

# Prednisolone replacement therapy is associated with significant weight loss in patients who switch from hydrocortisone with adrenal insufficiency.

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## BACKGROUND

Adrenal Insufficiency (AI) is a life-threatening disorder caused by dysfunction of the adrenal axis (primary AI) or of the hypothalamic-pituitary-adrenal axis (secondary AI).

Both result in glucocorticoid deficiency, requiring life-long replacement, with additional mineralocorticoid replacement required in primary AI. However, accurately reproducing the endogenous circadian and ultradian rhythm of cortisol secretion is challenging.

Current Endocrine Society guidelines recommend either hydrocortisone (thrice-daily) or once-daily prednisolone (3-5mg)<sup>1</sup>. Concerns around adverse metabolic outcomes associated with prednisolone have been based on evidence using higher prednisolone doses<sup>2</sup>. We have used low-dose (2-4mg) prednisolone once-daily since 2014 for glucocorticoid replacement in adults with AI. Since 2018 we have prospectively audited patients switched from hydrocortisone to prednisolone, and from prednisolone to hydrocortisone (HYPER-AID study (NCT03608943)).

## METHODS

Patients were clinically followed up at for least 4 months following the switch prior to repeat measurements being taken. Data was analysed using Microsoft Excel and GraphPad Prism version 9.3.1 (GraphPad, San Diego, CA,). Significance was assessed using paired t-tests, with significance defined at p<0.05.

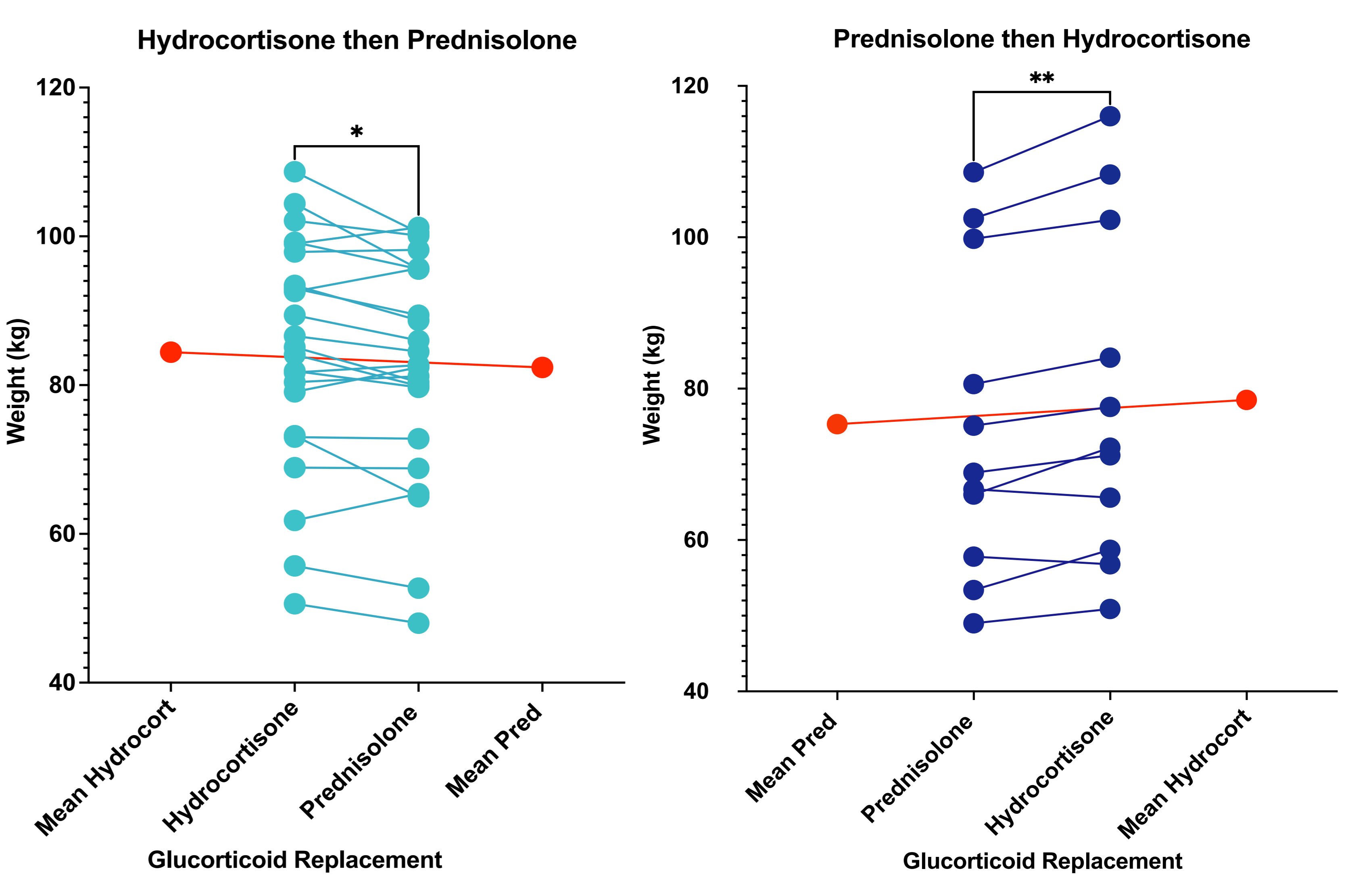
## RESULTS

Of the 23 patients who have completed both visits, 12 switched from hydrocortisone to prednisolone, and 11 from prednisolone to hydrocortisone.

The mean weights of patients on hydrocortisone and prednisolone were 80.2kg and 77.7kg respectively, with a difference of 2.6kg (p<0.01).

In those who switched from prednisolone to hydrocortisone, there was a significant weight gain of 3.2kg (p<0.004).

	Weight (kg) at baseline	Repeat weight (kg) at follow-up	Mean weight difference (kg) (SEM)	p-value
<b>All patients (n=34)</b>	82.5 on HC	80.1 on Pred	-2.43 (0.57)	p<0.001
<b>HC then Pred (n=23)</b>	84.4 on HC	82.4 on Pred	-2.06 (0.75)	p<0.02
<b>Pred then HC (n=11)</b>	75.3 on Pred	78.5 on HC	3.21 (0.84)	p<0.01



## DISCUSSION

The mechanism of the weight loss found with prednisolone may be due to overall less glucocorticoid exposure or because it mimics a more physiological circadian profile, avoiding supraphysiological cortisol levels later in the day<sup>4</sup>.

Once-daily low-dose prednisolone in the treatment of adrenal insufficiency is safe. Preliminary results of the HYPER-AID study suggest that prednisolone may have a beneficial effect on weight in those who are switched from hydrocortisone.

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