RELATIONSHIP BETWEEN TELOMERE LENGTH AND DYSLIPIDEMIA IN PATIENTS WITH CUSHING'S SYNDROME

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Introduction

- **Cushing's syndrome** (CS) is a rare disease caused by hypersecretion of cortisol and is associated with increased mortality and morbidities.
- Hypercortisolism is also present in **chronic mood disorders** (CMD) and **stress**, where **telomere length** (TL) has been found to be shorter than in matched controls.
- Since hypercortisolism is present in CS and CMD, we hypothesized that telomere shortening could also be present in CS.

Hypothesis

Chronic mood disorder (CMD) Stress → HYPERCORTISOLISM ⋯> Telomere length shortening → Premature ageing Increased mortality and morbidities

Cushing's Syndrome → HYPERCORTISOLISM

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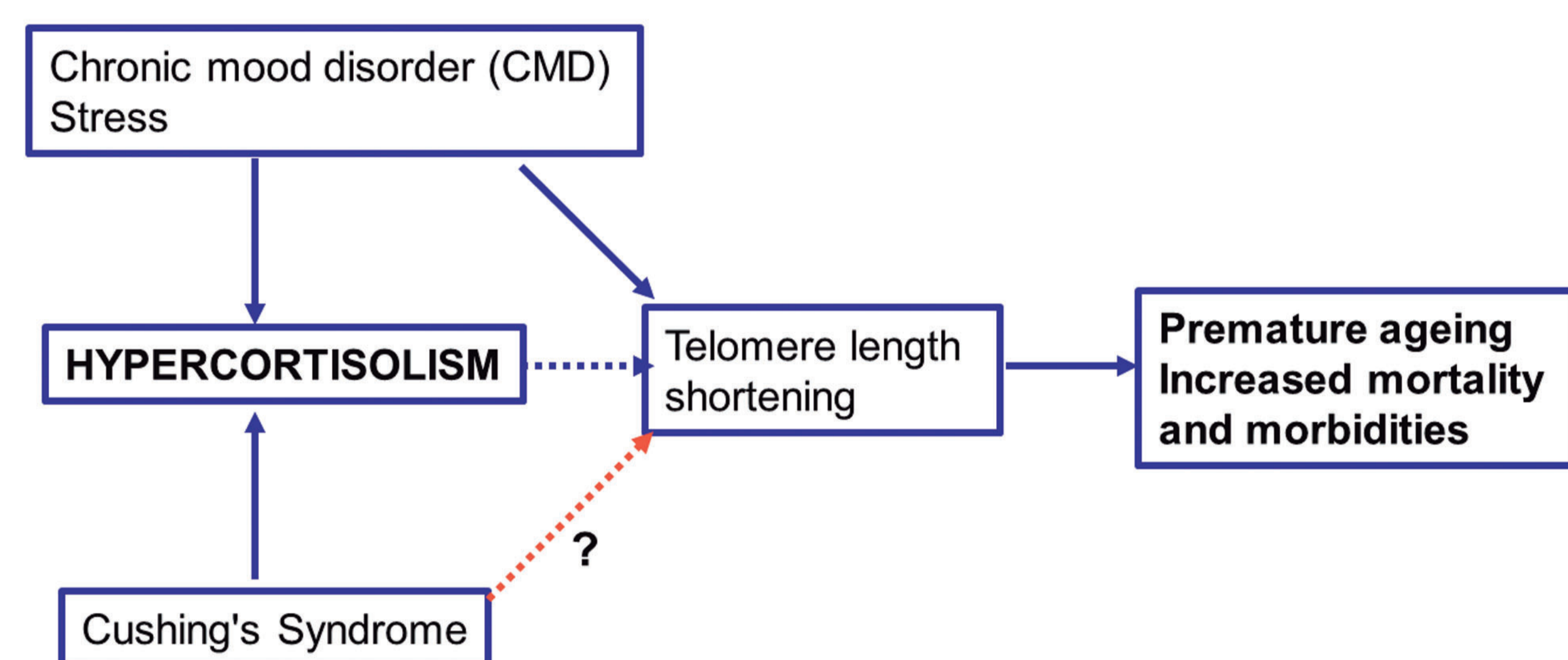
Aim

- To investigate TL in CS patients compared to matched controls.

