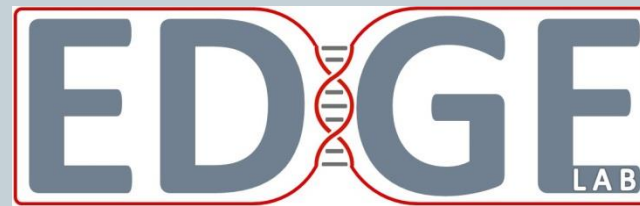# Affective symptoms across the life course and midlife cortisol: prospective birth cohort study

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Affective disorders

◉ Depression and anxiety are the most common forms of psychopathology in adolescents and adults

◉ Depression is the 2nd leading cause of disability by 2020 (WHO, 2001)

◉ The prevalence rate is rising among young people (WHO, 2014)

◉ Associated with age-related conditions: e.g., faster cognitive decline, obesity, the metabolic syndrome, and type 2 diabetes

◉ The hypothalamic-pituitary-adrenal (HPA) axis represents one possible brain circuit that may mediate the relationship between affective disorders and various age-related problems

HPA axis

- The function of the HPA axis can be altered early in life with long-term effects on cortisol secretion (Glover et al., 2010; Phillips and Jones, 2006) that affects human health (Reynolds et al., 2001)
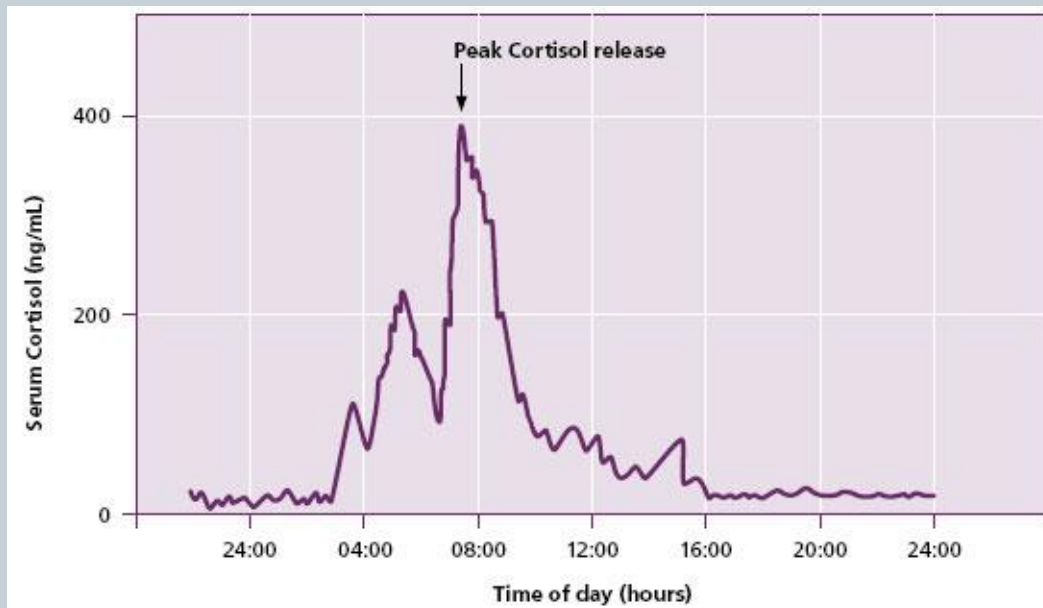
- Cortisol typically follows a **diurnal rhythm**, with a peak soon after waking in the morning and a gradual decline throughout the day
- Other patterns have been observed: absence, or prolongation of the high awakening level; or rises later in the day

HPA axis and affective symptoms: longitudinal studies

- In children and adolescents, **hyperactivity of the HPA-axis** (e.g., higher morning cortisol and higher cortisol awakening response) has been shown to predict onset and recurrence of affective disorders (Cicchetti and Rogosch, 2001; Goodyer et al., 1997; Kalmijn et al., 1998; Kaufman, 1991; Kuningas et al., 2007; Ruttle et al., 2011); although in the most recent and largest study this association was not confirmed (Carnegie et al., 2014).

- In adults, reported associations between affective disorders and cortisol are less consistent, with **both cortisol hyper- and hypo-secretion** being associated with affective disorders (Bremmer et al., 2007; Power et al., 2011; Wardenaar et al., 2011).

HPA-axis and affective symptoms: methodological issues

- There is a variation in salivary collection protocols;

- Different measures of cortisol are used (e.g., a single morning cortisol measure, CAR, or response to a stressor);

- The complexity of cortisol regulation is not always considered;

- Modest sample sizes combined with a wide range of potential ways to analyse cortisol may have increased type I errors;

- The timing of symptoms (i.e., adolescence or adulthood) and recurrence of affective symptoms across the life course need to be taken into account:

  - HPA-axis dysregulation may follow a natural history so that initially hyper-responsiveness (heightened CAR) may, with greater chronicity, evolve into hypo-responsiveness; attenuated CAR and smaller diurnal variability over the day (Ben-Shlomo et al., 2013).

