

# VITAMIN D LEVELS AND UVEITIS ACTIVITY: AN OBSERVATIONAL CASE-CONTROL STUDY

Zelia Karmen Chiu<sup>1</sup>, Sophie Rogers<sup>2</sup>, Ming-Lee Lin<sup>3,4</sup>, Robyn Troutbeck<sup>4</sup>, Cecilia Ling<sup>3,4</sup>, Lyndell Lim<sup>2,4</sup>, Anthony Hall<sup>3</sup>.

Monash University<sup>1</sup>, Clayton, Victoria; Centre for Eye Research Australia<sup>2</sup>, East Melbourne, Victoria; The Alfred Hospital<sup>3</sup>, Prahran, Victoria; Royal Victorian Eye and Ear Hospital<sup>4</sup>, East Melbourne, Victoria

## BACKGROUND

Vitamin D deficiency has been increasingly linked to the development of autoimmune conditions.<sup>1</sup> This association has been particularly strong with multiple sclerosis (MS).<sup>2</sup> There is a strong clinical link between MS and uveitis, and this has also been borne out of the experimental similarities between experimental autoimmune encephalomyelitis (EAE) and experimental autoimmune uveoretinitis (EAU), the animal models of MS and uveitis respectively.<sup>3</sup>

Experimental studies have demonstrated that calcitriol inhibits the development of EAU, and has the potential to reverse already-developed EAU.<sup>4</sup> Little research currently exists regarding the clinical relationship between serum vitamin D levels and uveitis activity.

**AIM: To investigate serum vitamin D levels in patients presenting with acute uveitis and compare them to levels of patients with inactive/chronic uveitis, and Victorian month-matched controls based on Australian government data**

## METHODS

A prospective observational case-control study. Patients were recruited from February to August 2017 inclusive, from the Royal Victorian Eye and Ear Hospital, The Alfred Hospital and Eye Surgery Associates in Melbourne, Australia.

Inclusion criteria:

- Noninfectious anterior, intermediate, posterior or panuveitis as diagnosed by a fellowship-trained ophthalmologist
- Able to provide informed consent
- Age >18yo

Exclusion criteria:

- Infectious or traumatic uveitis

Active uveitis was defined as activity (1+ cells or more on slit-lamp examination, as per SUN criteria<sup>5</sup>), up to 28 days prior to the serum vitamin D measurement.

All participants completed a questionnaire and had a serum vitamin D test.

