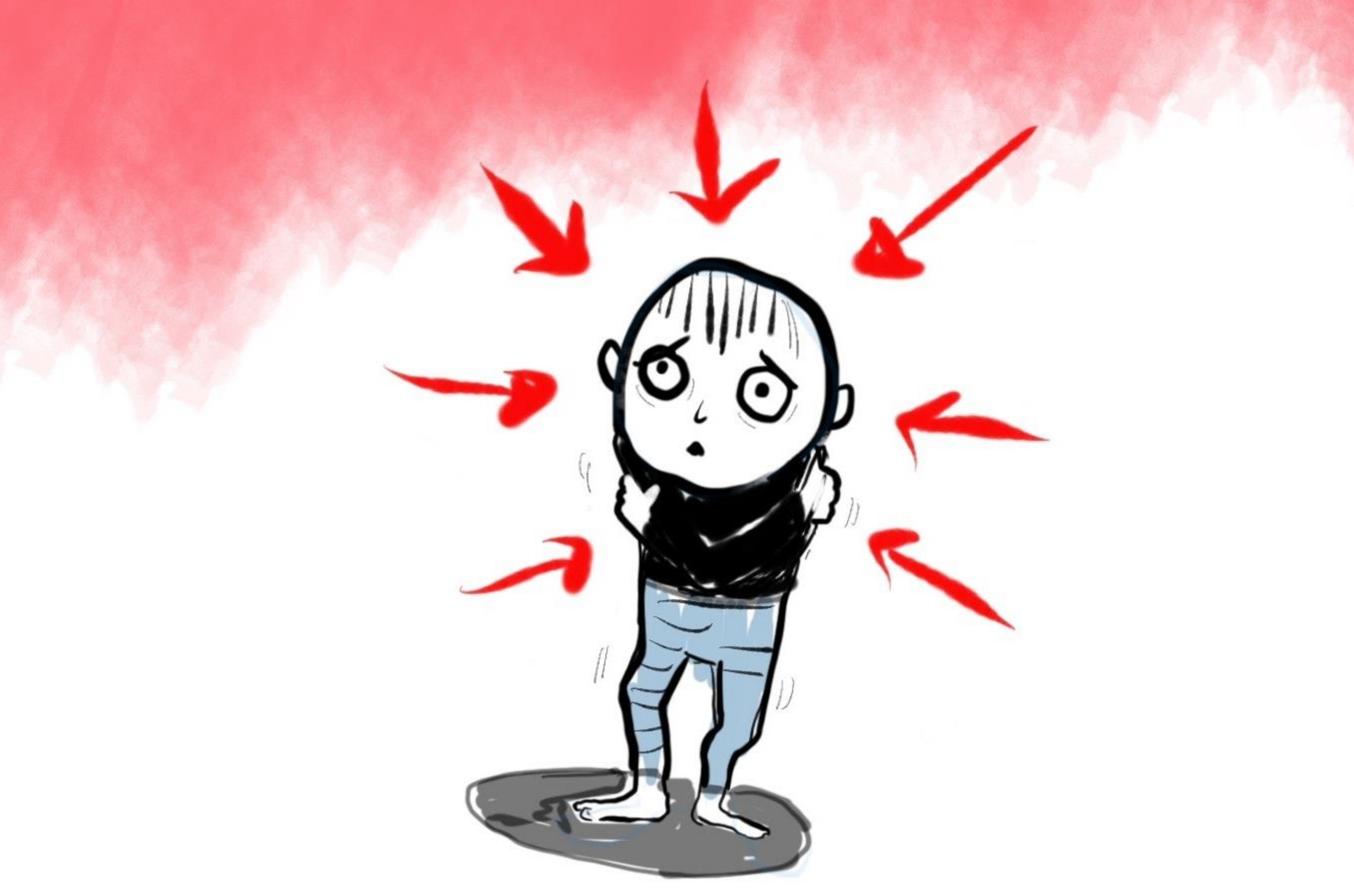
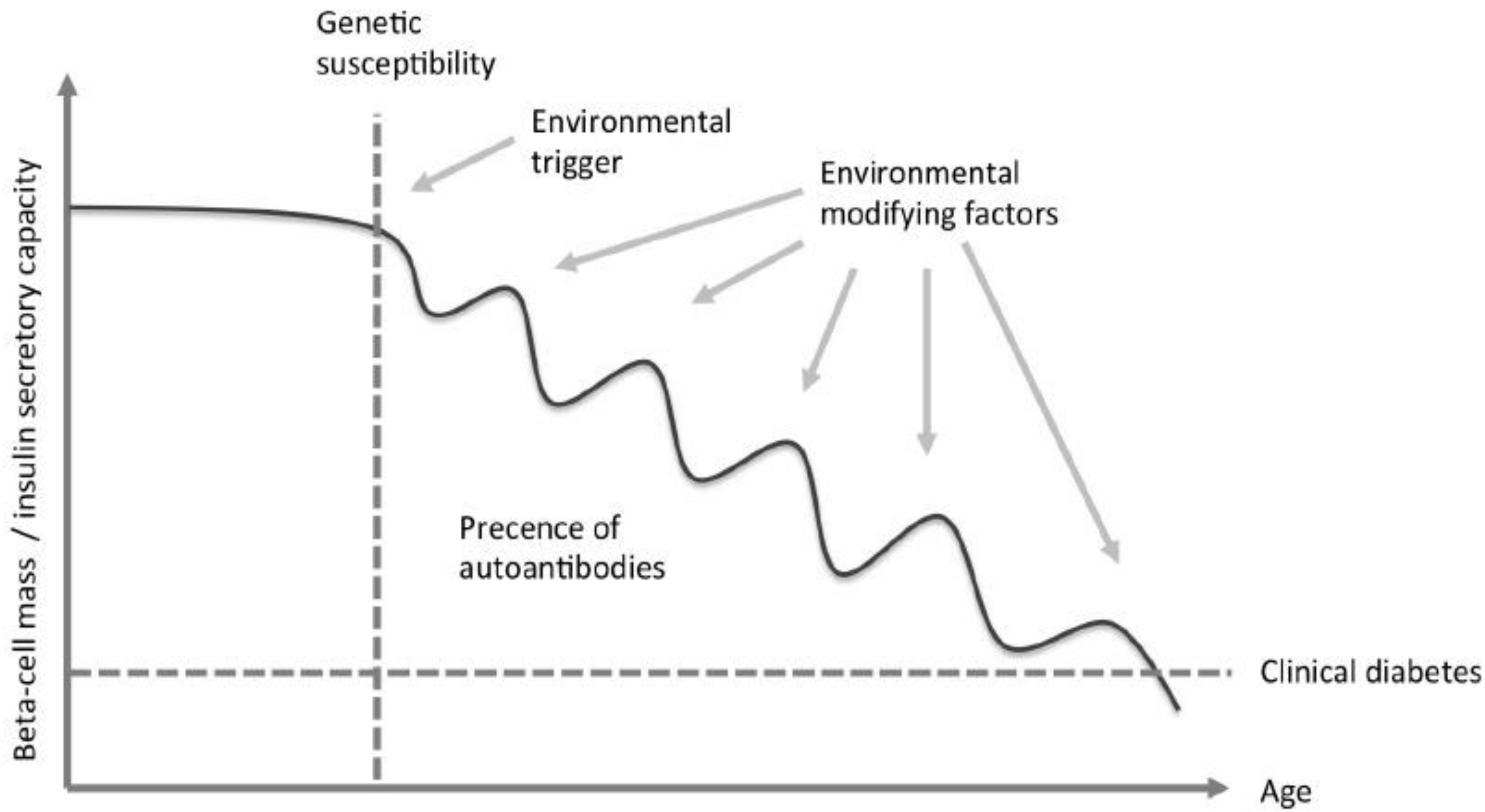
Accumulation of childhood adversities and the risk of type 1 diabetes:

A life course study of all children born in Denmark between 1980 and 2015

Jessica Bengtsson, Stine Byberg, Bendix Carstensen, Bianca L. De Stavola, Jannet Svensson, Marit Eika Jørgensen, Naja Hulvej Rod



The autoimmune process of type 1 diabetes



Nygren 2015 after Atkinson et al. 2014 and Knip et al. 2005

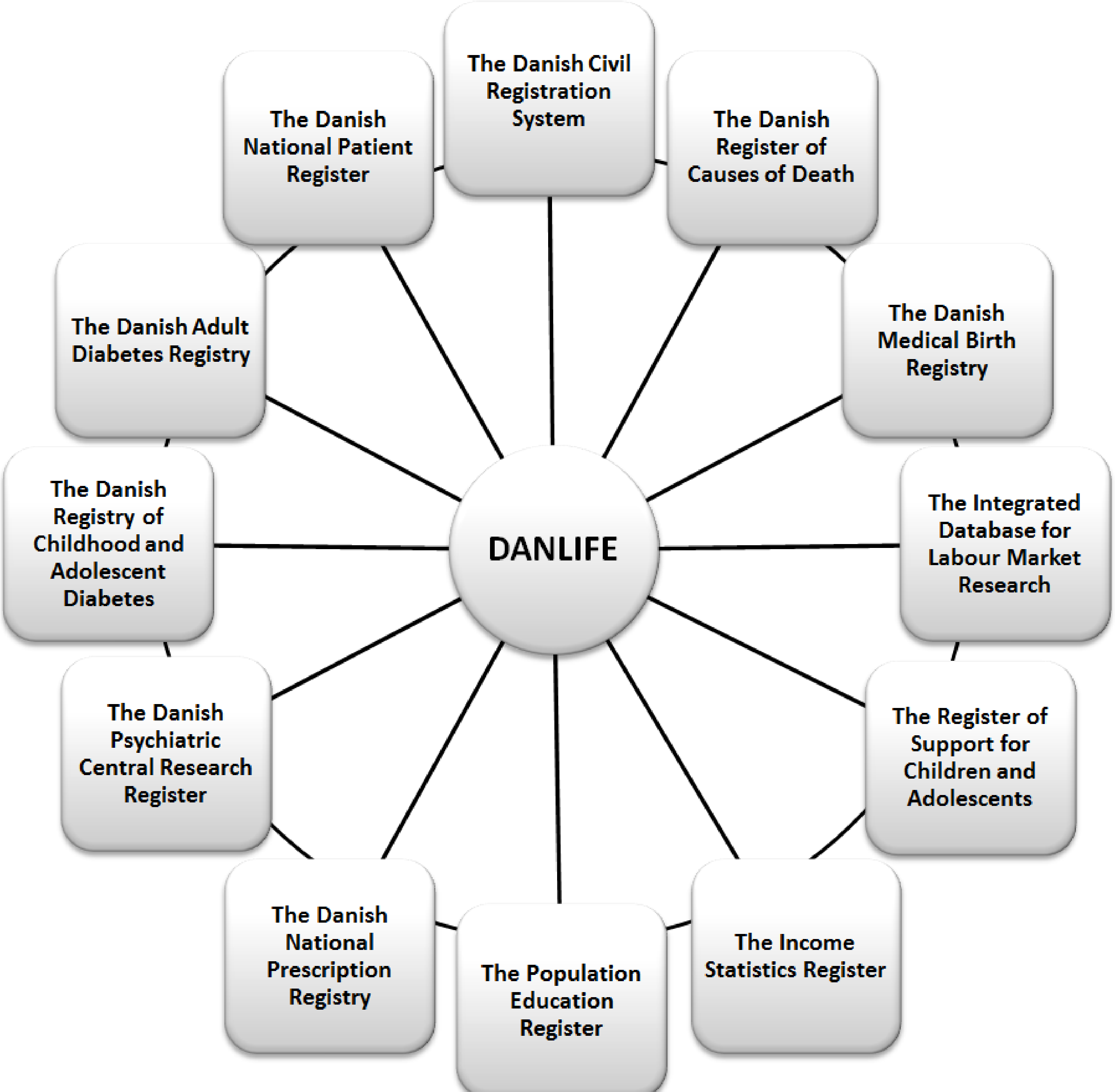
Background

“Childhood experience of a serious life event was associated with a higher risk of future diagnosis of type 1 diabetes (**HR 3.0 [95% CI 1.6, 5.6**], $p = 0.001$) after adjusting for heredity of type 1 diabetes and age at entry into the study.”

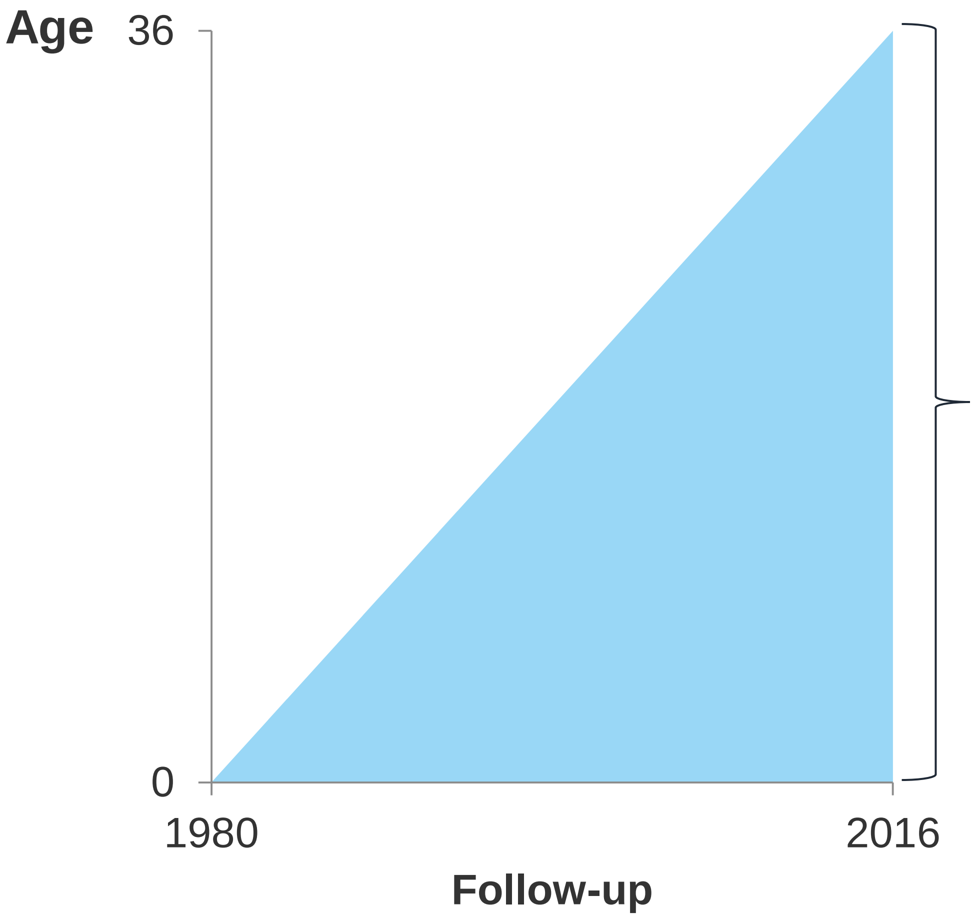
Nygren et al. 2015, Diabetologia

Objective

To quantify the effect of accumulation of childhood adversities on the incidence of type 1 diabetes and to assess whether the effect is different in boys and girls.