Results

Table1: Baseline characteristics

	CS	controls	P
Age (years)	46.8±12.8	46.8±12.6	ns
BMI (kg/m^2)	26.8±4.8	27.7±5.2	ns
W/H ratio	0.906±0.066	0.843±0.078	<0.001
Hypertension	47%	11%	<0.001
Osteoporosis	24%	2%	<0.01
Diabetis mellitus	9%	2%	ns
Dyslipidemia	36%	20%	ns
Psychiatric disease (mainly anxiety or depression)	31%	11%	<0.05

No other baselines differences among CS and controls were found

Methods/Design

- Transversal study.
- 45 CS patients and 45 matched control (age, gender, smoking):
  – 9 males, 36 females
  – Mean age 46.8±12.8 SC vs 46.8±12.6 controls
  – 36 pituitary Cushing's disease, 9 adrenal Cushing's syndrome
  – 9 with active disease, 36 biochemically cured (7 patient postoperative ACTH deficiency)
- DNA extraction from leukocytes using the phenol/chloroform method.
- Leukocyte TL was measured by TRF Southern technique (kit-telo TAGGG Telomere length Assay, Roche).
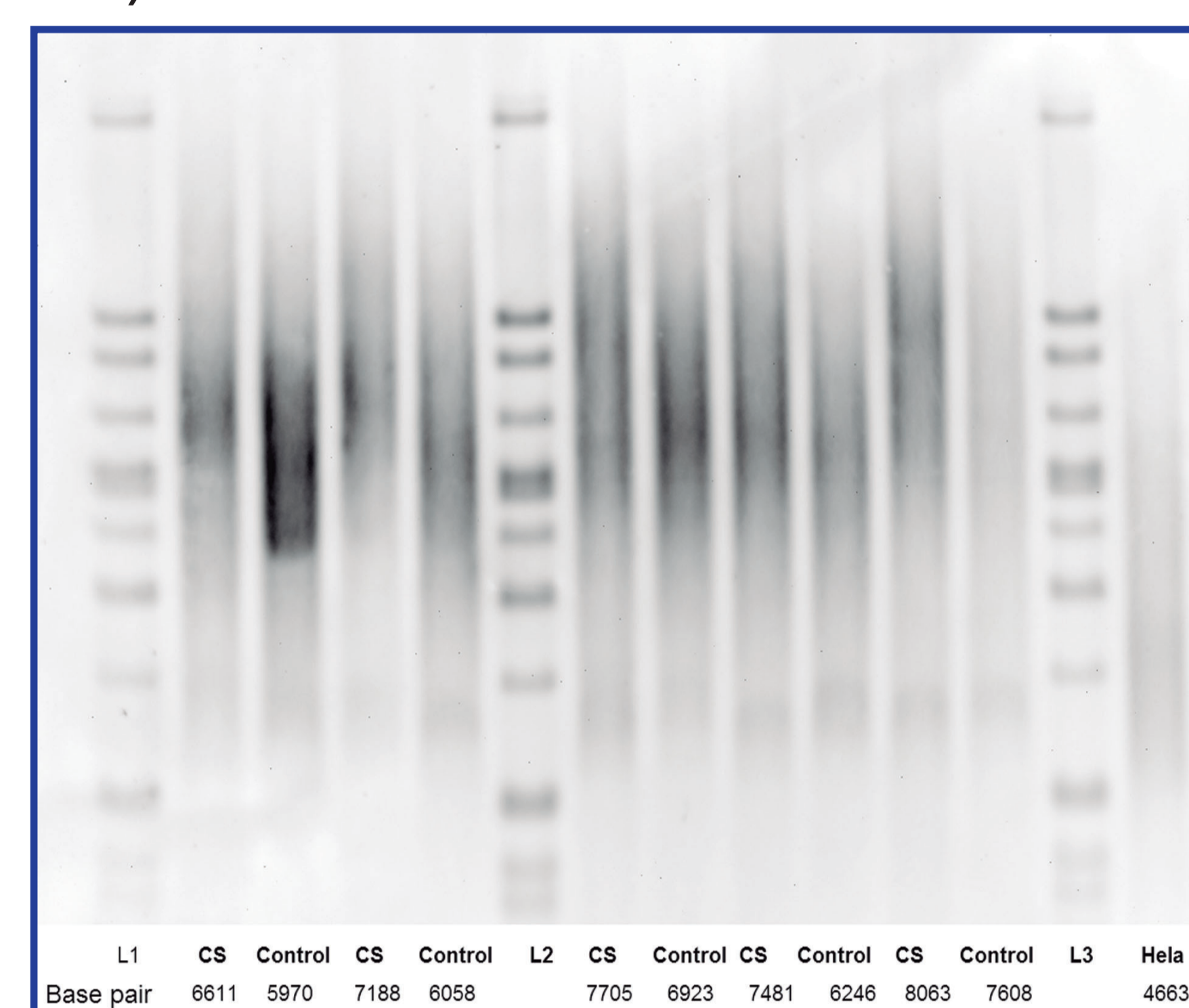

