EARLY BRAIN & BIOLOGICAL DEVELOPMENT: A SCIENCE IN SOCIETY SYMPOSIUM

Biological Embedding of Adverse Childhood Experiences

Andrea Danese, MD PhD

31 May 2011



Alberta family wellness initiative

Norlien Foundation

Introduction

Enduring effects of child stress

Timing matters

Biological embedding in children

Conclusion

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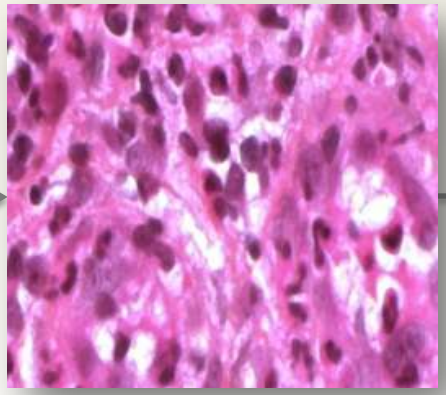
Conclusion



INFLAMMATION

Innate immunity

- Body physical barriers

(e.g., skin, gastrointestinal tract)

- Non-self recognition

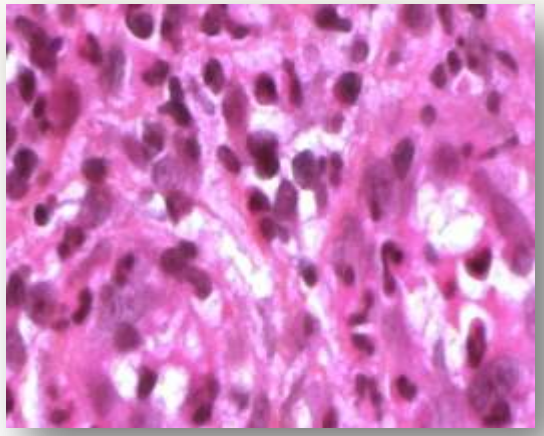
(complement system, Toll-like receptors)

- Activation

(cytokines, endothelial cells)

Response

(phagocytes, acute phase proteins)



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THE DUNEDIN STUDY

Representative birth cohort followed up from birth to age 32y

N=972 (at age 32 years)

Childhood maltreatment (multiple informants, multiple time points)

High-sensitivity CRP (>3mg/dL, cont), fibrinogen, white blood cell count

CHILDHOOD MALTREATMENT

Maternal rejection (14%)

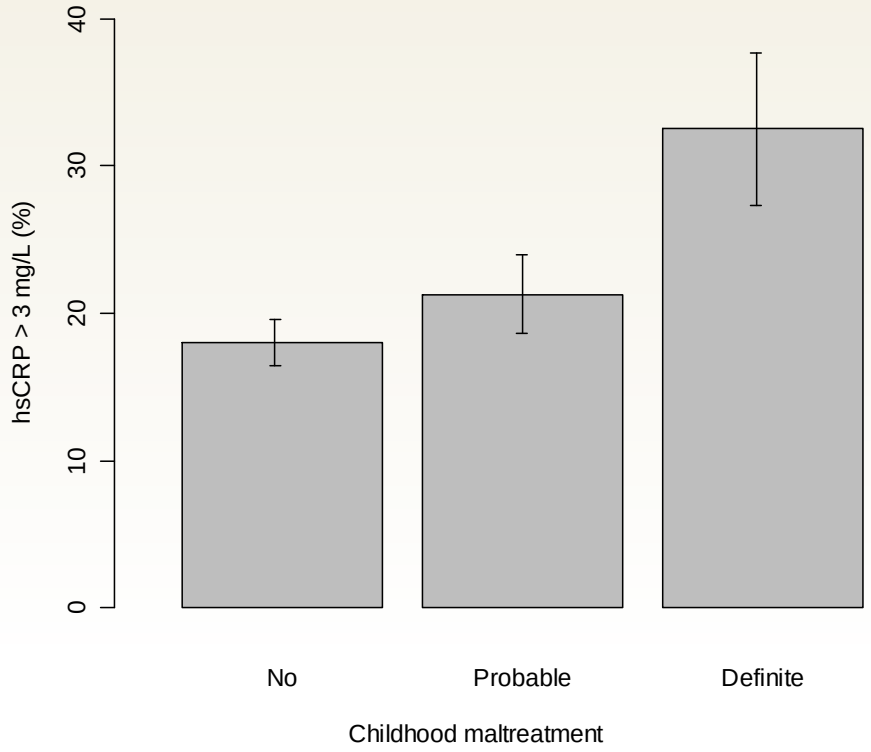
Harsh discipline (10%)

Disruptive caregivers changes (6%)

Physical abuse (4%)

Sexual abuse (12%)

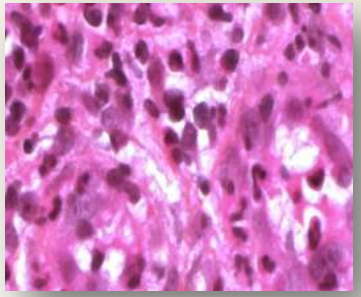
MALTREATMENT & ADULT INFLAMMATION



Danese A et al, PNAS 2007, 104:1319-24

MALTREATMENT & ADULT INFLAMMATION

RR = 1.80 [1.26-2.58]



MALTREATMENT & ADULT INFLAMMATION

CO-OCCURRING EARLY-LIFE RISKS

?

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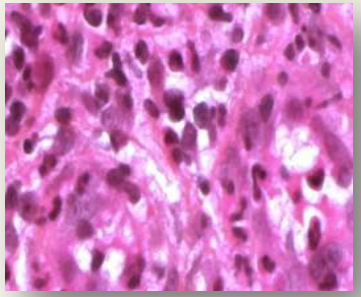


*Low birth weight. RR = 0.87 [0.49-1.53]

*Low child SES. RR = 1.89 [1.50-2.39]

*Low child IQ. RR = 2.12 [1.56-2.87]

*Low birth weight. RR = 1.60 [1.00-2.57]

*Low child SES. RR = 1.96 [1.19-3.25]

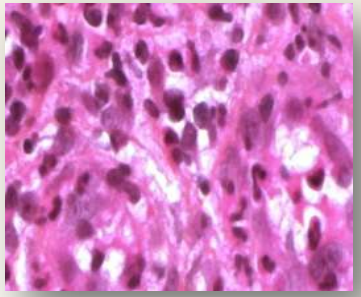
*Low child IQ. RR = 1.44 [1.03-2.01]

MALTREATMENT & ADULT INFLAMMATION

CO-OCCURRING EARLY-LIFE RISKS

RR = 1.58 [1.08-2.31]

RR = 1.80 [1.26-2.58]



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MALTREATMENT & ADULT INFLAMMATION

ADULT STRESS EXPOSURE

?

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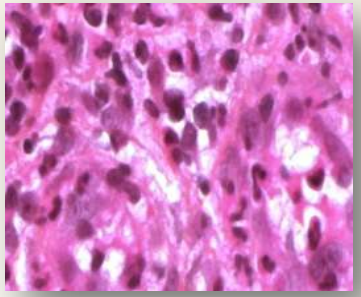


*Low adult SES. RR = 1.48 [1.23-1.73]

*Major Depression. RR = 1.46 [1.10-1.94]

*High Perc. Stress. RR = 1.43 [1.12-1.82]

*Low adult SES. RR = 1.44 [0.94-2.20]

*Major Depression. RR = 1.45 [1.06-1.99]

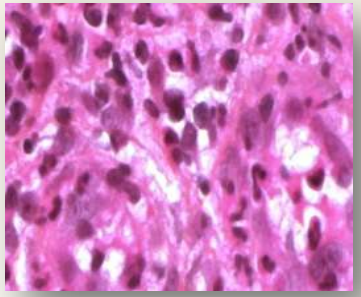
*High Perc. Stress. RR = 1.45 [1.08-1.94]

MALTREATMENT & ADULT INFLAMMATION

ADULT STRESS EXPOSURE

RR = 1.64 [1.13-2.40]

RR = 1.80 [1.26-2.58]



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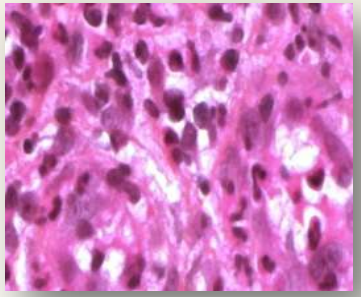
MALTREATMENT & ADULT INFLAMMATION

ADULT HEALTH & HEALTH BEHAVIOURS

?