Present study: aims

⊙ The aims of the present study:

1) to investigate whether affective symptoms at different ages across the life course were associated with cortisol levels and patterns at age 60-64 years

2) to explore the cumulative effect of affective symptoms on midlife cortisol levels and patterns
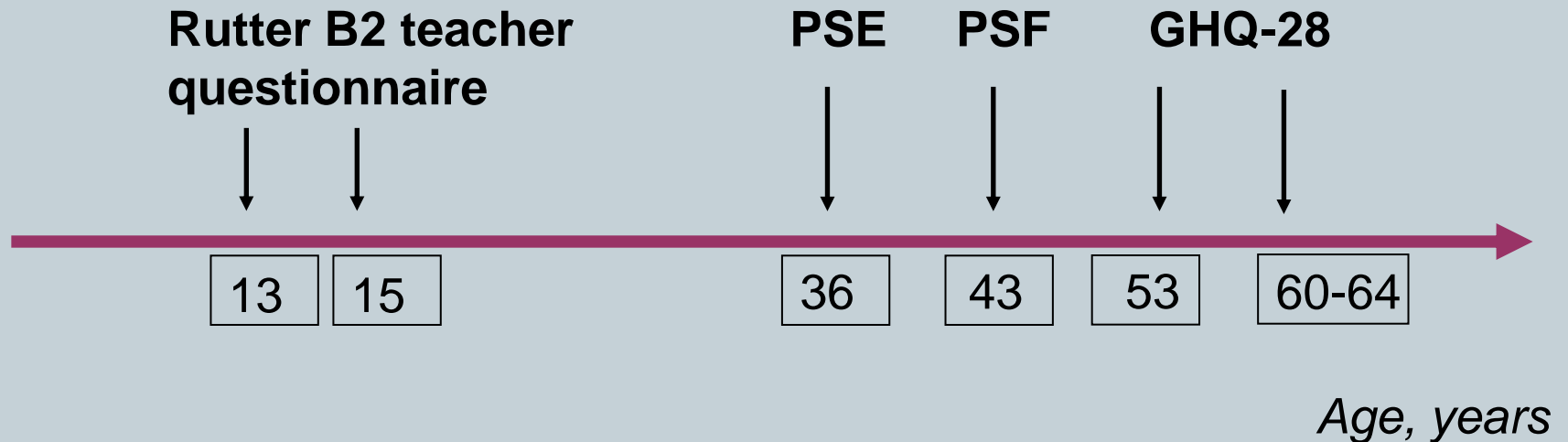
Present study: sample

- MRC National Survey of Health and Development (British 1946 birth cohort): 2547 women and 2815 men

http://www.nshd.mrc.ac.uk/

Present study: measures

⊙ <u>Affective symptoms</u>

Rutter B2 teacher questionnaire   **PSE**   **PSF**   **GHQ-28**
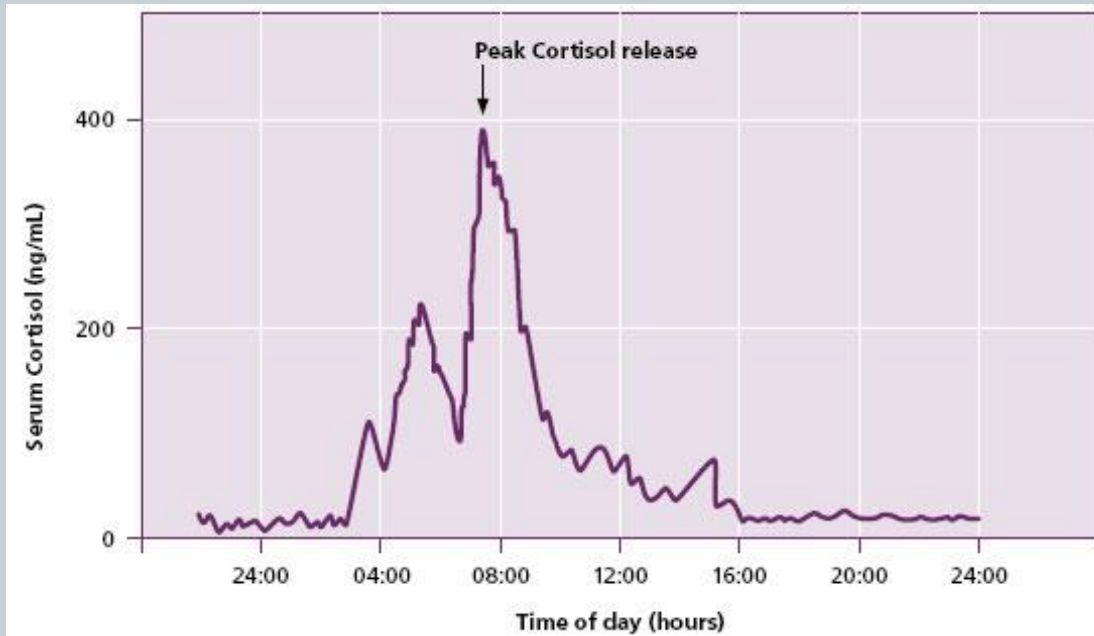
| 13 | 15 | | 36 | 43 | 53 | 60-64 |

Age, years

PSE = Present State Examination; PSF = Psychiatric Symptom Frequency; GHQ-28 = General Health Questionnaire

Present study: measures

◉ **Cortisol levels and patterns**

Saliva samples collected :
- at waking (T1)
- 30 minutes after wakening (T2)
- 2100h – 21.30h the same evening (T3)