DANLIFE
The Danish Civil Registration System
The Danish Register of Causes of Death
The Danish Medical Birth Registry
The Integrated Database for Labour Market Research
The Register of Support for Children and Adolescents
The Income Statistics Register
The Population Education Register
The Danish National Prescription Registry
The Danish Psychiatric Central Research Register
The Danish Registry of Childhood and Adolescent Diabetes
The Danish Adult Diabetes Registry
The Danish National Patient Register

Study population: DANLIFE



Total N: 2,153,164

Deaths: 18,531 (0.9%)

Emigrations: 151,630 (7%)

Person years: 37.2 million

Mean follow-up: 16.9 years

Type 1 diabetes: 8335 (0.4%)

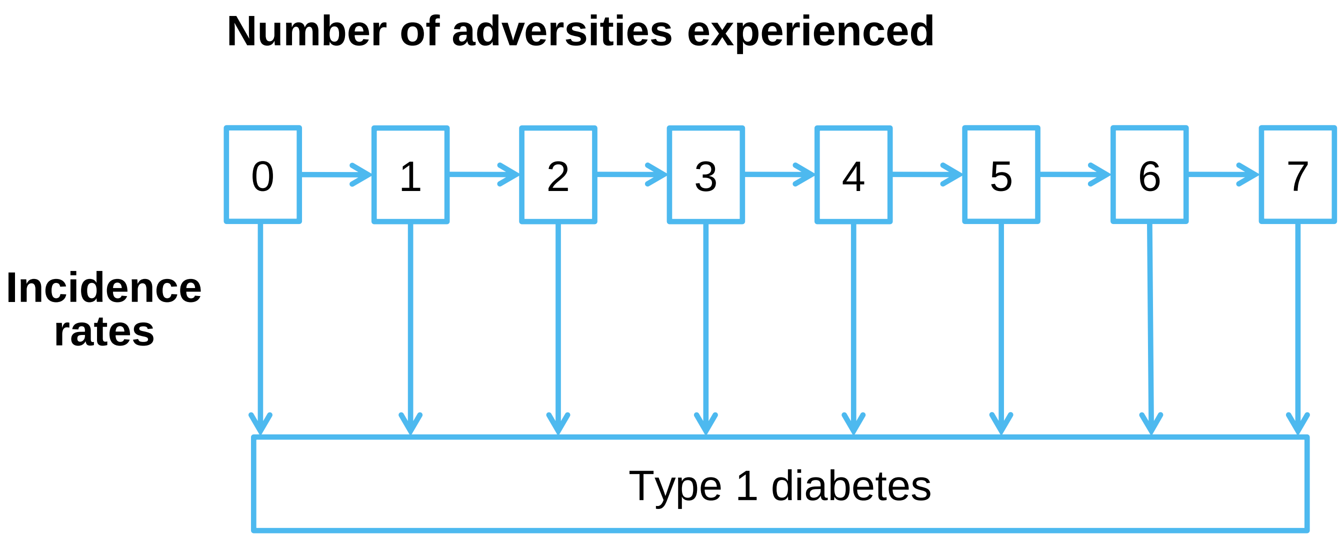
Boys: 51.3%

Childhood adversities

- Death of a parent
- Death of a sibling
- Parental somatic illness
- Sibling somatic illness
- Parental psychiatric illness
- Sibling psychiatric illness
- Foster care
- Parental separation
- Parental long-term unemployment
- Family poverty
- Parental alcohol abuse
- Parental drug abuse

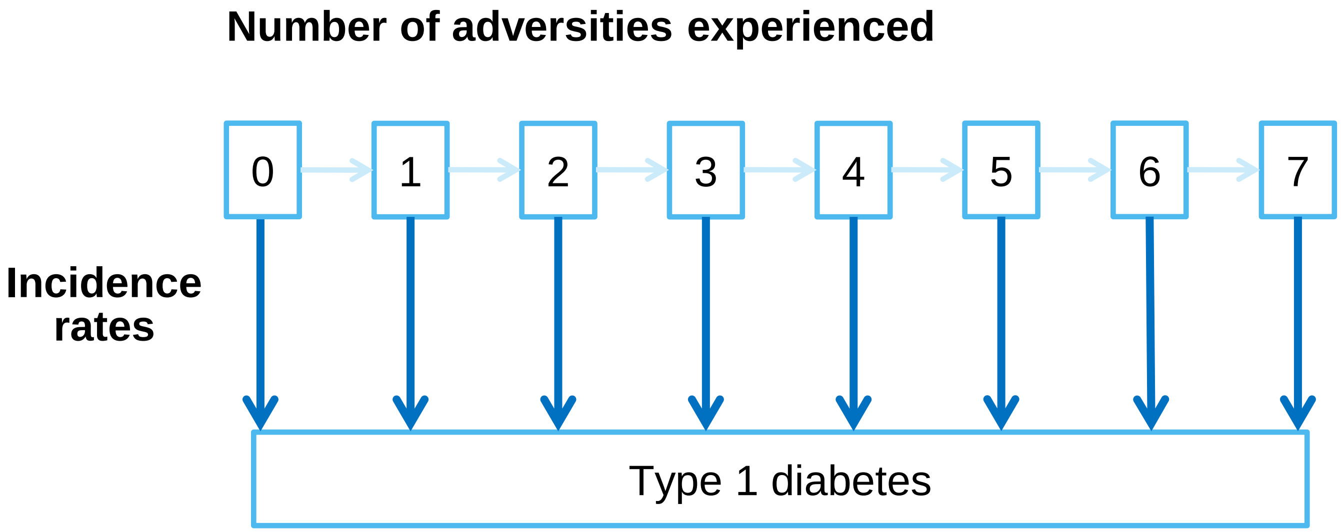
Statistical analyses

In a **multi-state model,** we let each additional adversity occurrence represent a new state of exposure and calculated hazard ratios of developing type 1 diabetes in each state with age as the underlying time scale.



