

# Psychological stress, but not physiological stress, is associated with inflammation among residents of a peri-urban community in Vanuatu

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## Introduction

Understanding the relationship between stress and inflammation is critical for mitigating chronic disease risk in settings where rapid social change is accompanied by increasing risk for chronic disease.

Inflammation begins when immune cells detect an infectious agent or tissue damage and are activated to produce inflammatory mediators. These mediators promote vasodilation and permeability, recruit additional immune cells to the site, initiate edema, activate innate immune responses (e.g., complement) and coagulation, and potentiate adaptive immune responses. Activated long-term, inflammation can be damaging and has been implicated in multiple chronic disease processes [1, 2].

Stress likely acts on inflammation through many pathways, and is in turn affected by multiple aspects of physiology, psychology, and the environment [1]. Rapid social change (e.g., due to market integration) may cause stress in multiple ways; it is possible that stress and downstream inflammation are connected in populations undergoing economic development and increased chronic disease risk.

We investigated the relationship between **stress** and **inflammation** in the Republic of Vanuatu, a South Pacific island nation currently undergoing rapid economic development and an associated health transition [3, 4].

We conceive of stress in two ways:

- Psychological stress:** expressed stress as captured with a survey instrument
- Physiological stress:** the stress hormone cortisol (activity of the hypothalamic-pituitary-adrenal axis) [1, 2]

We characterized inflammation via the biomarker **C-reactive protein (CRP)** [2]. Variation in CRP <5 mg/l reflects background levels of inflammation that are characteristic of an individual.

We hypothesized a positive association between background inflammation and stress, particularly cortisol, as an indicator of physiological stress.

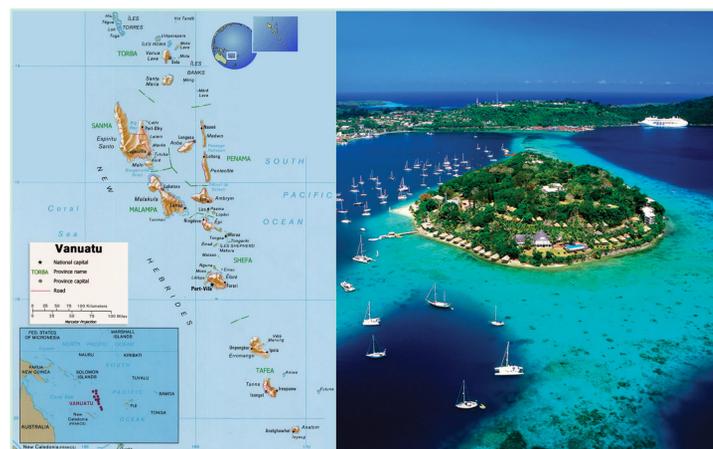


Figure 1. Map of The Republic of Vanuatu (left) including the island Efate, home to the urban capital Port Vila (right). Images from [pacificcollectionsreview.wordpress.com](http://pacificcollectionsreview.wordpress.com) & [jactarsuperyachtcharter.com](http://jactarsuperyachtcharter.com)

## Methods

Participants were residents of a peri-urban community on Efate.

Physiological stress was characterized via hair cortisol (1-3 cm hair samples) [5]; this provides a weeks-to-months long picture of cortisol secretion and HPA axis activity. Psychological stress was characterized via scores constructed from a 14-item distress survey.

Inflammation was characterized with CRP measured in dried blood spot specimens via enzyme immunoassay [6]. Individuals with CRP>5 mg/l were excluded from all models.

Associations between CRP and stress were assessed by estimating generalized linear regression models with a log link using STATA v15 software.

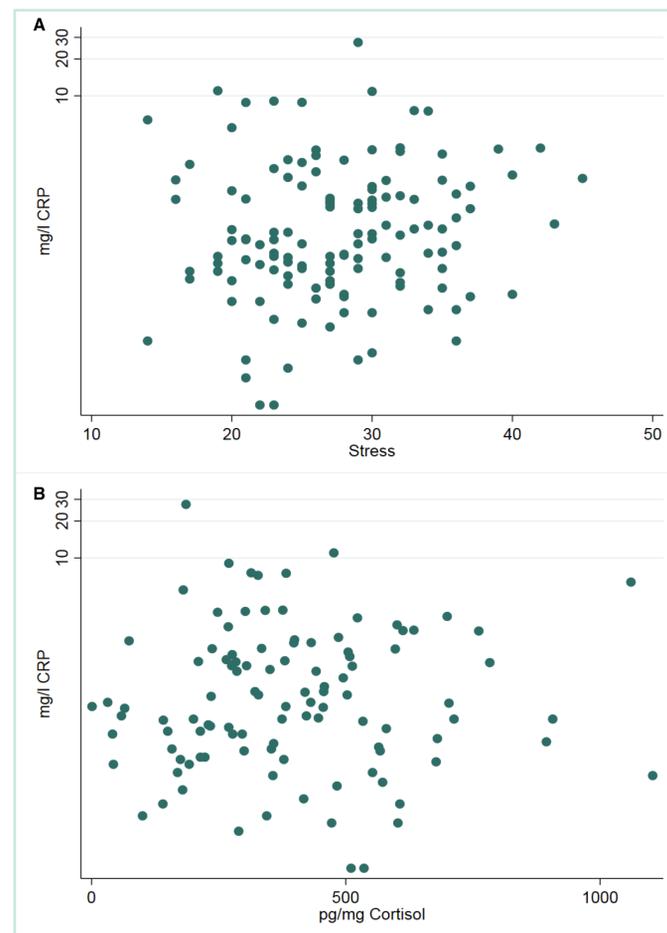


Figure 2. Scatter plots: (A) stress score and CRP (B) hair cortisol and CRP, with CRP log-transformed