RR = 1.80 [1.26-2.58]



*CV risk cluster.	RR = 1.48 [1.10-2.00]
*Smoking.	RR = 1.91 [1.13-3.23]
*Physical inactivity.	RR = 0.87 [0.69-1.11]
*Diet.	RR = 0.98 [0.78-1.23]

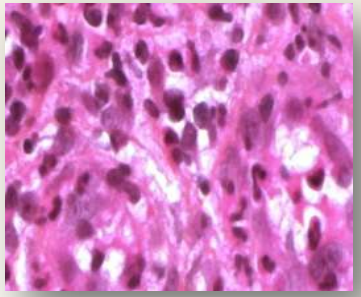
*CV risk cluster.	RR = 2.38 [1.84-3.10]
*Smoking.	RR = 1.18 [0.69-2.03]
*Physical inactivity.	RR = 1.57 [1.05-2.34]
*Diet.	RR = 1.01 [0.68-1.48]

MALTREATMENT & ADULT INFLAMMATION

ADULT HEALTH & HEALTH BEHAVIOURS

RR = 1.76 [1.23-2.51]

RR = 1.80 [1.26-2.58]



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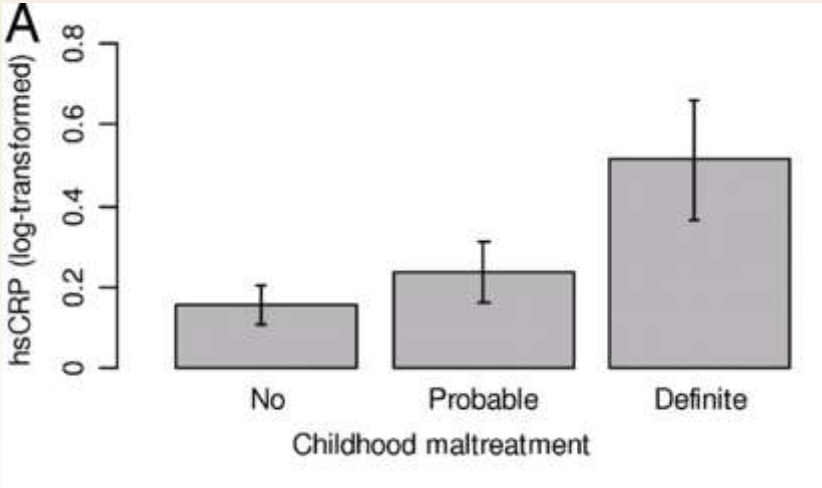

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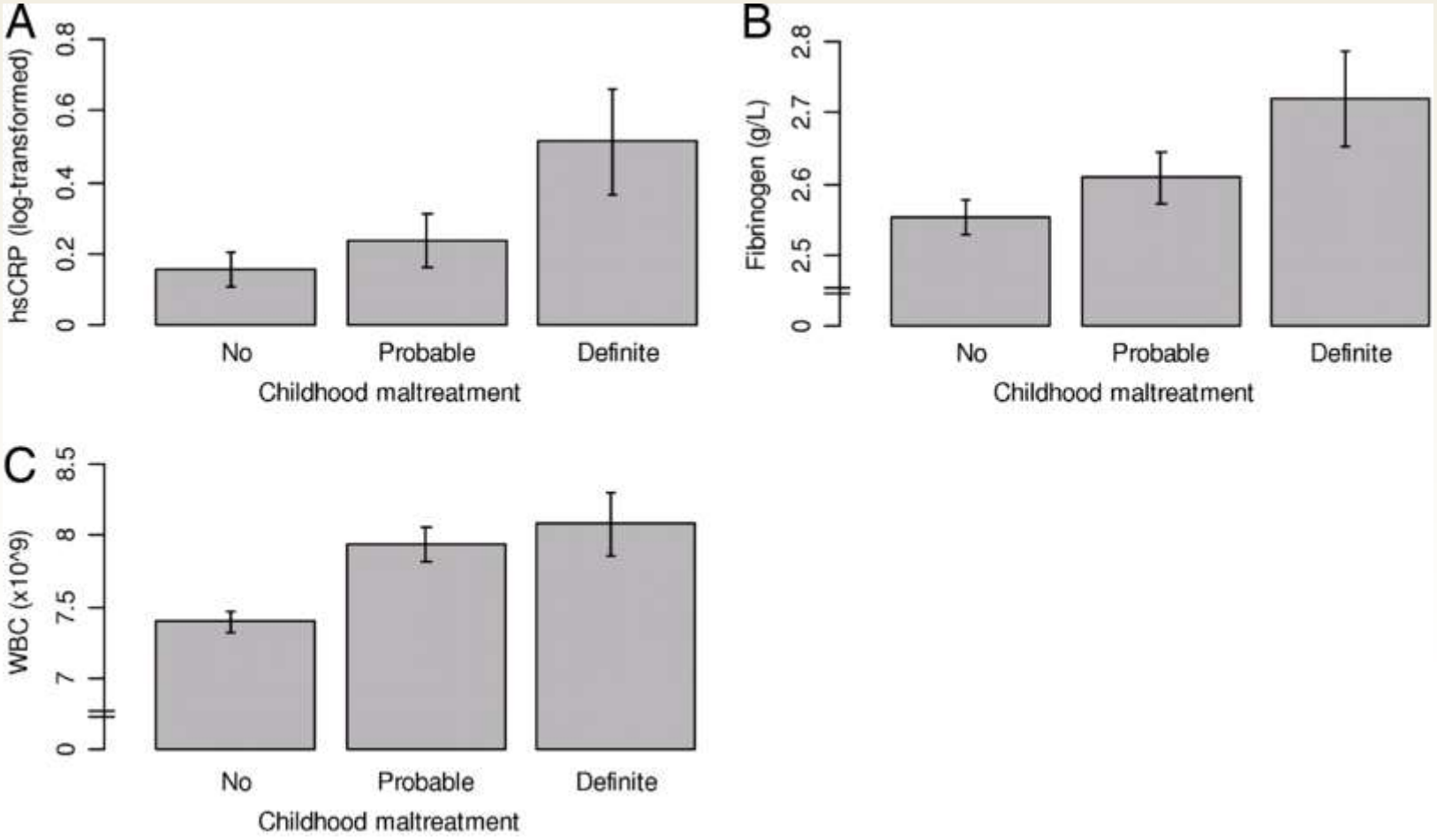

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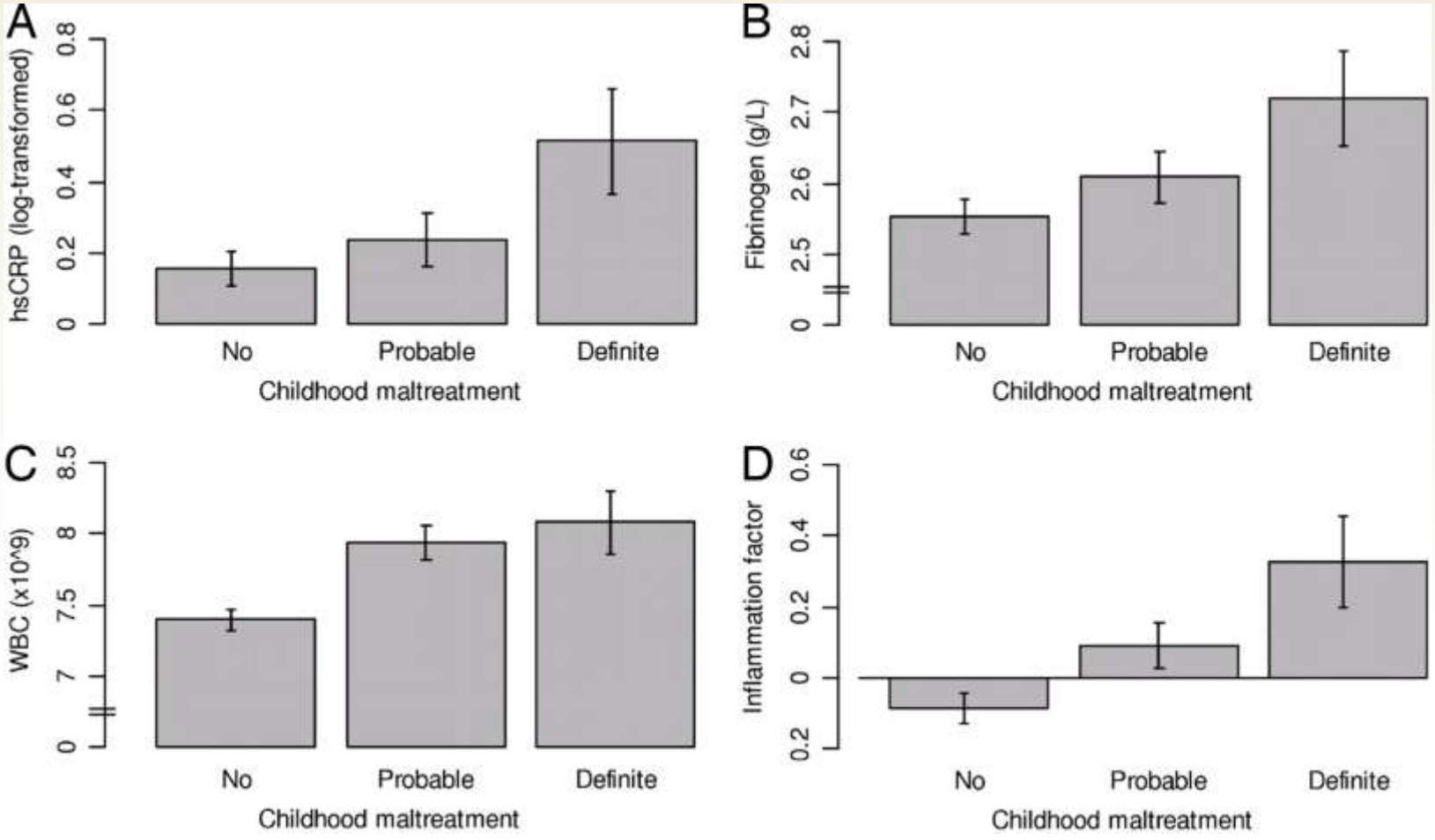