Statistical analyses

In a **multi-state model,** we let each additional adversity occurrence represent a new state of exposure and calculated hazard ratios of developing type 1 diabetes in each state with age as the underlying time scale.



Statistical analyses

- Followed from birth until type 1 diabetes diagnosis, emigration, death or the 31st of December 2015
- Stratified analyses for boys and girls adjusted for:
    - Parental type 1 diabetes
    - Sibling type 1 diabetes
    - Date of birth
    - Birth weight
    - Parity
    - Maternal age at birth
    - Parental education at birth
    - Ethnicity

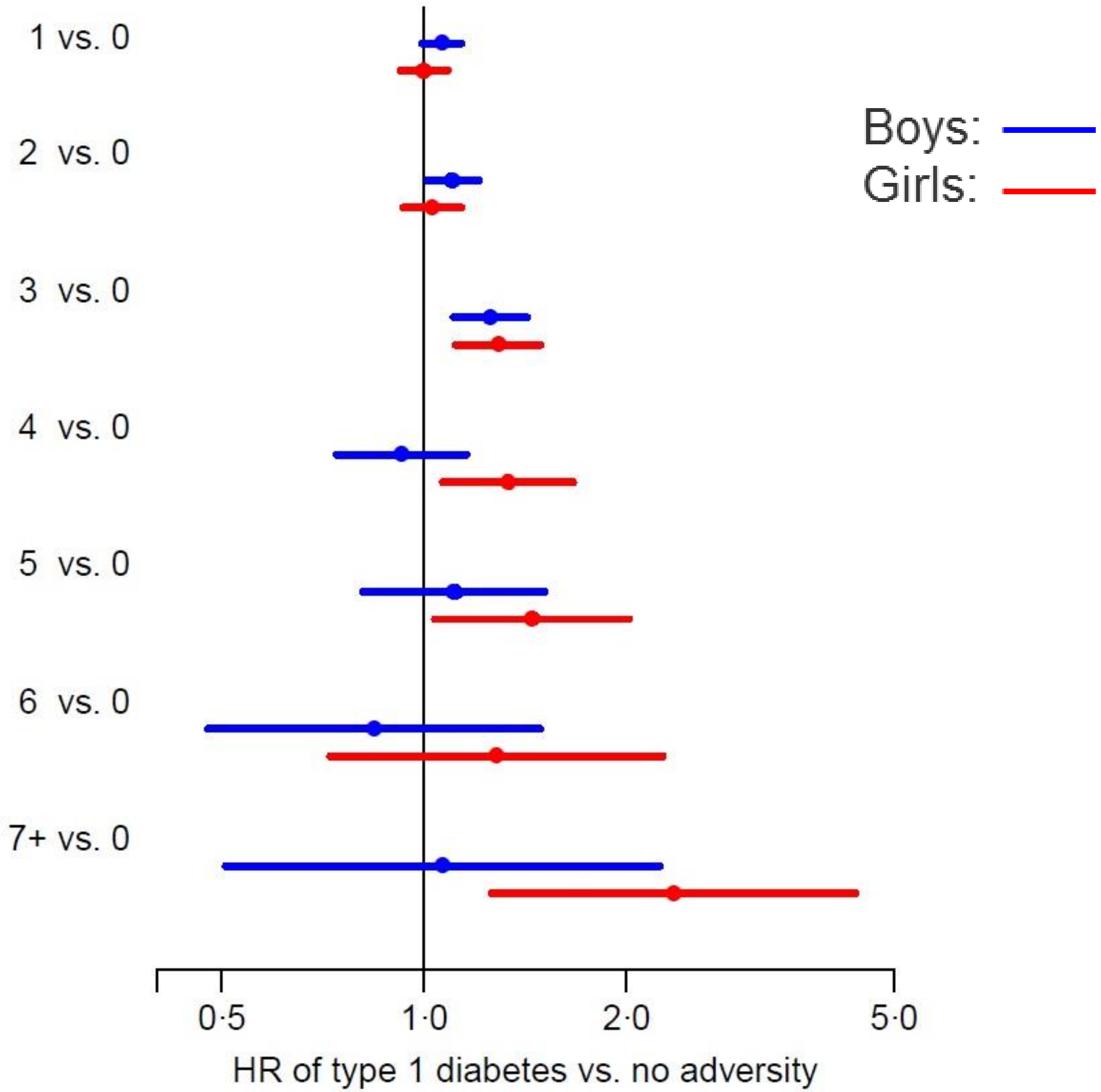
REGION

Results

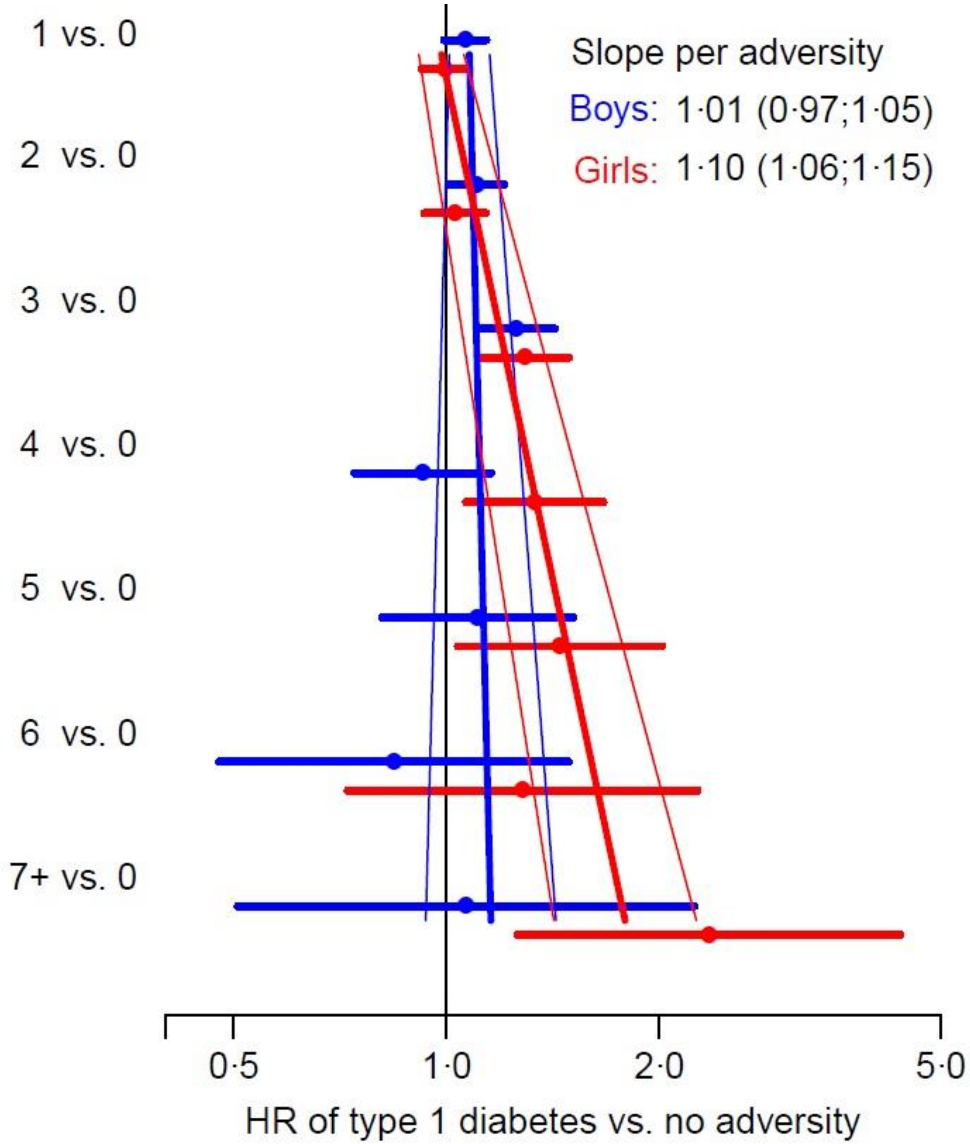
Number of adversities

Adversities	N	%	Mill. PY
0	994 517	46.2	18.59
1	634 849	29.5	10.98
2	316 353	14.7	4.90
3	124 947	5.8	1.69
4	49 335	2.3	0.63
5	20 796	0.9	0.26
6	8 214	0.4	0.10
7+	4 153	0.2	0.05
Total	**2 153 164**	**100**	**37.20**