L1	CS	Control	CS	Control	L2	CS	Control	CS	Control	CS	Control	L3	Hela
Base pair 6611	5970	7188	6058		7705	6923	7481	6246	8063	7608			4863

Figure 1: Southern Blot results

Table 2: Characteristics of CS patients

Variables	
ACTH postoperative deficiency	7 (15.6%)
Biochemically cured:	29 (64.4%)
Mean years of cure	7.4±7
Active disease	9 (20%)
Months hypercortisolism	68±43.1
Delay in diagnosis (months)	38.3±28.6
Radiotherapy treatment	12 (26.7%)
Previous recurrence	11 (24.4%)

No correlation was found BETWEEN concomitant **cortisol values**, length of **exposure to hypercortisolism** or endocrine **cure** AND **telomere length**
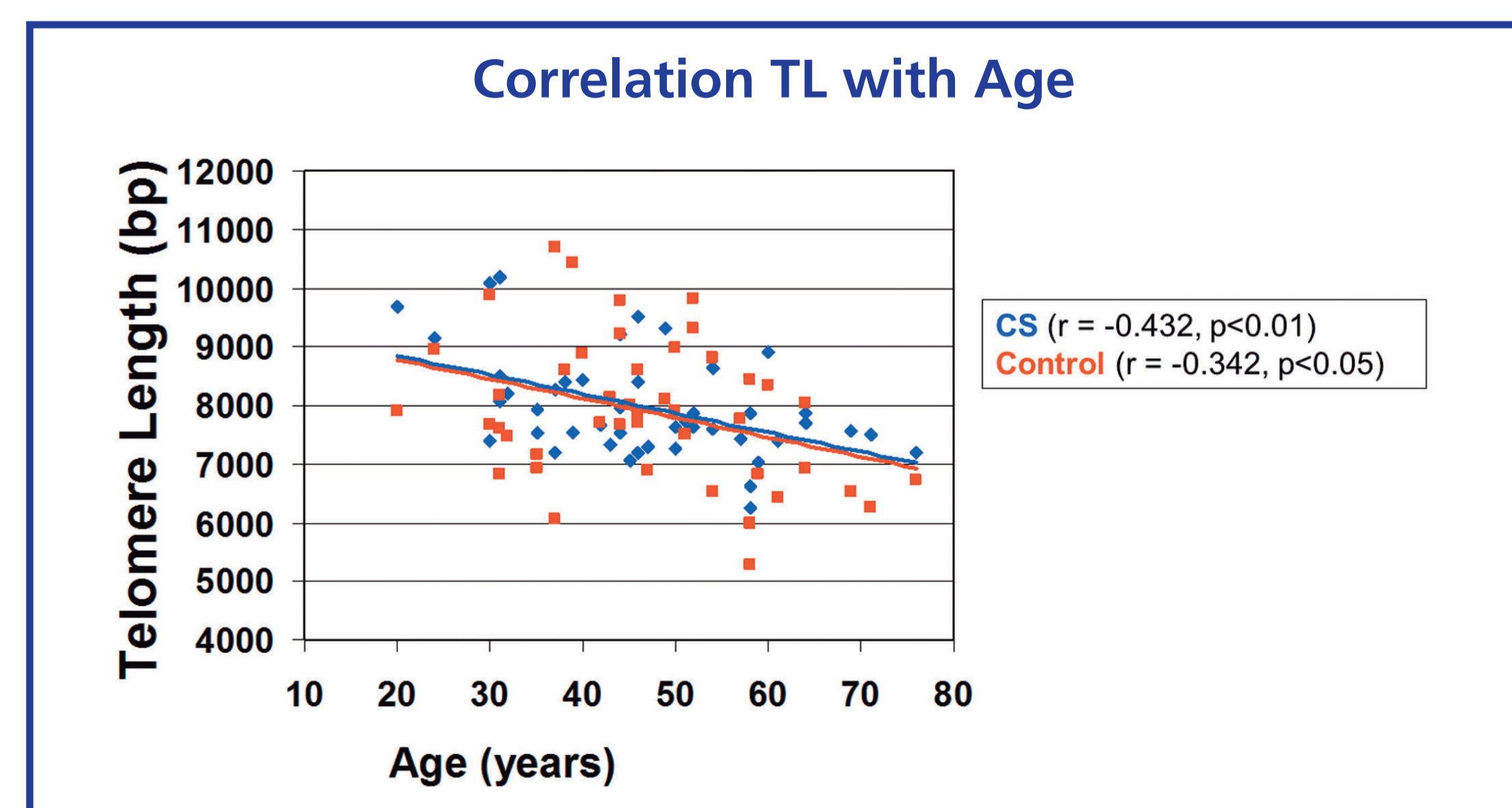
Correlation TL with Age

CS (r = -0.432, p<0.01)
Control (r = -0.342, p<0.05)

Figure 2: Correlation of Telomere Length (TL) with age.
(CS: Cushings's syndrome, bp: base pairs)