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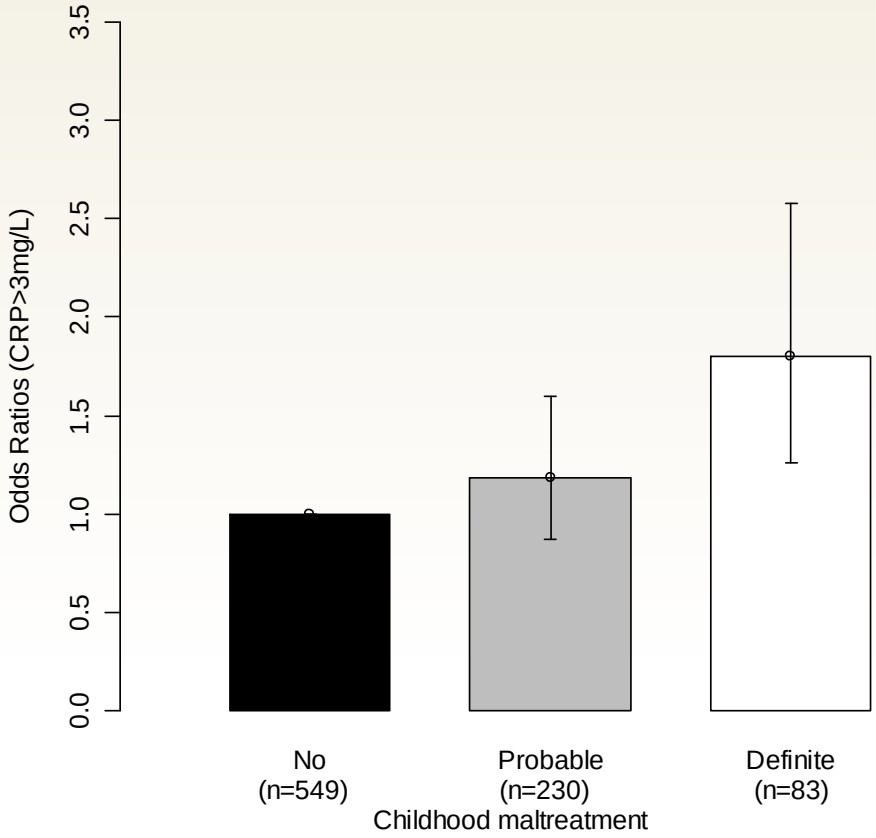
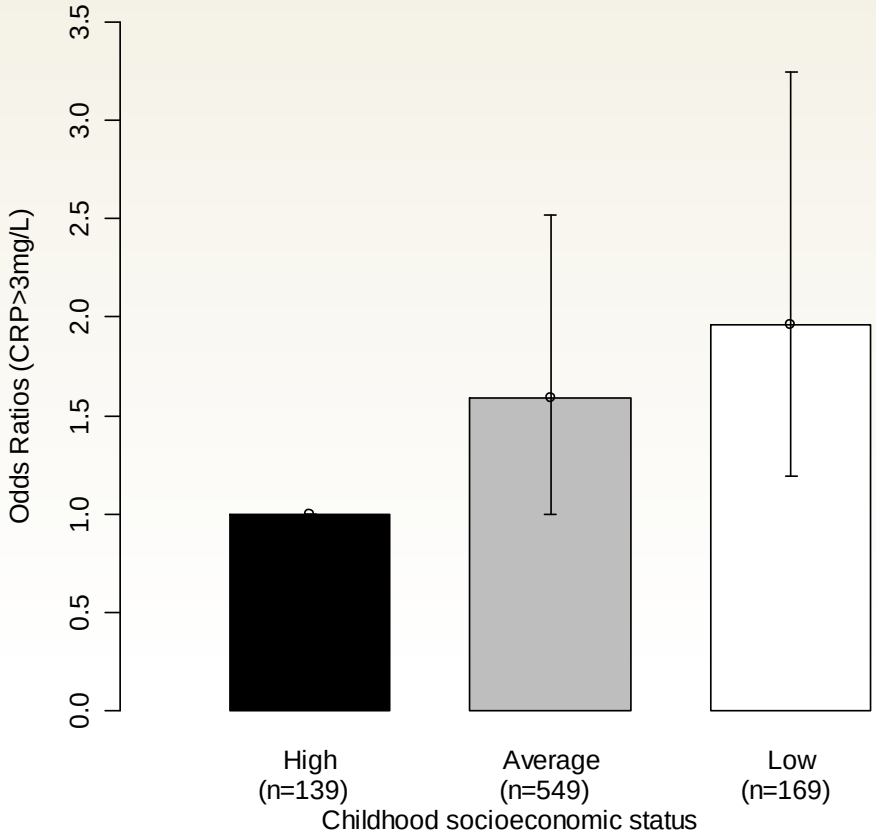
CHILD MALTREATMENT
AND ADULT INFLAMMATION



Danese A et al, Arch Pediatr Adolesc Med 2009, 163: 1135-43

CHILD SOCIO-ECONOMIC DISADVANTAGE

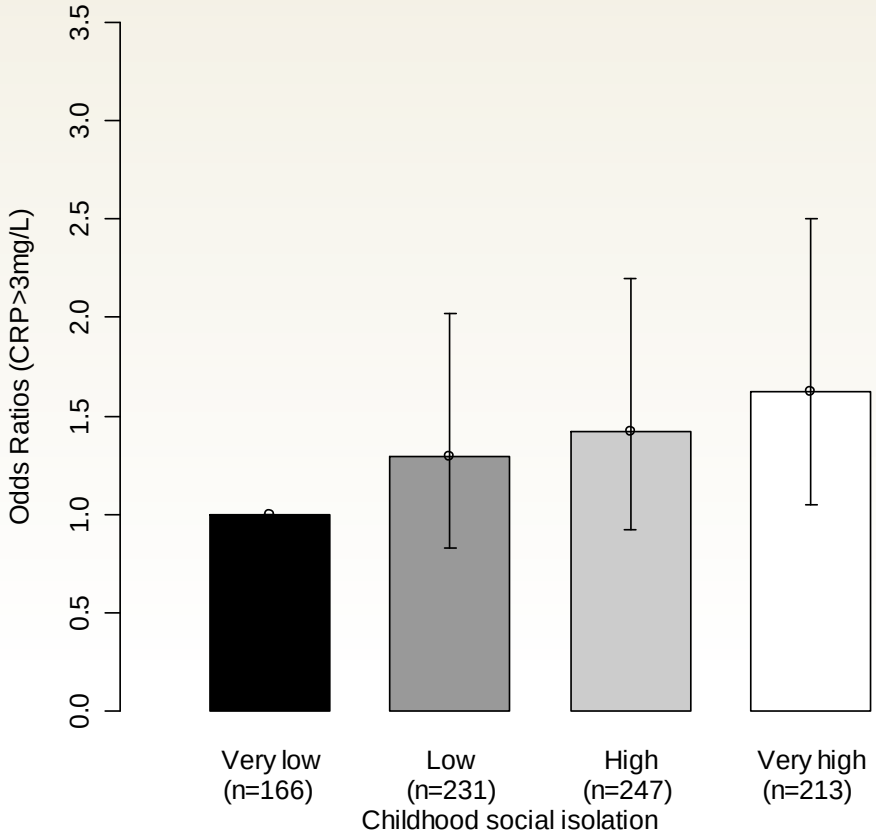
AND ADULT INFLAMMATION



Danese A et al, Arch Pediatr Adolesc Med 2009, 163: 1135-43

CHILD SOCIAL ISOLATION

AND ADULT INFLAMMATION



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SUMMARY (1)

> Children who experienced maltreatment, socio-economic disadvantage and social isolation show a significant and graded elevation in inflammation levels 20 years later, in adulthood.