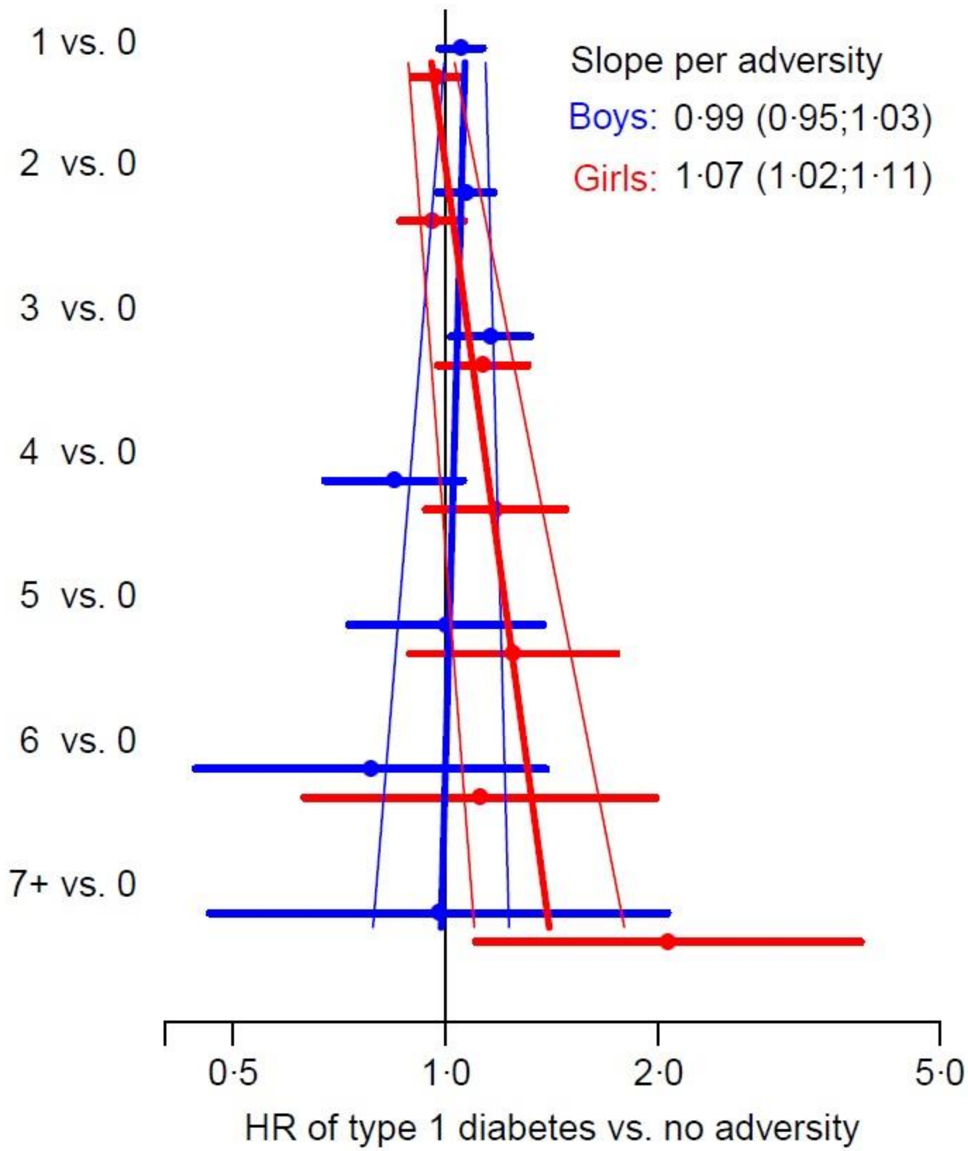
Unadjusted hazard ratios for the number of adversities experienced vs. 0 adversities



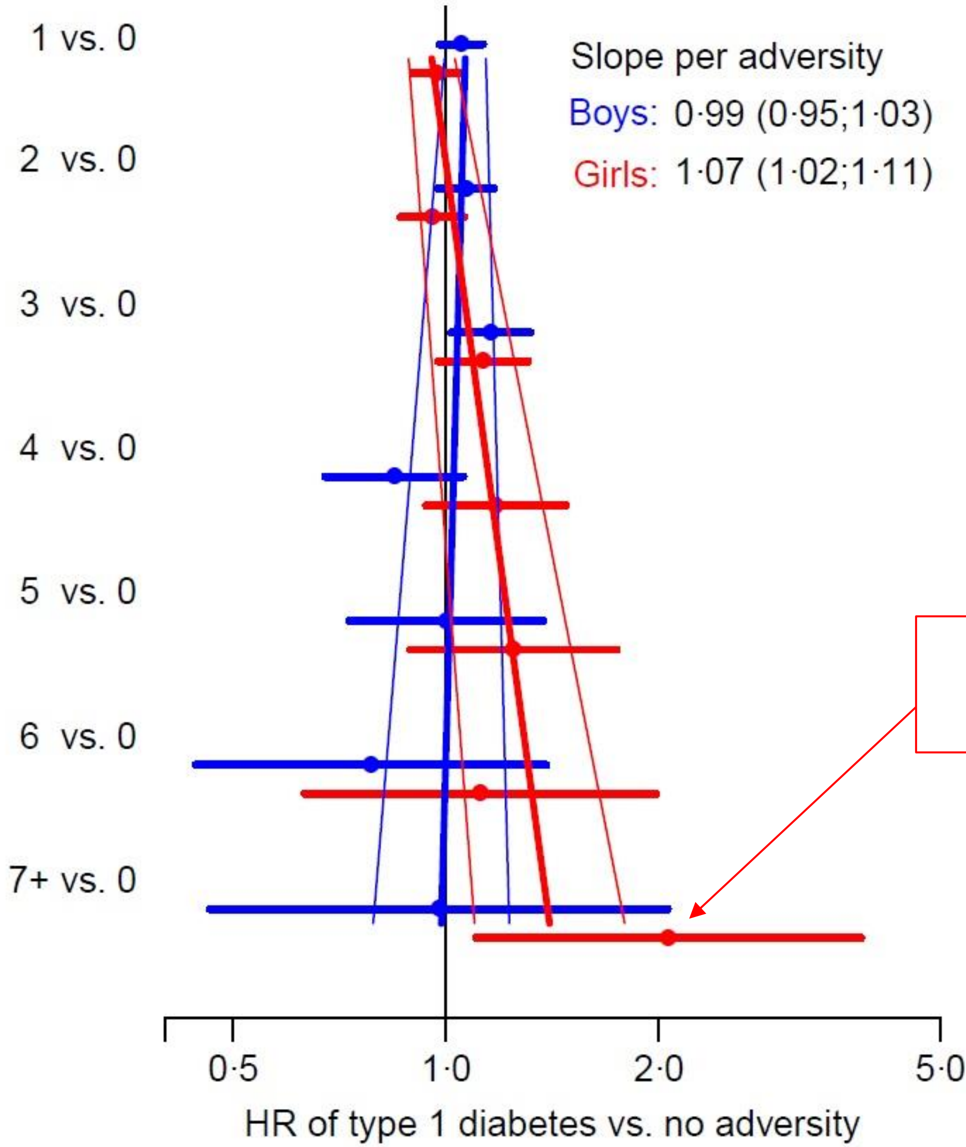
Unadjusted linear trend from 1 adversity onwards