Plus:
- cortisol awakening response, CAR = (T2-T1).
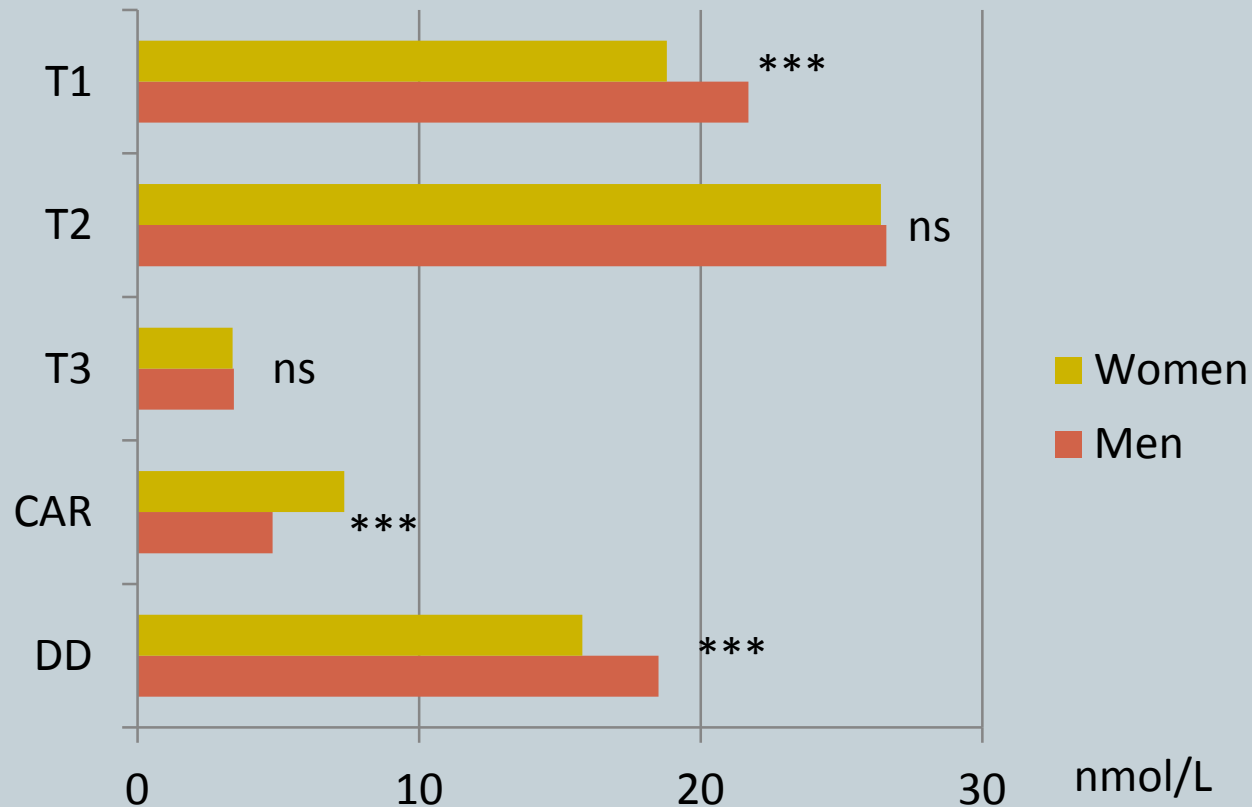- diurnal drop, DD = (T1-T3)
                        = (T1+T2)/2

T1 T2   T3

Gaysina et al, PNEC, 2013

Present study: measures

- Covariates
  - Sex
  - SEP at age 53:
    - manual
    - non-manual
  - Life-course smoking status:
    - lifelong smoker,
    - predominantly smoker,
    - predominantly non-smoker,
    - never smoker
  - BMI at age 53: weight kg/height m^2
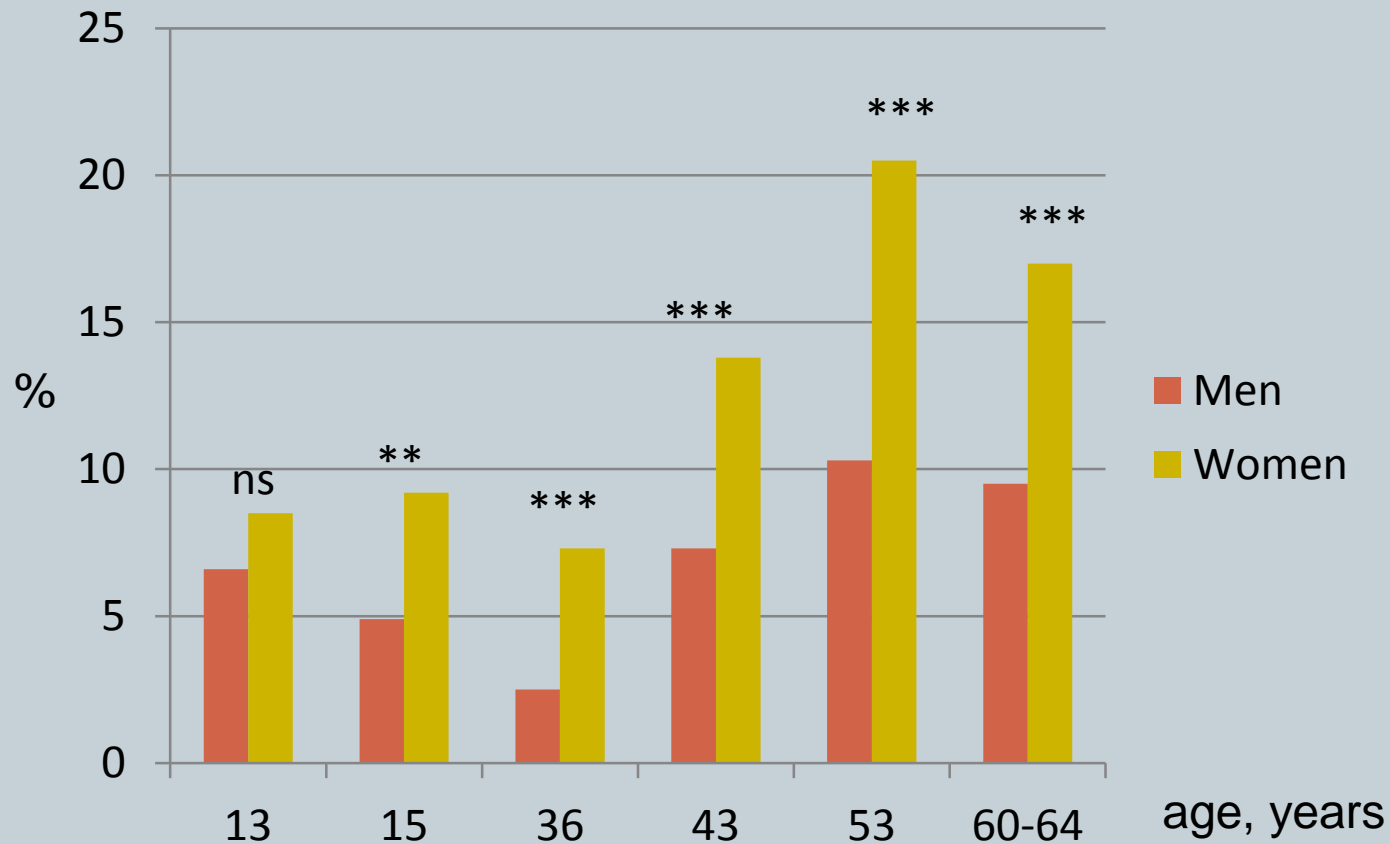
Results: descriptives