> The effects of adverse childhood experiences on adult inflammation are independent of the influence of co-occurring risk factors.

> 10% of the cases of inflammation in the population may be attributable to childhood maltreatment.

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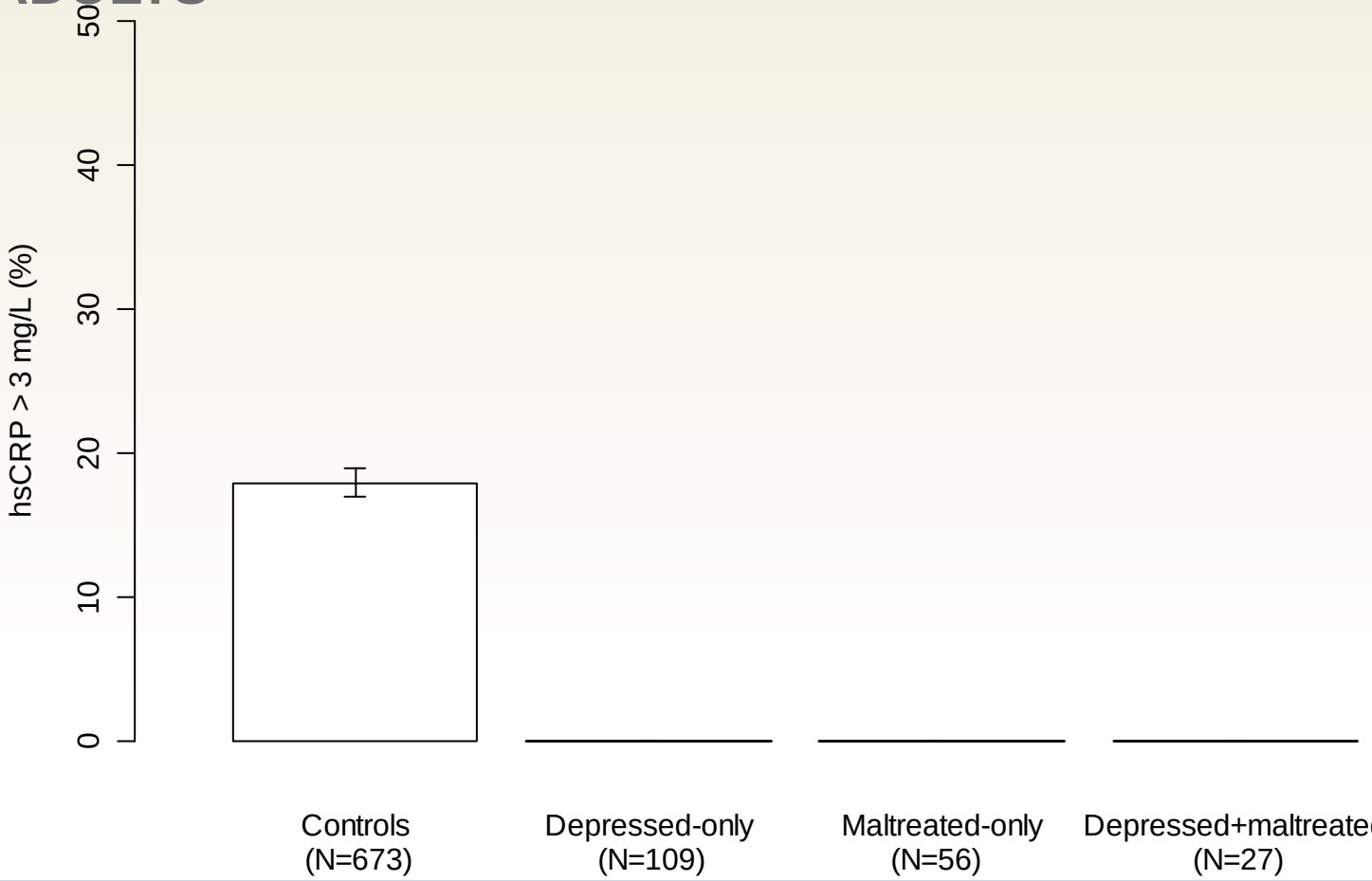
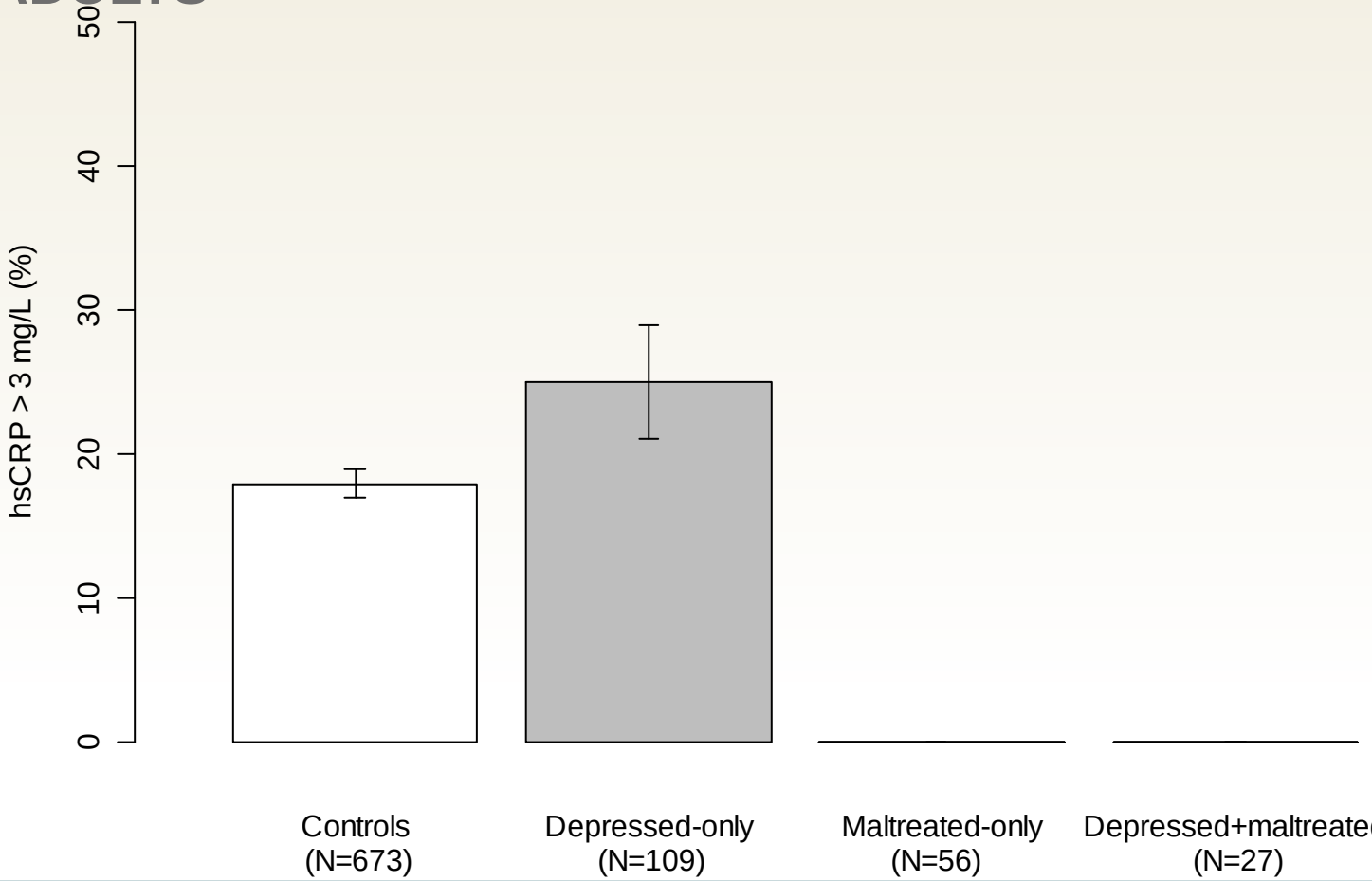
MALTREATMENT, DEPRESSION & INFLAMMATION IN ADULTS