CS 7971   Controls 7892
ns
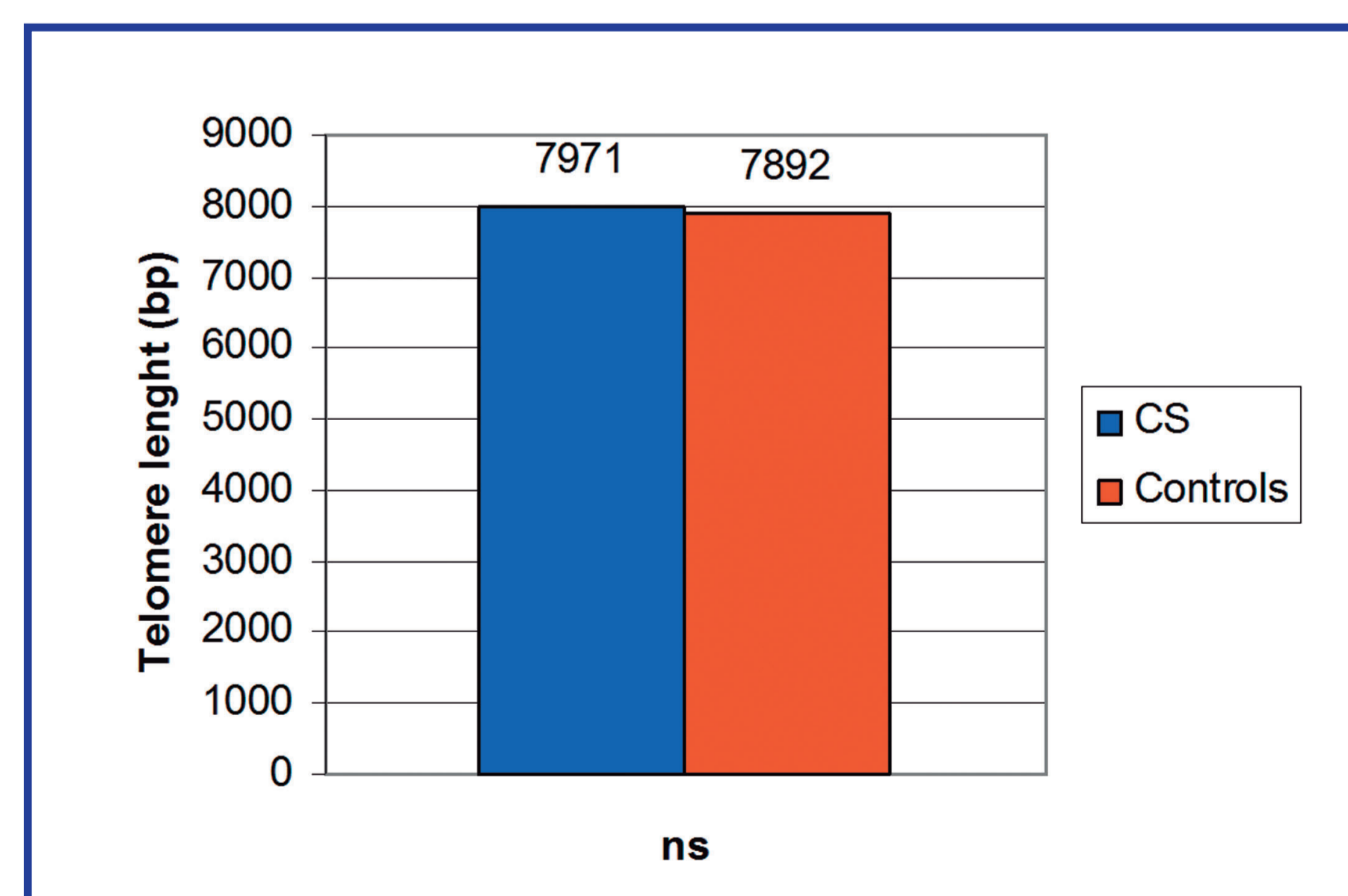
Figure 3: Comparison of Telomere Length between CS and controls

	Active disease (ns)	Dyslipidemia (p <0,05)	Diabetes (p = 0,067)
Yes	7831	7457	7272
No	7950	8184	7989