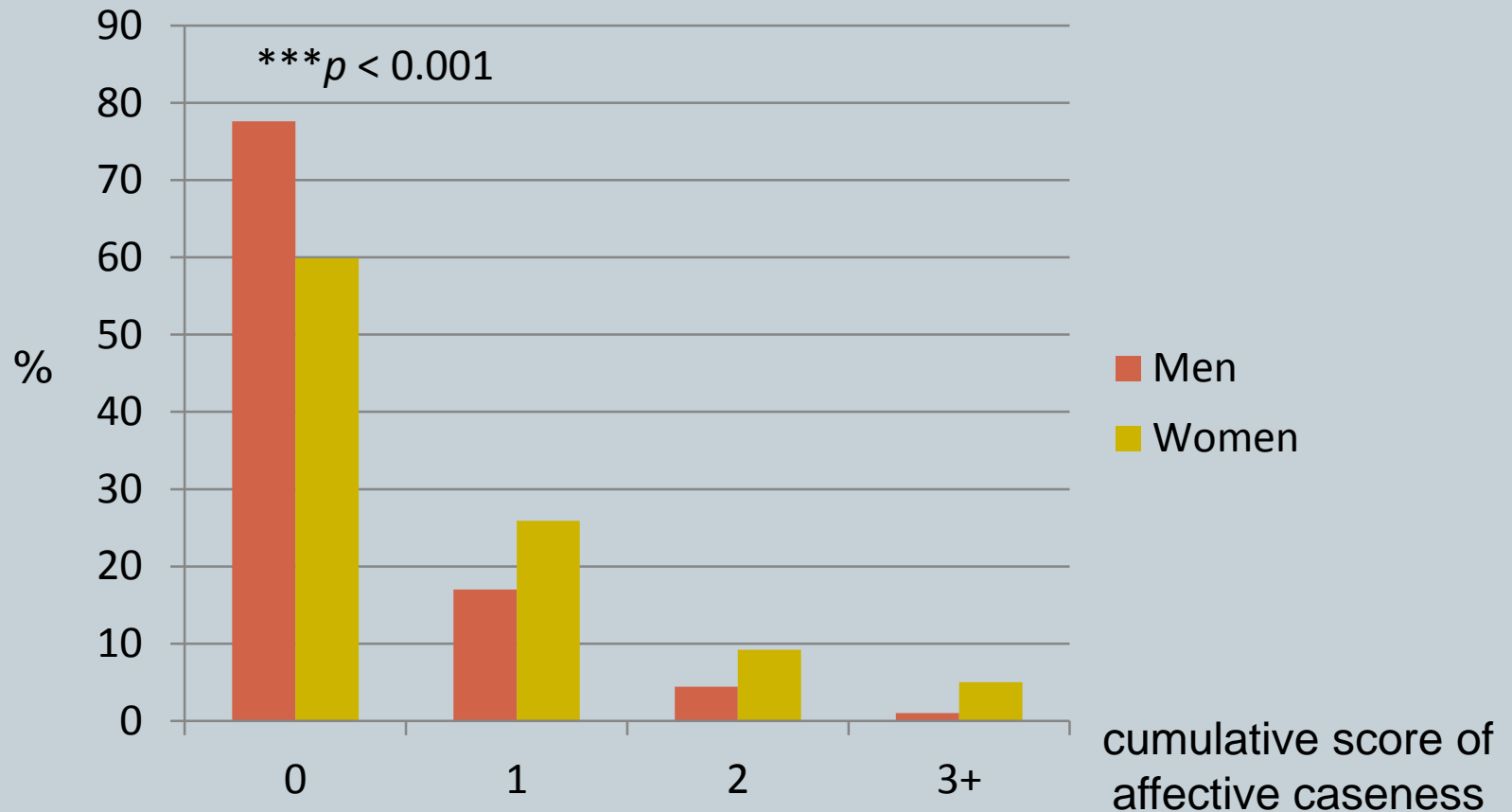◉ <u>Cortisol measures, nmol/L</u>

***$p < 0.001$

Results: descriptives

◉ <u>Affective caseness at different ages, %</u>

**p < 0.01; ***p < 0.001

Results: descriptives