Danese A et al, Arch Gen Psychiatry 2008, 65: 409-15

MALTREATMENT, DEPRESSION & INFLAMMATION IN ADULTS



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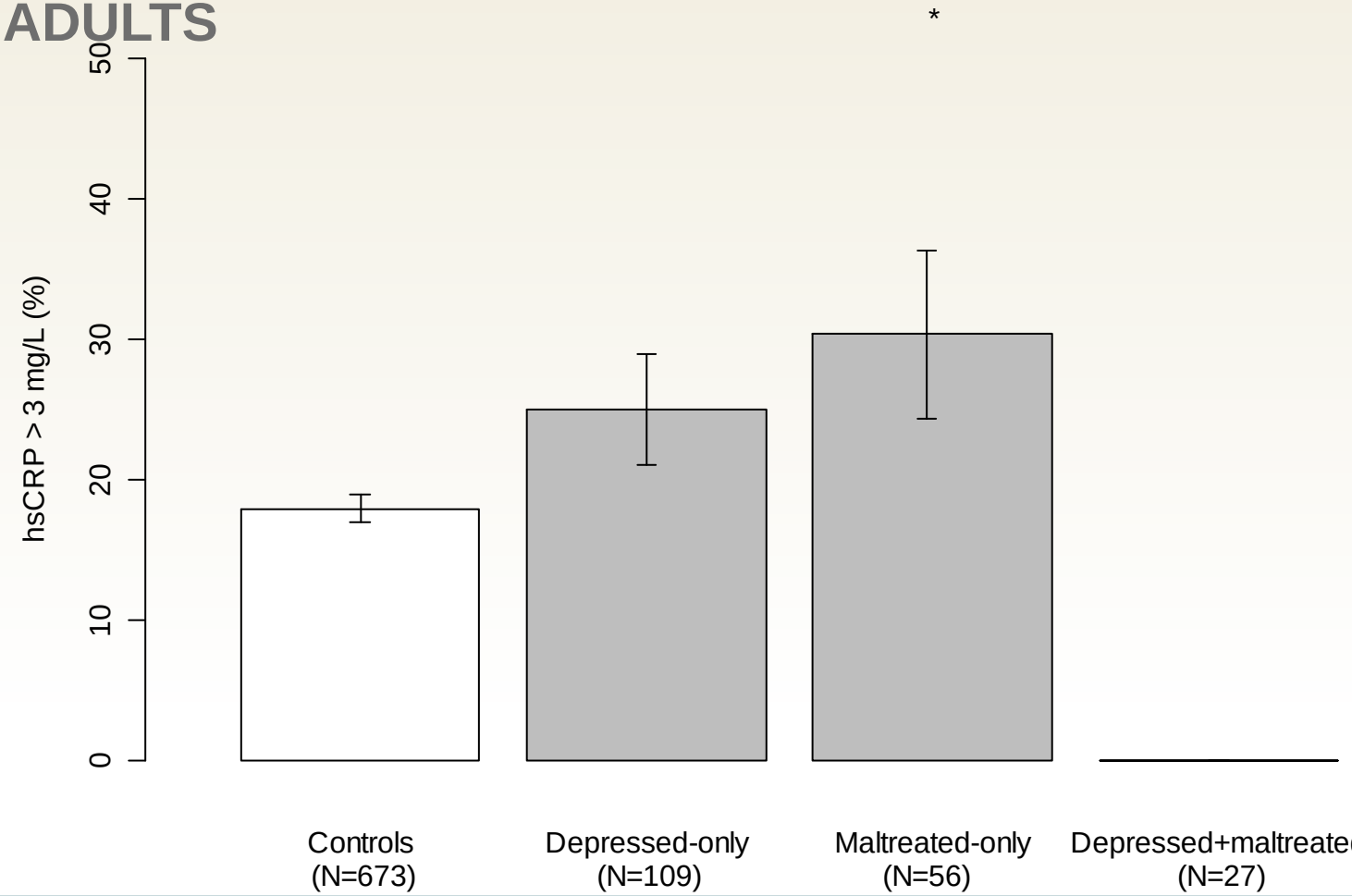

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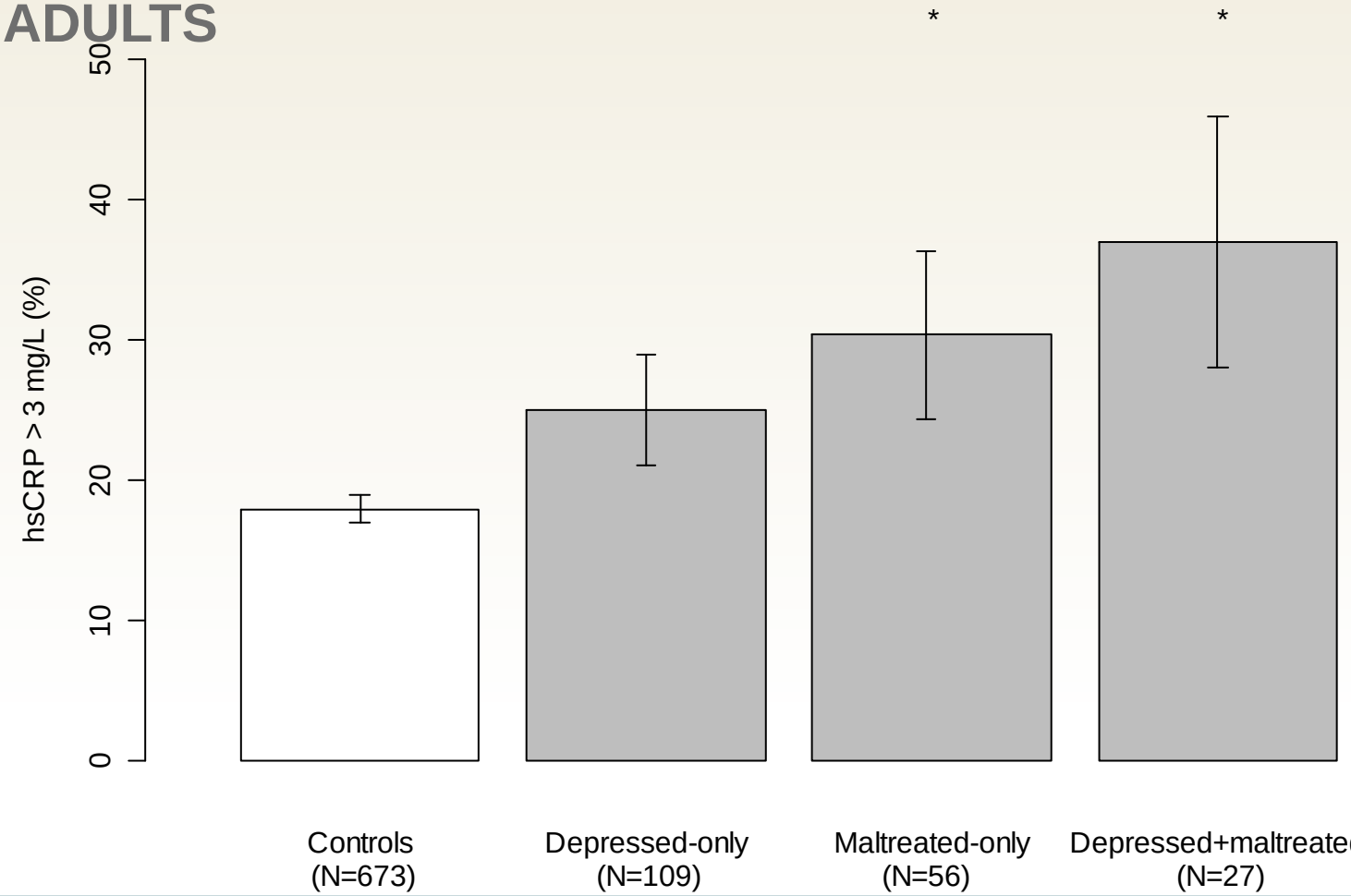

