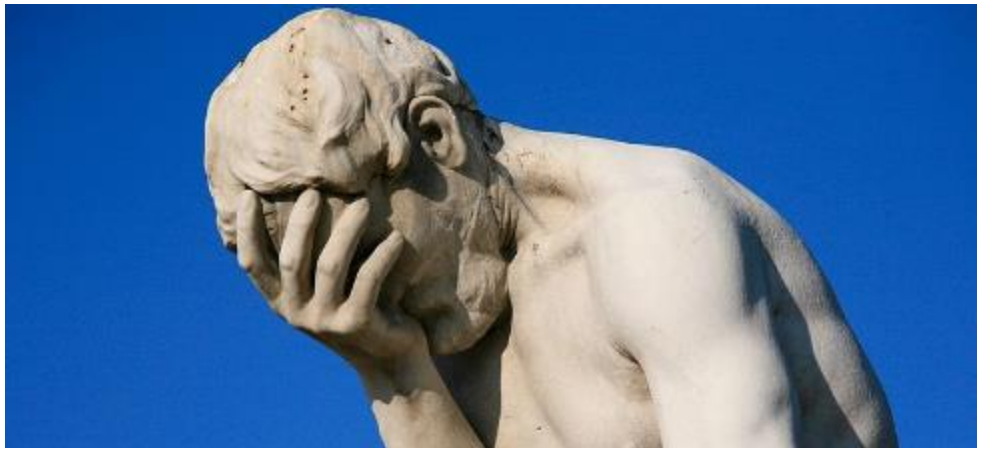

Intermediate confounders
Interleukin-6
C-reactive protein
Age 9 ½ years
ACEs
Age 0-9 years
Covariates (all paths)
Self-harm
Age 16 years

Results


Inflammatory markers
Indirect effect
RR 1.00
95% CI 1.00, 1.01
ACEs
Self-harm
Direct effect
RR 1.11
95% CI 1.05, 1.18

Sensitivity analysis: suicide attempt





The Journal of Child Psychology and Psychiatry

Journal of Child Psychology and Psychiatry 59:8 (2018), pp 829–830 doi:10.1111/jcpp.12952

Editorial: Sweet nothings – the value of negative findings for scientific progress

- Altered inflammatory response rather than systemic inflammation?
- Timing of measures
- Prior studies detecting inflammatory consequences of self-harm?
- Population-based vs clinical samples

In conclusion…

- Young people who have been exposed to childhood adversity are a group at high risk of self-harm
- The association between ACEs and self-harm does not appear to be mediated by an inflammatory process in childhood
- Further research is needed to identify alternative psychological and biological mechanisms underlying this relationship

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Thank you

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a.e.russell@bristol.ac.uk

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