No differences with any other analysed clinical features were found
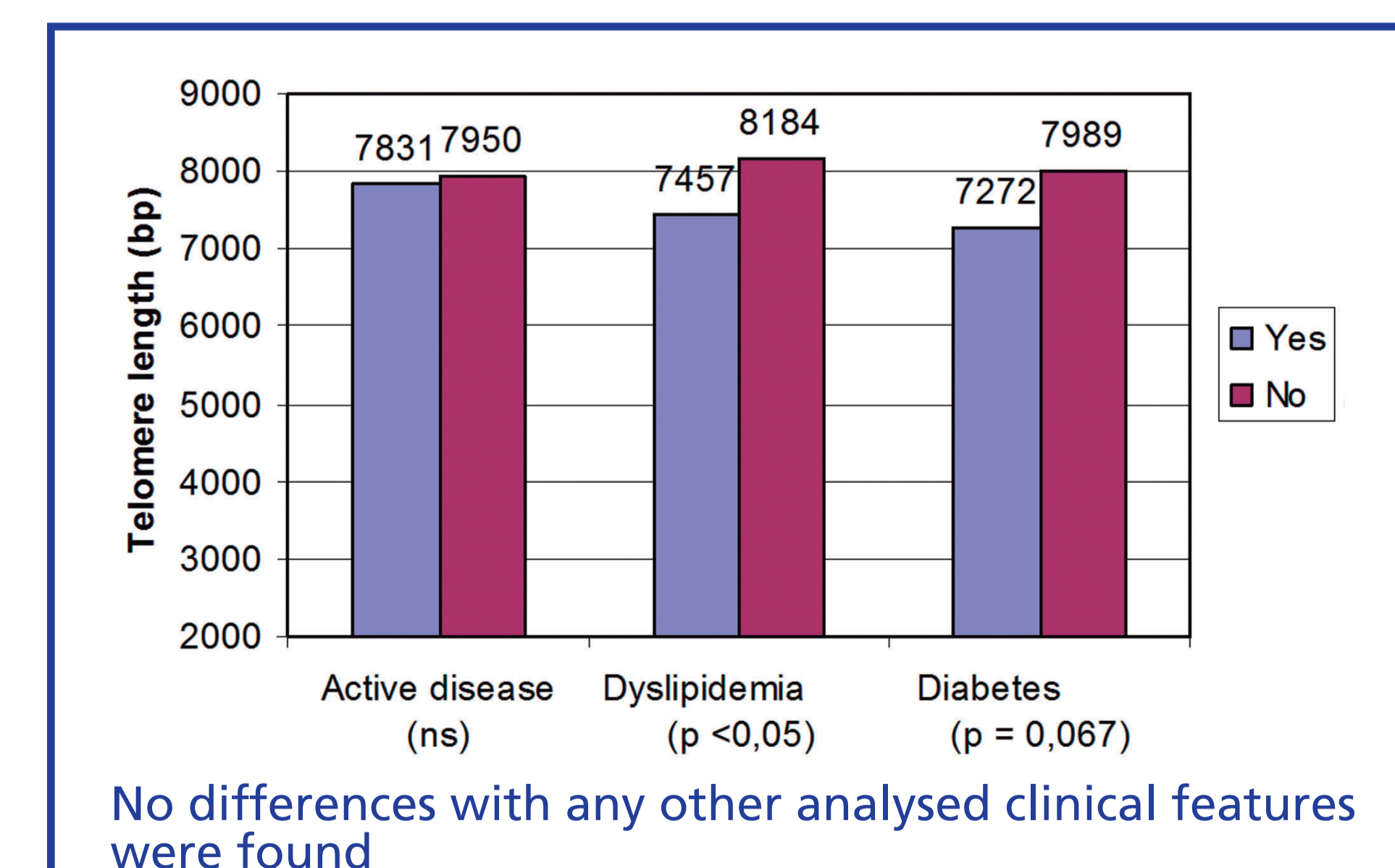
Figure 4: Relation of Telomere Length with disease activity and comorbidities

Conclusions

- **In this small group of matched CS/controls we did not find any differences in TL; however, in CS with dyslipidemia TL was shorter than in CS patients with normal lipid values.**
- **Further studies will be necessary to confirm this finding and define any possible relationship between hypercortisolism and TL.**

References

- Simon MN et al. Telomere Shortening and Mood Disorders: preliminary support for a Chronic Stress Model of Accelerated Aging. 2006. Biol Psychiatry; 60: 432-435.
- Epel ES et al. Accelerated telomere shortening in response to life stress. 2004. PNAS; 101: 17312-5.
- Choi J et al. Reduced telomerase activity in human T lymphocytes exposed to cortisol. 2008. Brain Behav Immun. 22: 600-5.
- Tomiyama AJ. Does cellular aging relate to patterns of allostasis? An examination of basal and stress reactive HPA axis activity and telomere length. 2012. Physiol Behav. 106: 40-5