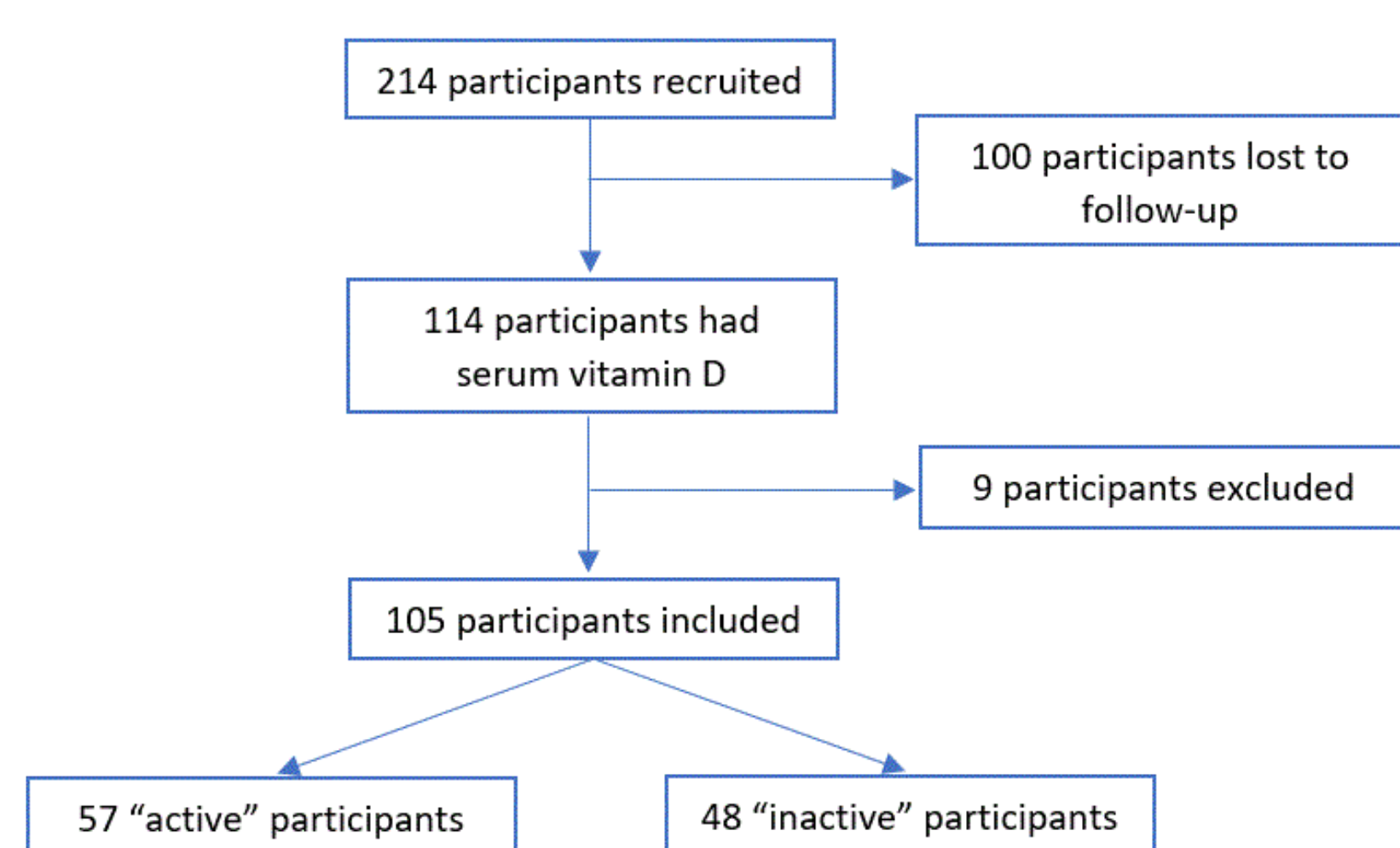


Figure 1: Flowchart of Methodology

Statistical analysis was performed using a statistical program (Stata/IC version 15.0). The Mann-Whitney U-test was used for testing the difference between vitamin D levels between active and inactive uveitic groups. The t-test and Fischer's exact tests were used to compare demographics.

## RESULTS

We recruited 214 patients, and included 105 participants in our study. Of these, there were 62 female participants. 57 participants were deemed active and 48 were deemed inactive (Table 1).

Table 1: Demographics of Participants

	Active	Inactive	p-value
N, no	57	48	
Age, mean (SD)	42.2 (14)	48.8 (15)	0.02
Male, n	23	20	0.891
Classification, n			0.659
Anterior	41	34	
Intermediate	8	7	
Posterior	1	3	
Panuveitis	5	3	
Vit D supplementation, n	14	15	0.552

Active uveitic patients recorded a significantly lower serum vitamin D level than inactive uveitic participants and matched controls from ABS data. This was found both throughout the study period (Fig 2) and when sub-grouped into months (Fig 3). These differences were significant (p = 0.01) (Table 2).