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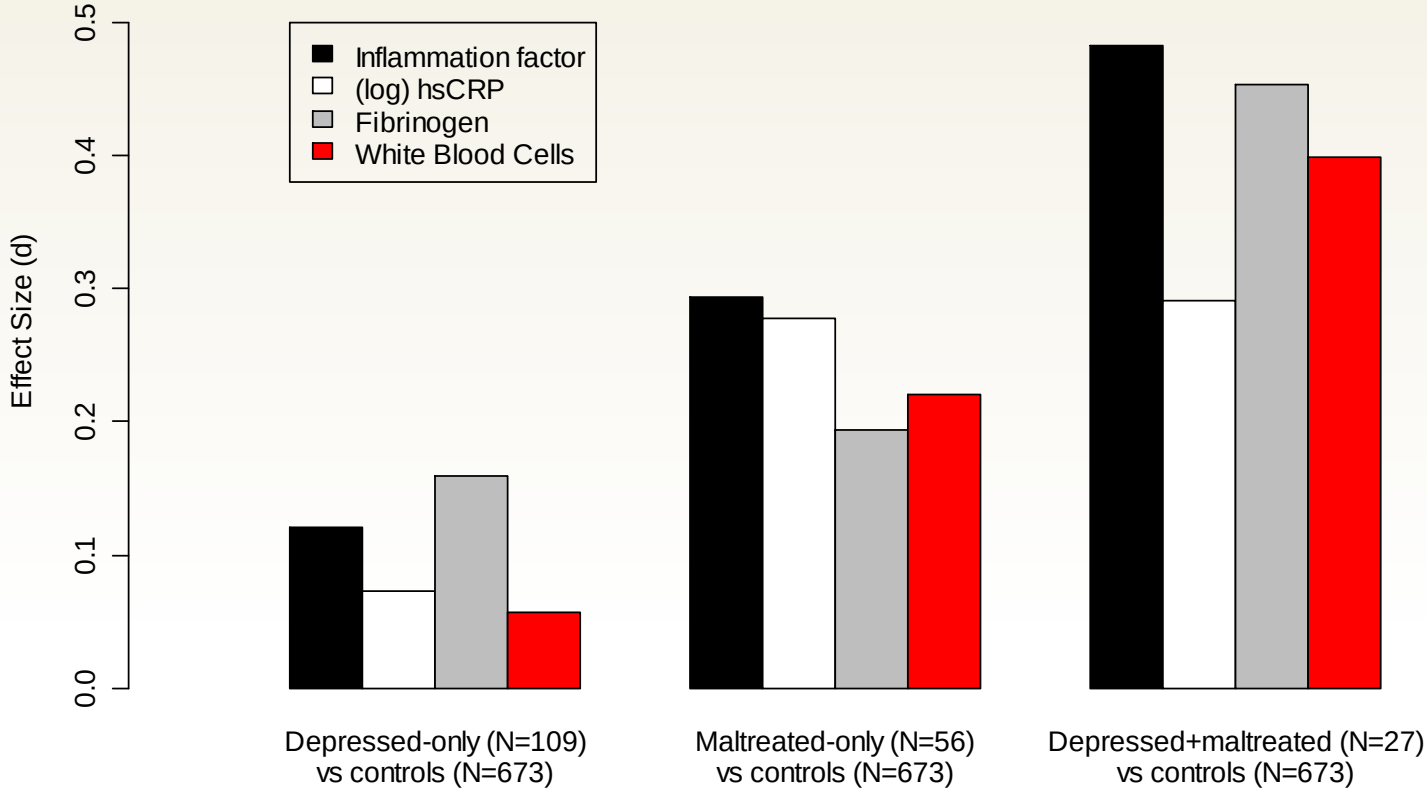
MALTREATMENT, DEPRESSION & INFLAMMATION

IN ADULTS



Danese A et al, Arch Gen Psychiatry 2008, 65: 409-15

SUMMARY (2)

> Stress in childhood may modify developmental trajectories and have long-term effect on disease risk.

> Stress later in life may have a smaller effect on disease risk, because it acts on a more developed system.

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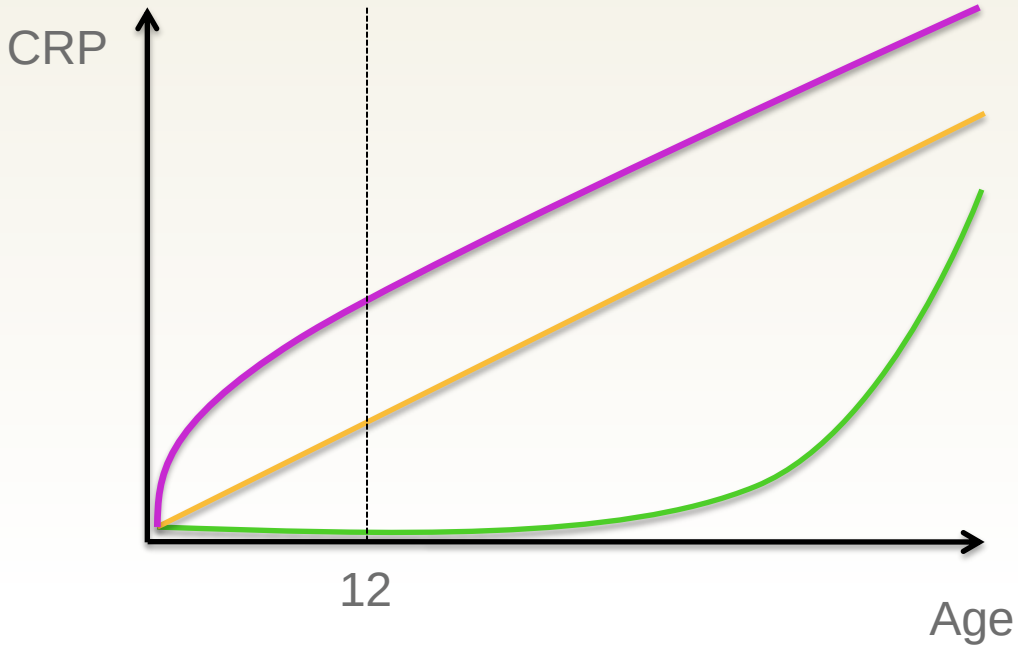
HEALTH TRAJECTORIES

AND CHILD DEVELOPMENT



THE E-RISK STUDY

Sampling from 2 consecutive Twins' Early Development Study (TEDS) birth cohorts

Target sample N=172, age 12 years

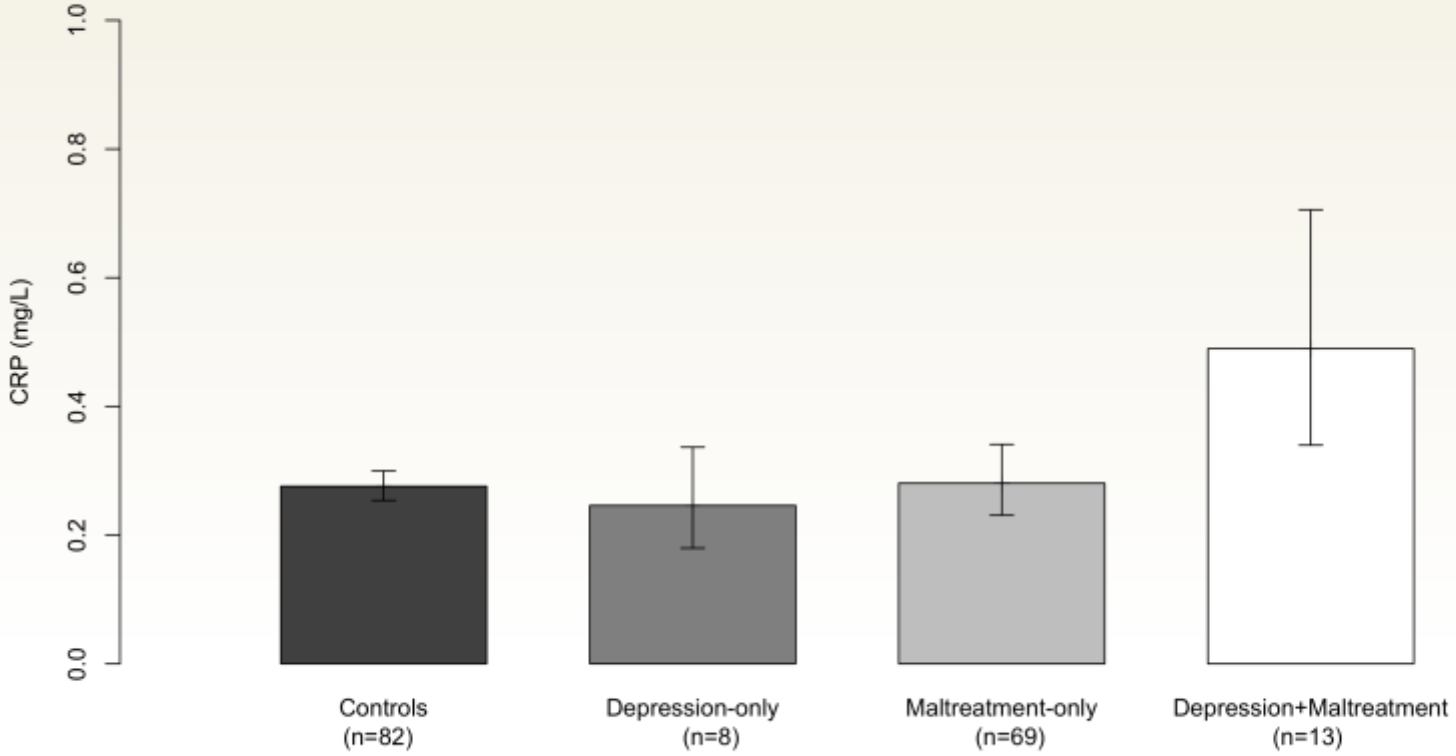
Childhood physical abuse: K Dodge's interview with mothers (prospectively collected)