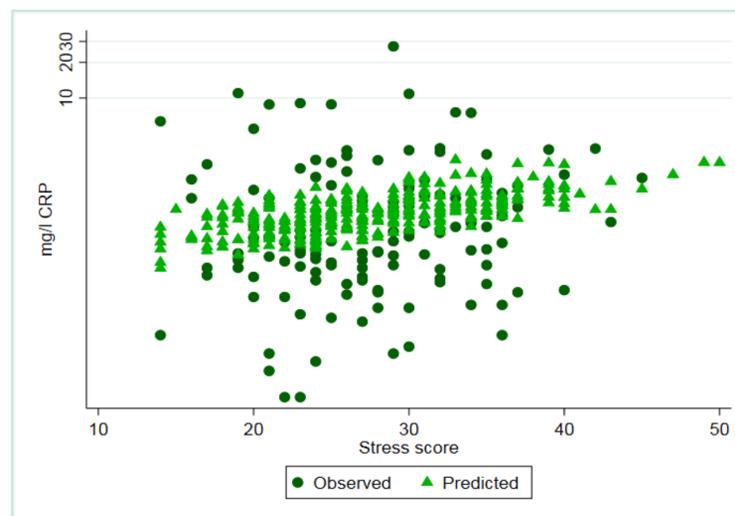


Figure 3. Psychological stress score and observed and predicted CRP (from the model in Table 1)

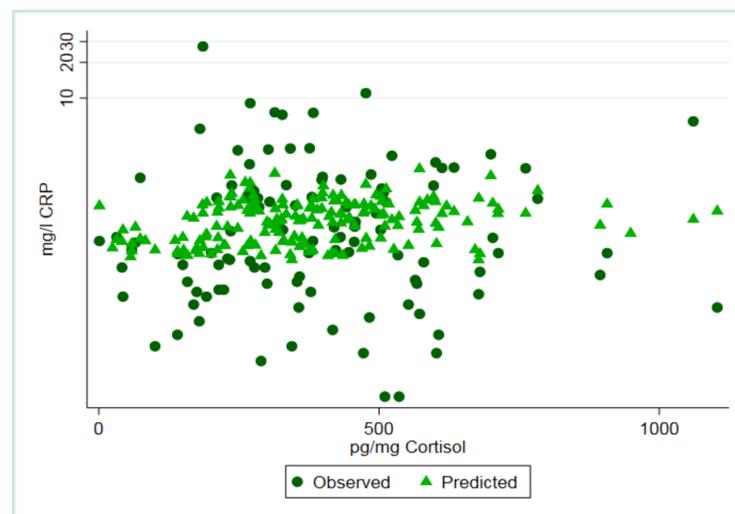


Figure 4. Hair cortisol and observed and predicted CRP (from the model in Table 2)

## Results

213 Efate residents participated (86 males and 127 females; age 41.5 ± 16.9).

CRP ranged from 0.03 - 27.3 mg/l, with a right-skewed distribution; CRP was below 5 mg/l for 132 participants. Hair cortisol ranges from 1.02 - 1,103.47 pg/mg, with a slightly right-skewed distribution. Psychosocial stress scores ranged from 14 - 50, with a normal distribution.

Controlling for sex, age, and BMI, CRP was positively associated with psychosocial stress (Table 1 and Figure 2), but not with hair cortisol (Table 2 and Figure 3). **Each 1-point increase in stress score was associated with a 4% increase in CRP** (Table 1).

Table 1. Generalized linear model of CRP (log-linked) and stress score

	$\beta$	Exp $\beta$	95% CI	p
<i>Stress score</i>	0.04	1.04	0.01 0.06	0.004
<i>Age</i>	0.01	1.01	-0.00 0.02	0.131
<i>Sex</i>	0.29	1.03	-0.07 0.65	0.116
<i>BMI</i>	0.02	1.02	-0.01 0.06	0.214

Table 2. Generalized linear model of CRP (log-linked) and hair cortisol

	$\beta$	Exp $\beta$	95% CI	p
<i>Hair cortisol</i>	0.00	1.00	-0.00 0.00	0.970
<i>Age</i>	0.01	1.01	-0.01 0.03	0.346
<i>Sex</i>	0.59	1.06	-0.01 1.19	0.053
<i>BMI</i>	0.04	1.04	-0.00 0.08	0.078

## Discussion

These findings suggest that psychological and physiological stress do not have the same impact on inflammation, and so may affect health differently.

Our findings suggest that psychosocial stress may act through pathways other than the HPA axis (reflected in hair cortisol) to affect inflammation.

Future studies should compare psychological and physiological stress and their relationship to inflammation between different islands on Vanuatu that are experiencing these transitions at different rates.

Measures of expressed psychosocial stress remain important in health research, even with the availability of objective, physiological measures of stress, such as hair cortisol.

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