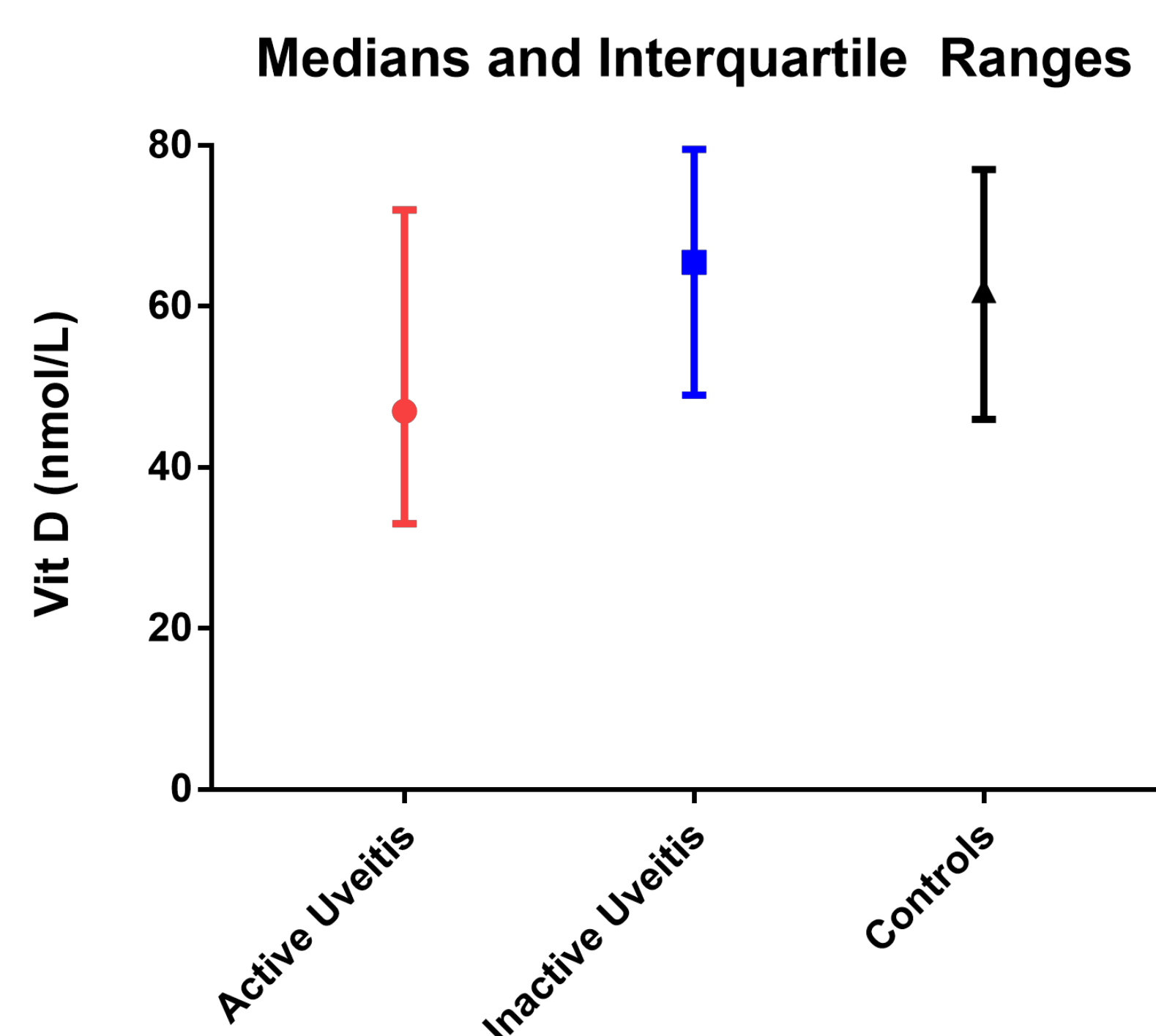


Figure 2: Medians and IQRs of Serum Vitamin D in Participants

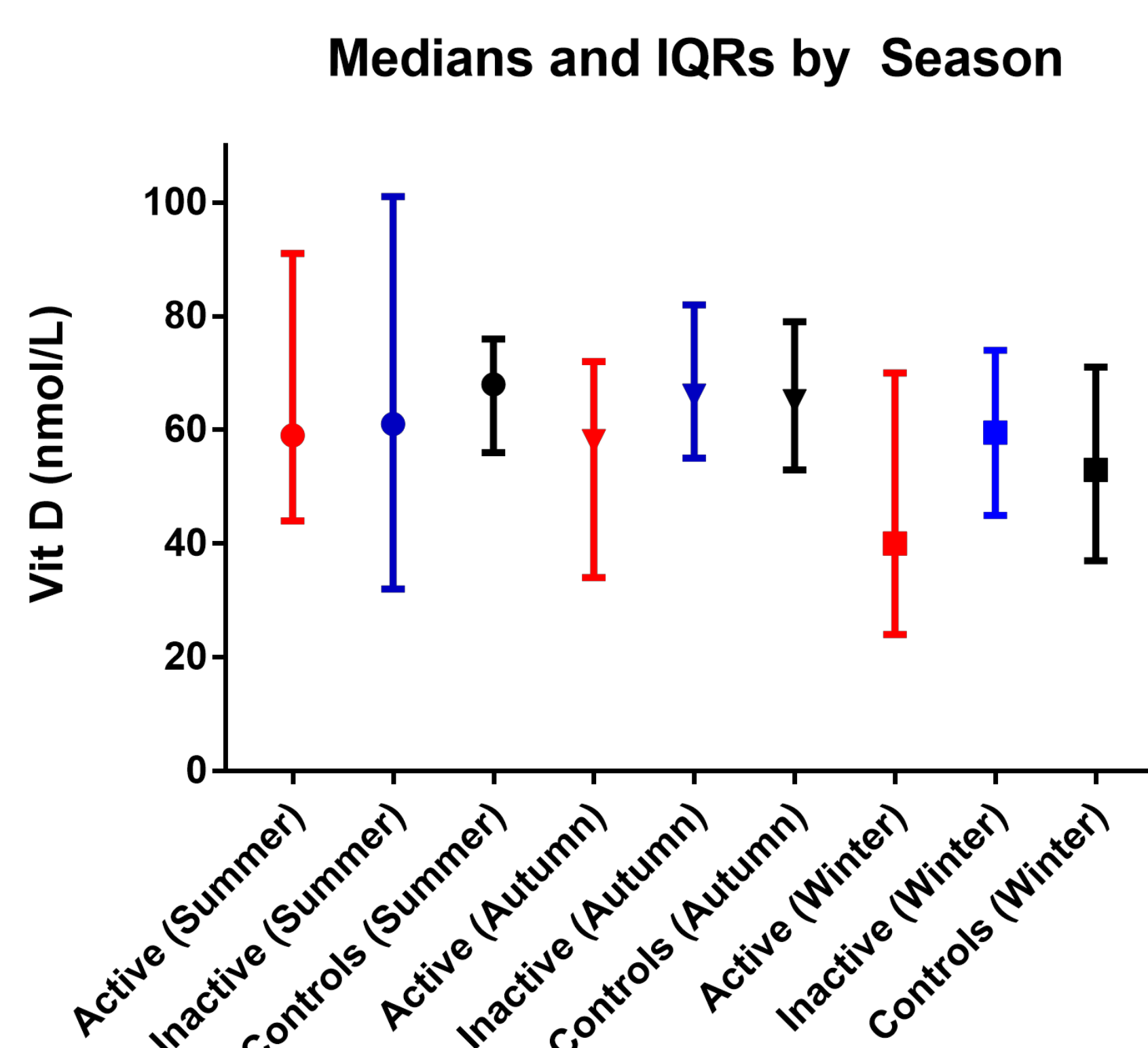


Figure 3: Medians and IQRs of Serum Vitamin D in Participants, Divided into Seasons

## CONCLUSION

To the best of our knowledge, this is the largest study demonstrating that patients with active uveitis have lower serum vitamin D levels than inactive and healthy controls. This indicates a potential relationship between low vitamin D levels and recurrence of uveitis.

Further studies are recommended to test the efficacy of vitamin D supplementation in decreasing relapse rates of uveitis, thereby having the potential to decrease poor visual outcomes for patients with recurrent uveitis.

Table 2: Vitamin D Levels and Uveitis Activity

Season	Group	n	Median (nmol/L)	p-value
All	Active	57	47	0.01
	Inactive	48	65.5	
	Control	594	62	
Summer	Active	7	54	0.909
	Inactive	3	61	
	Control	79	68	
Autumn	Active	29	58	0.029
	Inactive	31	66	
	Control	317	65	
Winter	Active	21	40	0.0424
	Inactive	14	59.5	
	Control	198	53	

## DISCUSSION

In this study, patients with active non-infectious uveitis were found to have significantly lower serum vitamin D levels than patients with inactive non-infectious uveitis and healthy controls. This expands on research conducted which found uveitic patients have lower serum vitamin D levels than healthy controls.<sup>6,7</sup>