Depression: Children's Depression Inventory (CDI≥20)

Inflammation: minimally-invasive collection of CRP through dried blood spots

MALTREATMENT, DEPRESSION & INFLAMMATION

IN CHILDREN

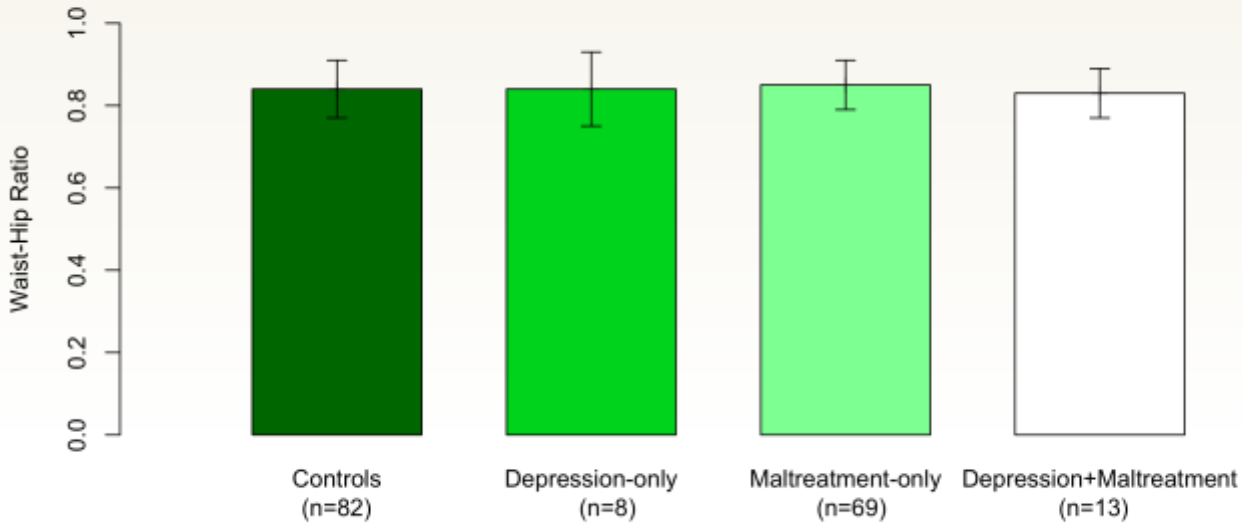


Danese A et al, Mol Psychiatry 2011, 16: 244-6

MALTREATMENT, DEPRESSION & INFLAMMATION

IN CHILDREN

r(CRPdbs,WHR)=.22, p=0.005

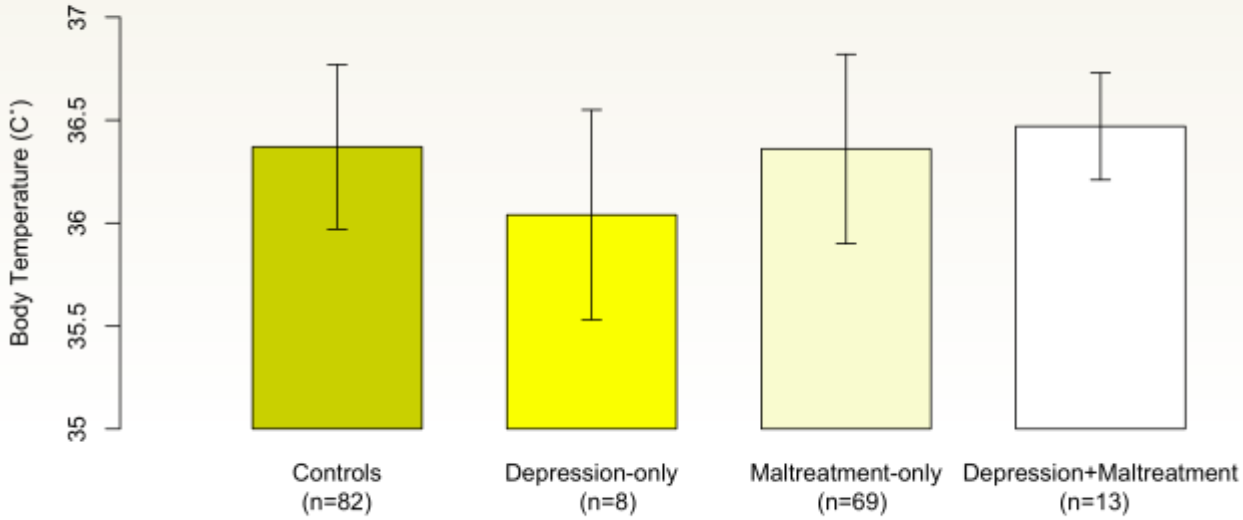


Danese A et al, Mol Psychiatry 2011, 16: 244-6

MALTREATMENT, DEPRESSION & INFLAMMATION

IN CHILDREN

r(CRPdbs,T°)=.18, p=0.020



Danese A et al, Mol Psychiatry 2011, 16: 244-6

SUMMARY (3)

> Stress-related elevation in inflammation biomarkers can already be observed in childhood.

> Childhood elevation in inflammation levels has been linked to the presence of key preclinical indicators of adult disease risk in children, such as advanced atherosclerosis progression.

> Interventions targeting stress in children could prevent the translation of psychosocial risks into enduring biological risks