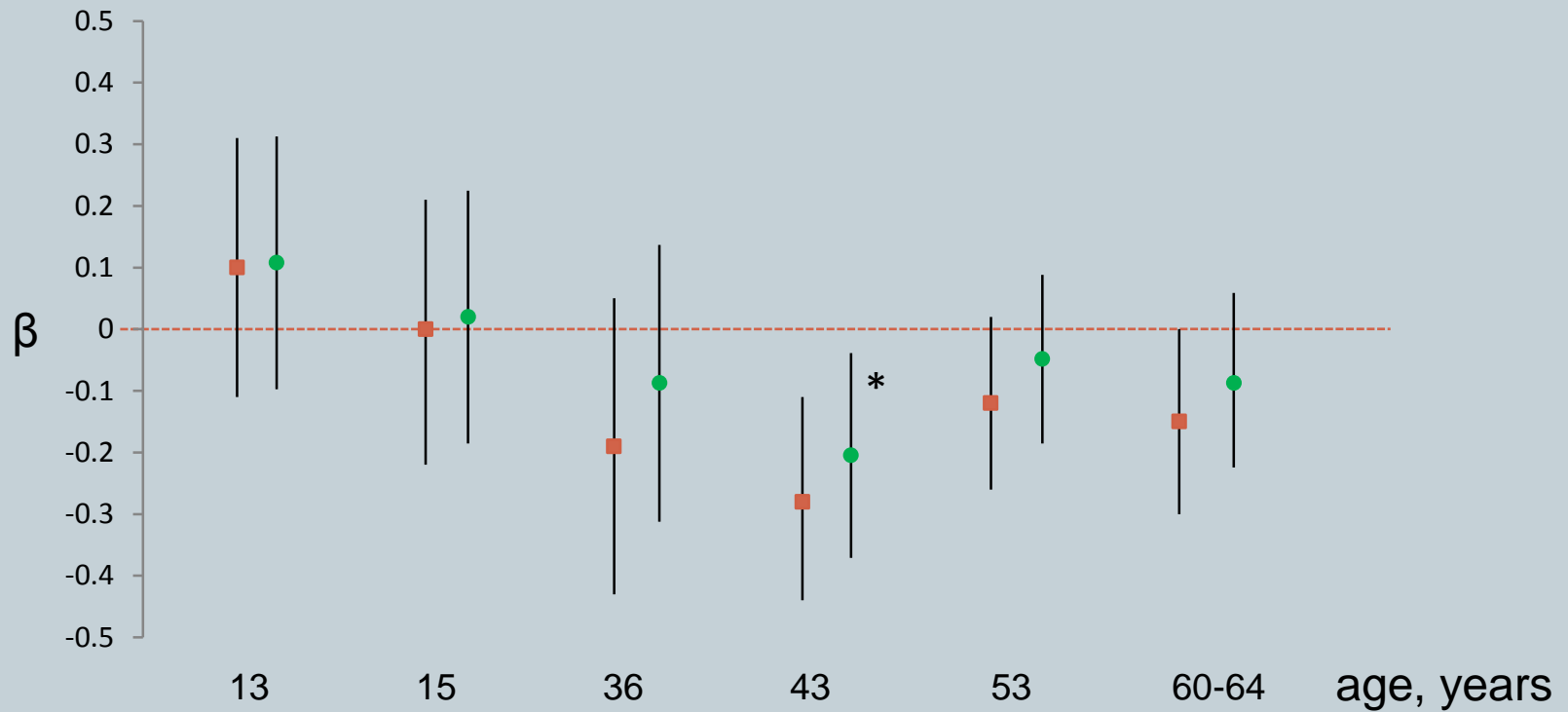
- Affective caseness cumulative score, %
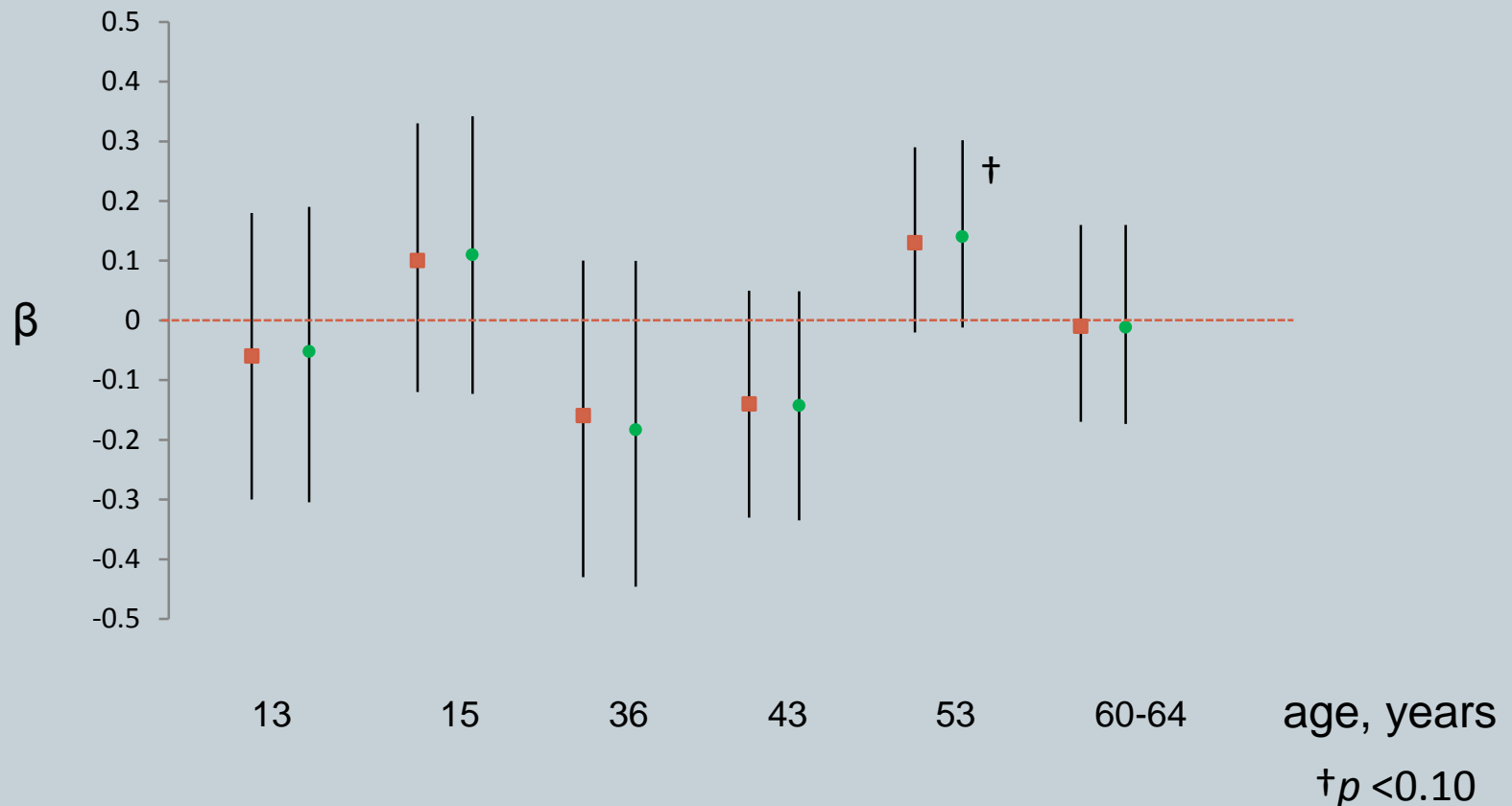
⊙ <u>Waking cortisol (T1) and affective caseness across the life course</u>