Adjusted linear trends from 1 adversity onwards

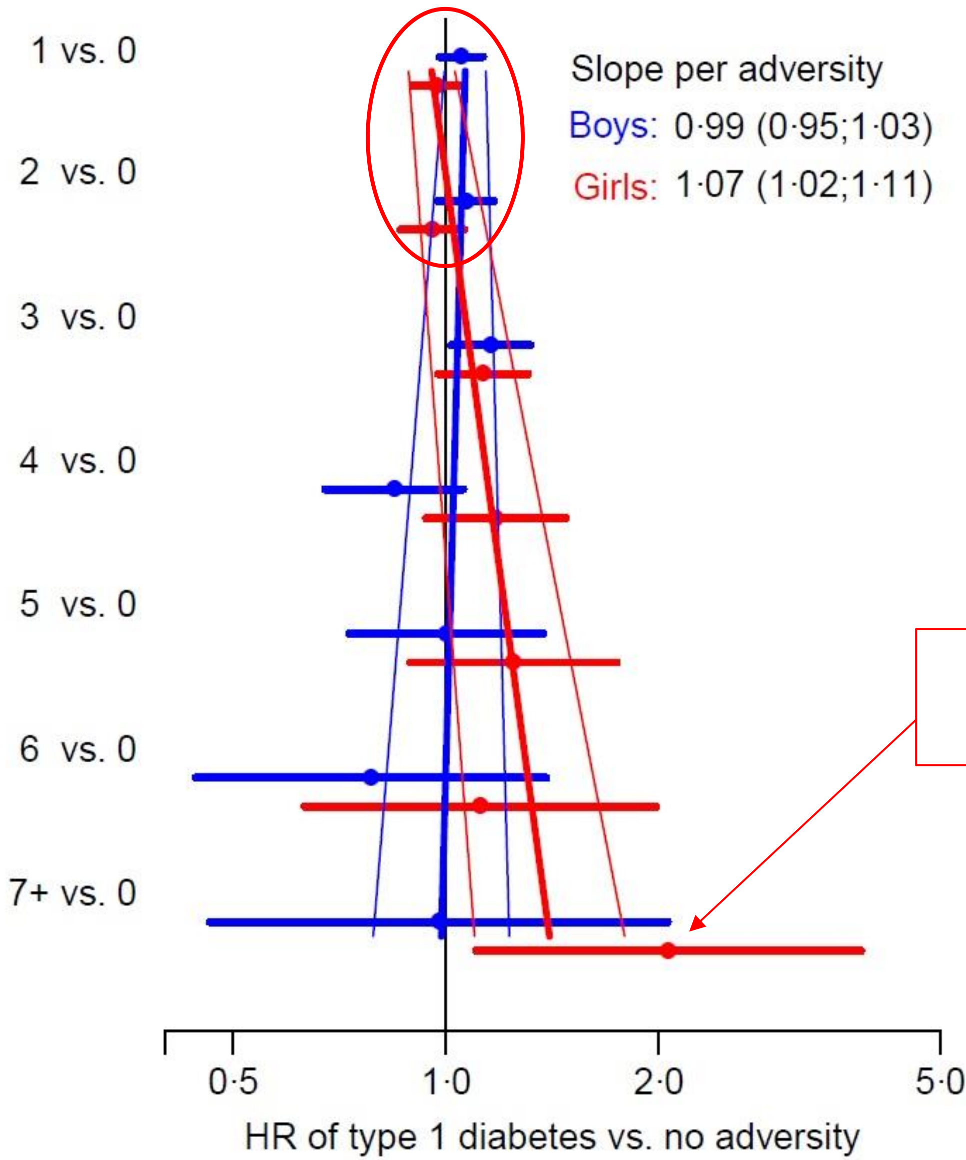


Adjusted linear trends from 1 adversity onwards



Adjusted HR, 7+:
2.06 (1.10-3.86)

Adjusted linear trends from 1 adversity onwards



Adjusted HR, 7+:
2.06 (1.10-3.86)

Strengths:

- The size of the study
- Avoiding:
  - Selection bias
  - Recall bias

Limitations:

- Limitations in register data
- Misclassification

Conclusion

- We find a quantitatively <u>small</u> effect of accumulation of childhood adversities on type 1 diabetes development in girls, but not in boys.
- There is a very small group of girls exposed to a high degree of adversity who may be more vulnerable to adversities and this group needs further attention.

Thank you!

Jessica.linnea.bengtsson@regionh.dk