MS has been associated with vitamin D deficiency, with both experimental and clinical studies demonstrating a strong link.<sup>2,8</sup> Notably, MS relapse rates have been shown to be inversely correlated with vitamin D levels.<sup>9</sup>

A longitudinal prospective study is recommended to confirm the causality of vitamin D levels in uveitis. Further to this, therapeutic trials of vitamin D supplementation are recommended to establish its efficacy in reducing relapse rates.

## REFERENCES

1. Perricone C, Agmon-Levin N, Shoenfeld Y. BMC Medicine. 2013;11:101.
2. Goldberg P. International Journal of Environmental Studies. 2007;6(1):19-27.
3. Calder VL, Lightman SL. Clinical and Experimental Immunology. 1992;89(2):165-9.
4. Tang J, Zhou R, Luger D, Zhu W, Silver PB, Grajewski RS, et al. J Immunol. 2009;182(8):4624-32.
5. The Standardization of Uveitis Nomenclature Working Group. American Journal of Ophthalmology. 2005;140(3):509-16.
6. Dadaci Z, Cetinkaya S, Acir NO, Oncel M, Borazan M. Ocular Immunology and Inflammation. 2016;1-5.
7. Grotting LA, Davoudi S, Palenzuela D, Papaliodis GN, Sobrin L. JAMA Ophthalmol. 2016.
8. Cantorna MT, Hayes CE, DeLuca HF. Proceedings of the National Academy of Sciences of the United States of America. 1996;93(15):7861-4.
9. Simpson S, Jr., Taylor B, Blizzard L, Ponsonby AL, Pittas F, Tremlett H, et al. Ann Neurol. 2010;68(2):193-203.

## ACKNOWLEDGEMENTS

This project was funded by the Alfred Hospital Ophthalmology Department SPF. CERA receives Operational Infrastructure Support from the Victorian Government