*$p < 0.05$

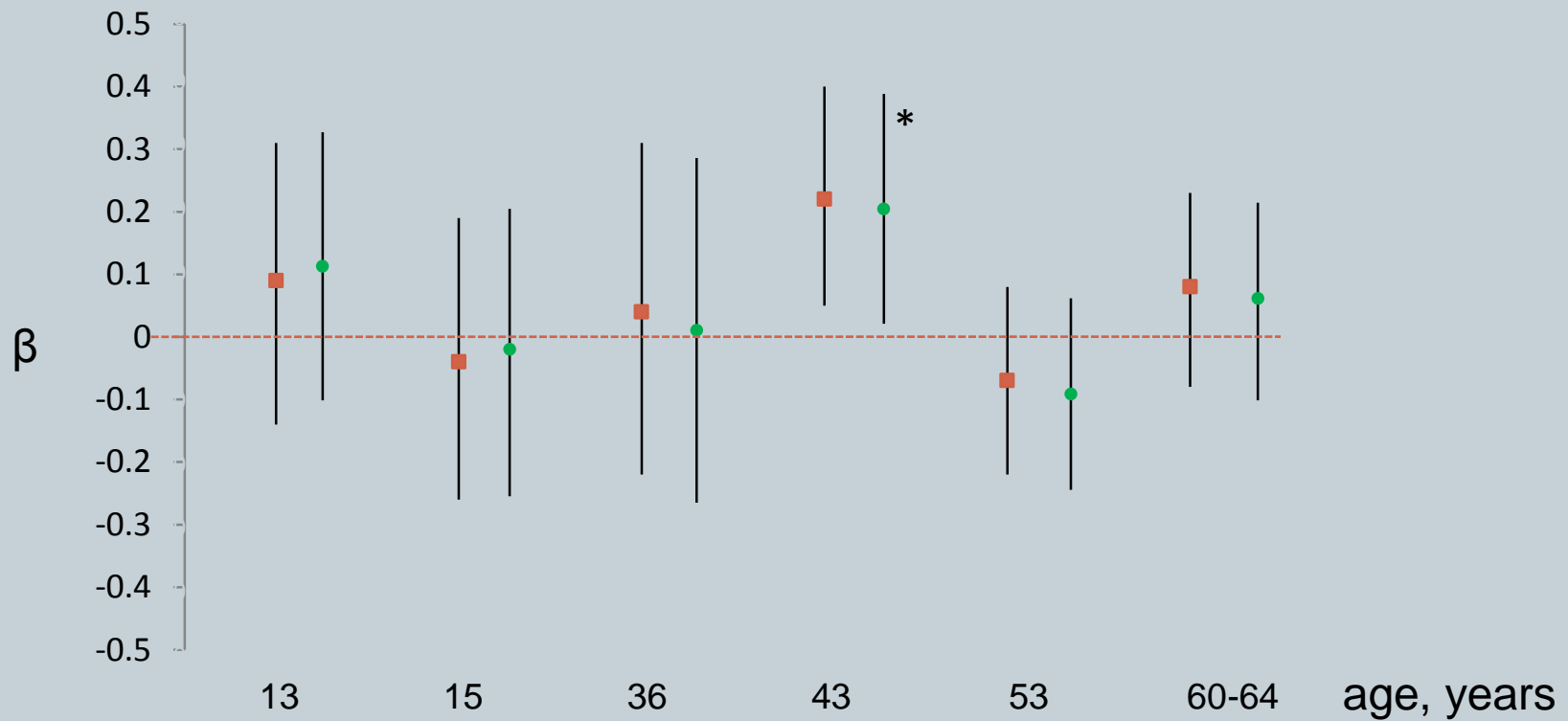# Results: Question 1

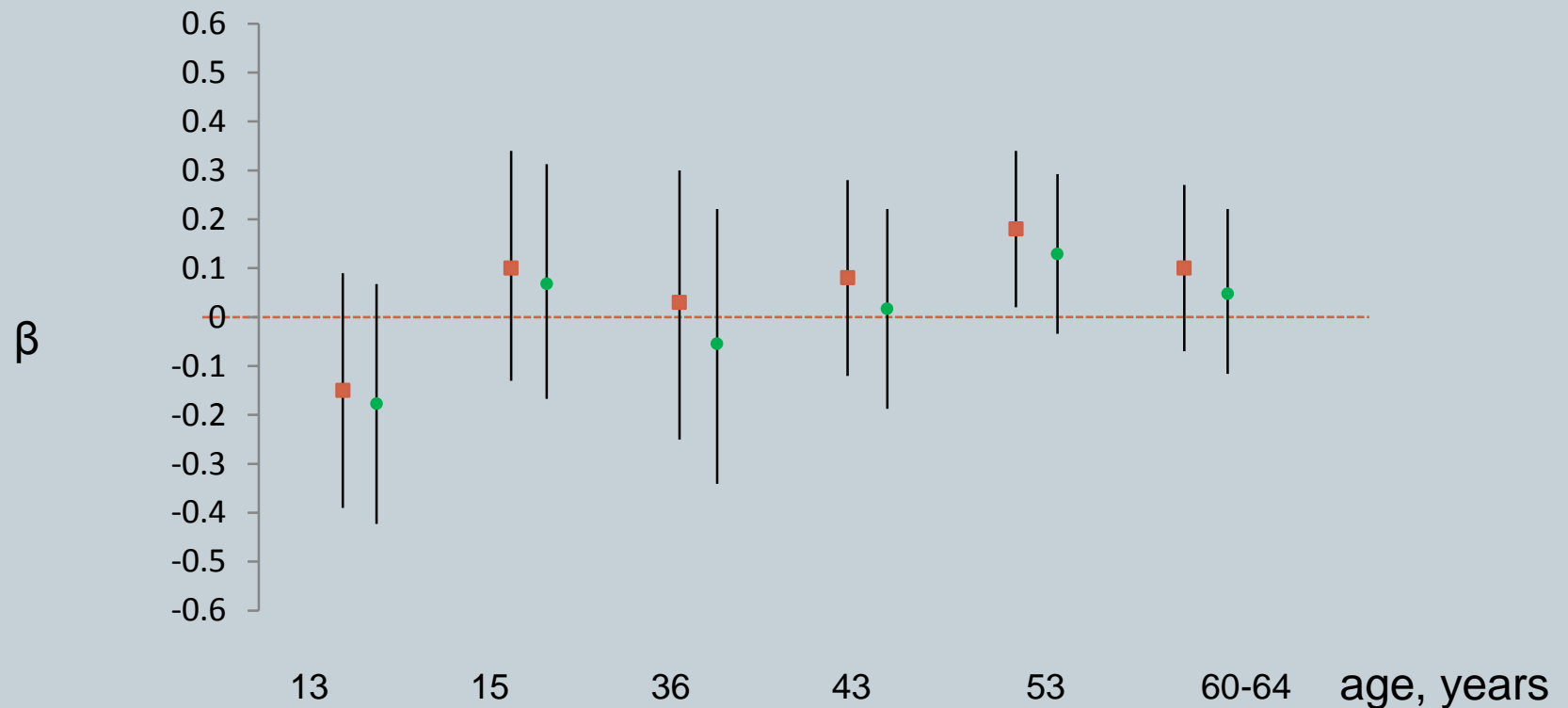- 30 minutes after wakening cortisol (T2) and affective caseness across the life course

age, years

†p <0.10

Results: Question 1

- Evening cortisol (T3) and affective caseness across the life course

β

age, years

*$p < 0.05$

- Cortisol awakening response (CAR) and affective caseness across the life course