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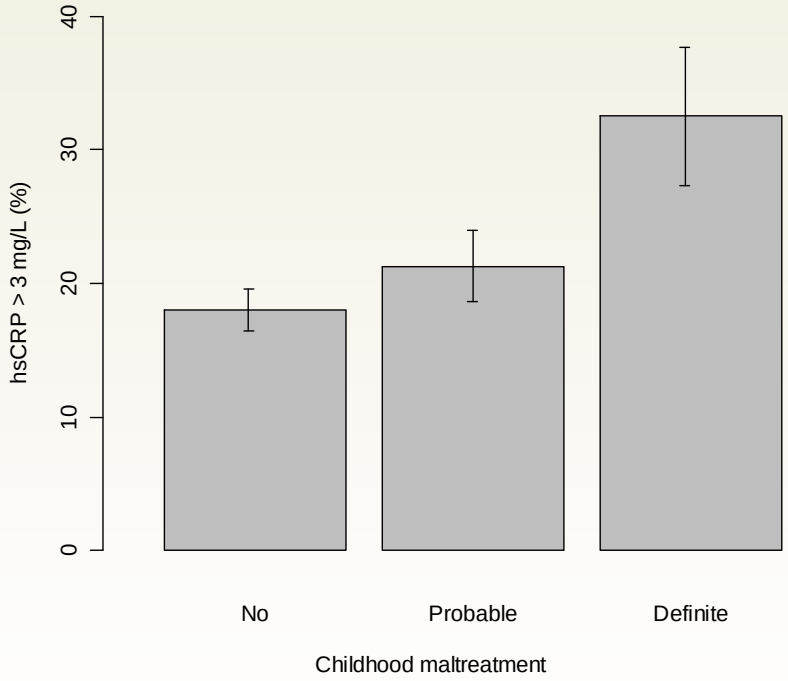
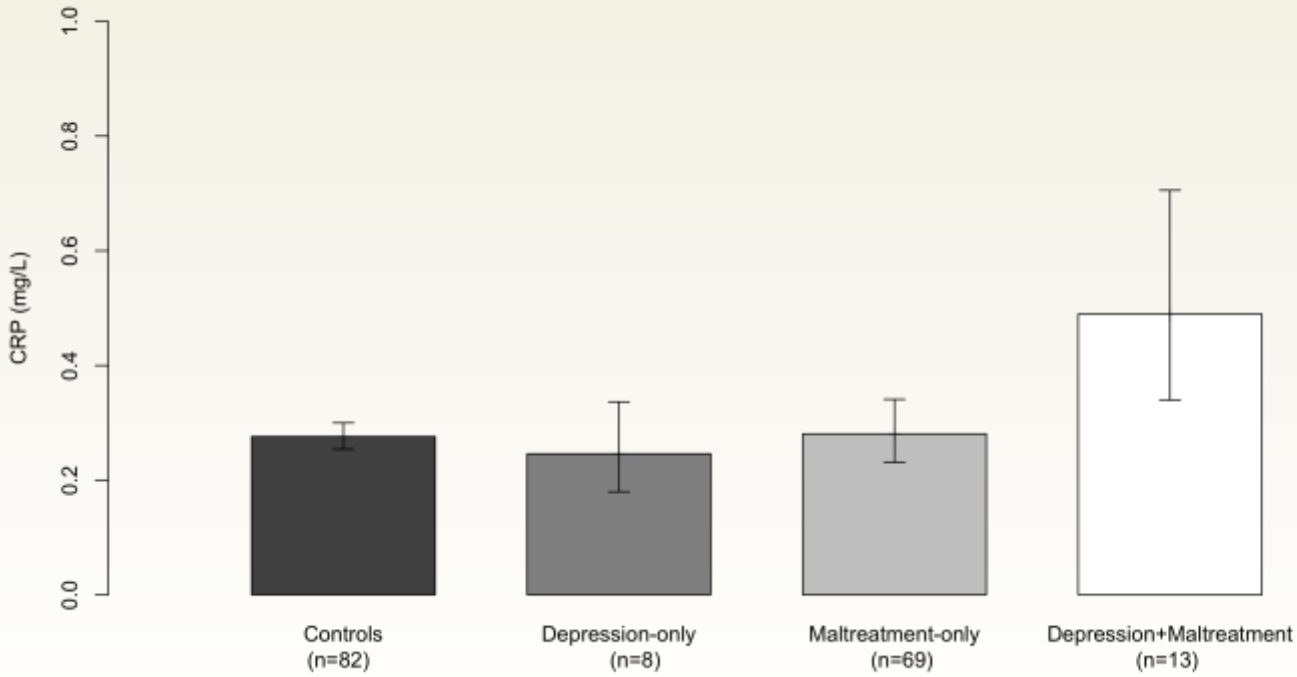


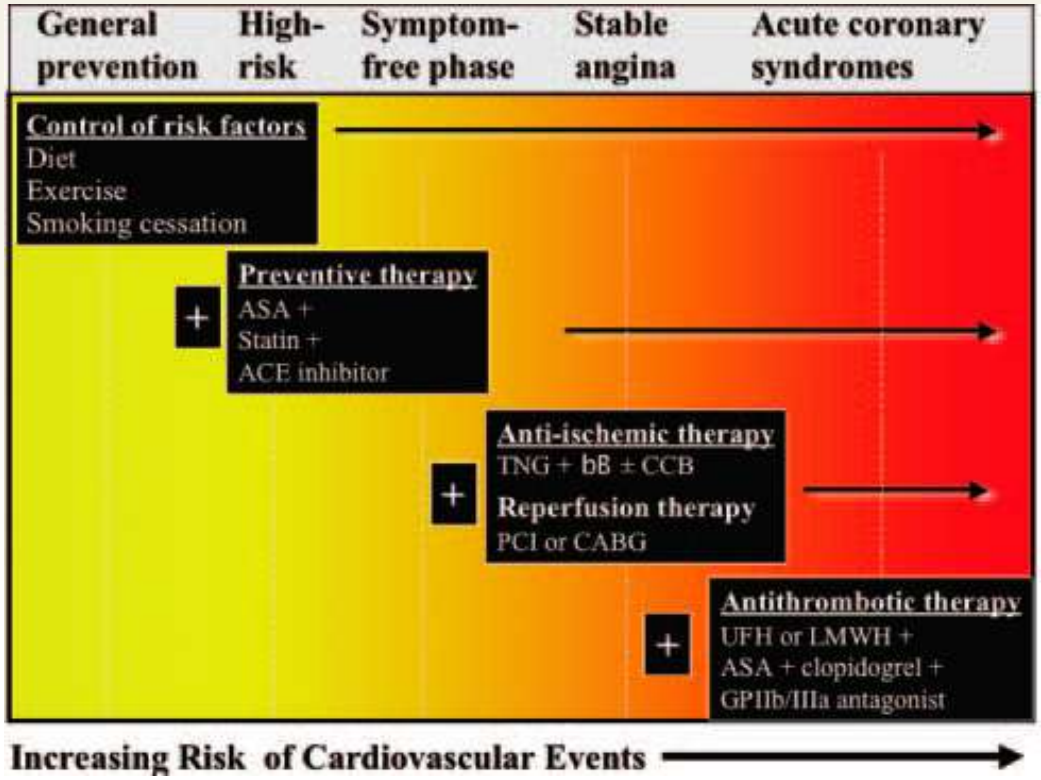
> Inflammation could be an important biological mediator of the effect of childhood maltreatment on adult health.

CONCLUSIONS



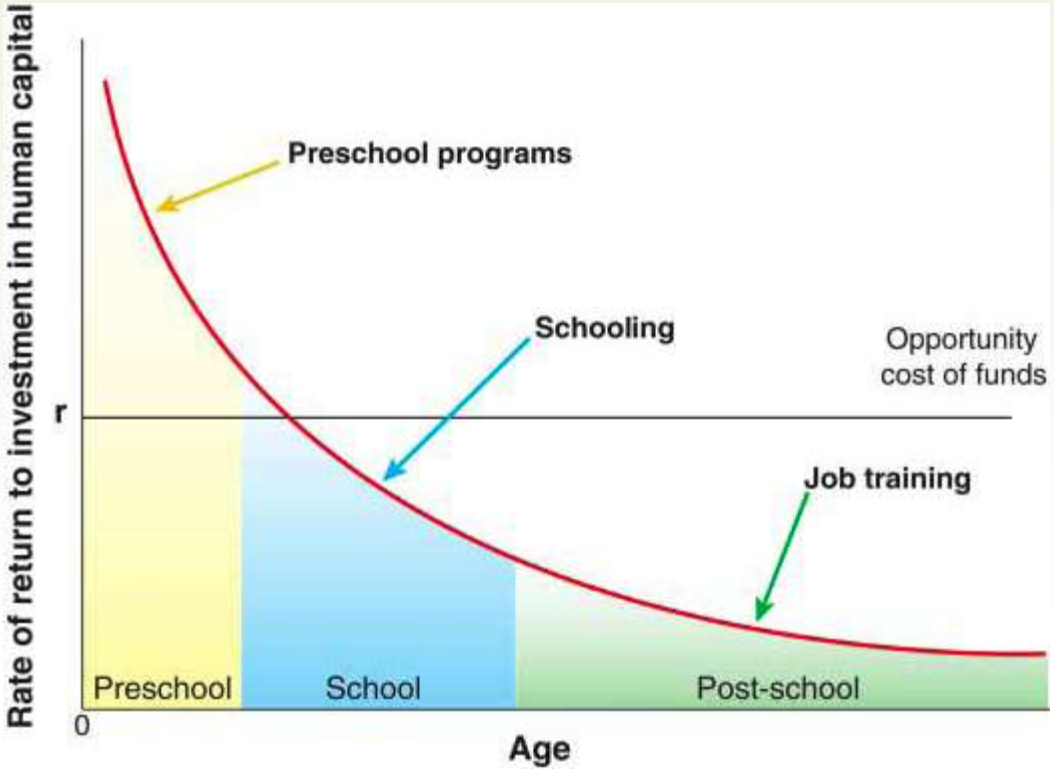
> Effective preventive strategies for adult disease should start from an early age.

ADULT RISK MODEL



Libby P, Circulation 2005, 111: 3481-88

LIFE-COURSE RISK MODEL



Heckman JJ, Science 2006, 312: 1900-2

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