- Diurnal drop (DD) and affective caseness across the life course
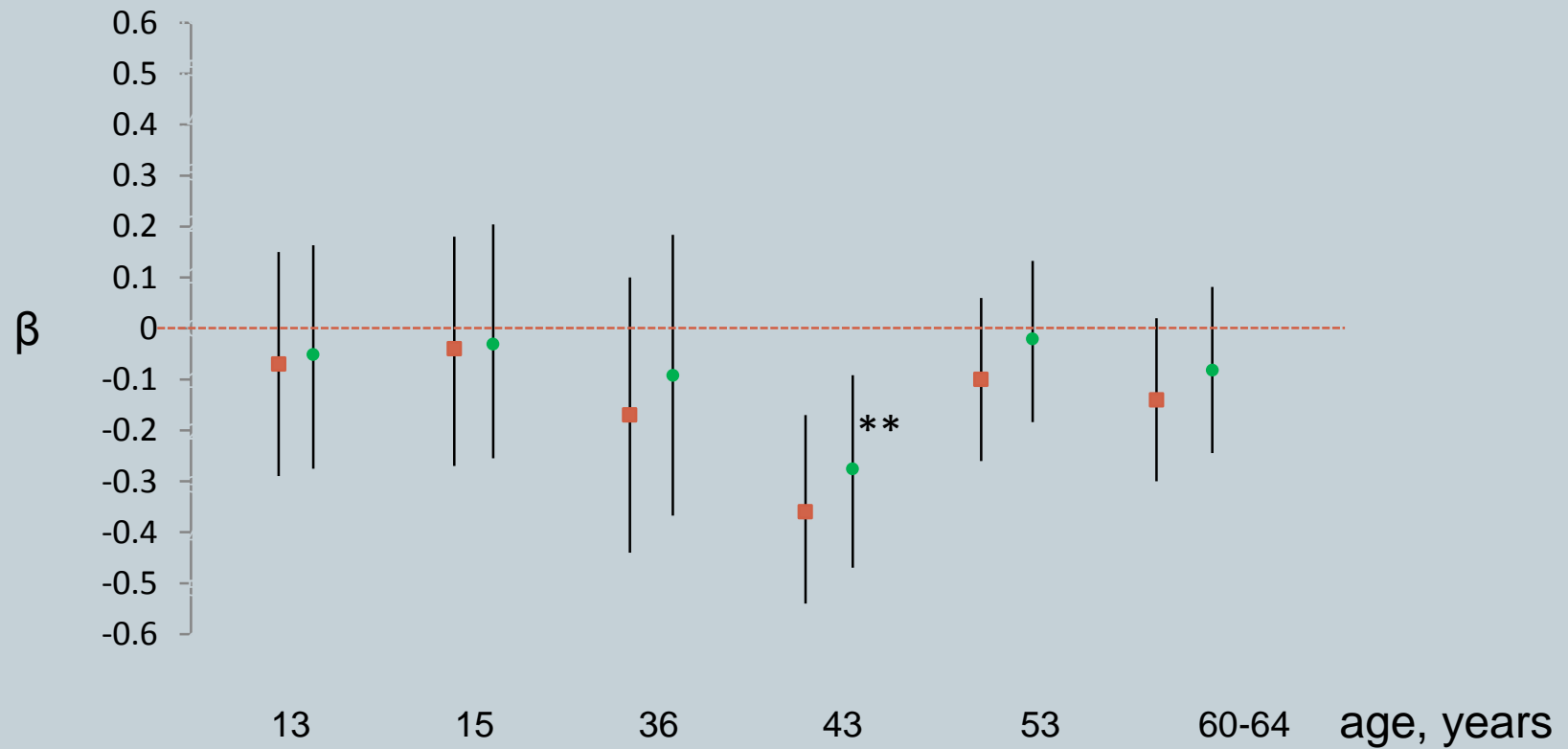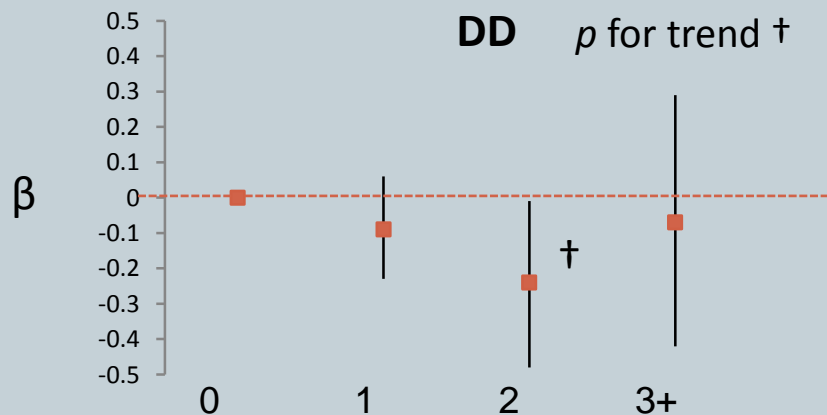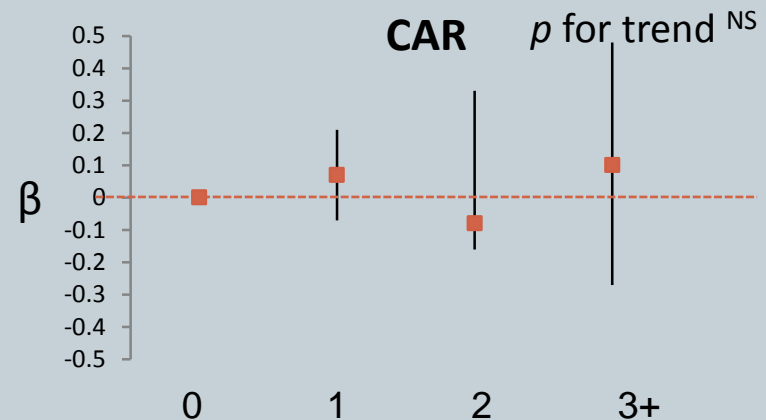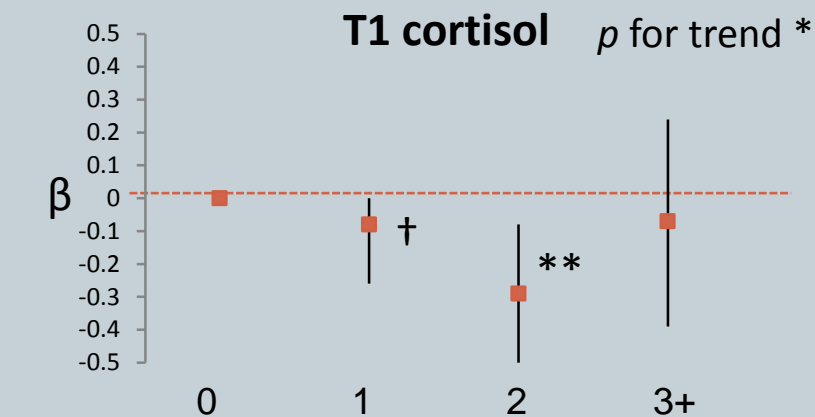

**p < 0.01

Results: Question 2

◉ <u>Cumulative score of caseness and midlife cortisol</u>

Affective caseness cumulative score	Midlife cortisol				
	T1	T2	T3	CAR	DD
None	0.07 (1.06)	0.01 (0.97)	0.00 (0.97)	-0.05 (1.03)	0.08 (1.01)
1	-0.07 (0.90)	0.04 (1.03)	0.11 (1.06)	0.06 (1.03)	-0.08 (0.95)
2	-0.29 (0.89)	-0.20 (1.03)	-0.22 (1.04)	0.10 (0.90)	-0.23 (0.90)
3+	-0.13 (1.01)	0.27 (1.22)	0.23 (1.00)	0.23 (0.84)	-0.11 (1.06)
p for trend	***			*	*

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

Results: Question 2

◉ <u>Cumulative score of caseness and midlife cortisol</u>

T1 cortisol *p* for trend *

CAR *p* for trend [NS]

DD *p* for trend †

Models adjusted for sex, SEP, smoking status, and adult BMI;
†$p < 0.10$; *$p < 0.05$; **$p < 0.01$

Conclusions

- There was the weak and inconsistent evidence for associations between affective symptoms across the life course and cortisol in midlife

- Those with case-level affective symptoms at one or more-time points had lower waking cortisol and flatter diurnal drop than those with no symptoms

- The effects of cortisol on affective symptoms in midlife can depend on lifetime psychological health, in particular, on adult repeated symptoms

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