

# THE DEVELOPMENT OF ANTIVIRAL GUIDELINES FOR THE TREATMENT OF HERPES SIMPLEX KERATITIS

CATHY VLOUHOS<sup>1</sup>, JUDITH HAMPSON<sup>1</sup>, DR MARIA CABRERA-AGUAS<sup>2</sup>, PROF STEPHANIE WATSON<sup>1,2</sup>

1. SYDNEY AND SYDNEY EYE HOSPITAL, SYDNEY, NSW, AUSTRALIA  
2. SAVE SIGHT INSTITUTE, SYDNEY, NSW, AUSTRALIA

## Background

Herpes simplex keratitis (HSK) is the leading cause of infectious blindness in developed countries<sup>1</sup>. About one-fifth of people with ocular herpes virus infection develop HSK which is the blinding manifestation of the infection<sup>2</sup>.

Despite the impact of HSK in the population<sup>3</sup>, there have been limited randomised clinical trials to determine the best management to reduce visual loss. The Herpetic Eye Disease Study (HEDS) were a series of informative clinical trials conducted in the USA in the 1990s<sup>(4-7)</sup> that provided key evidence for management guidelines to reduce corneal scarring from HSK.

## Aim

To review the current prescribing trends in the treatment of Herpes Simplex Keratitis (HSK), compare these with published literature, develop and implement guidelines for use by ophthalmology medical officers for the treatment and management of HSK.

## Method

A retrospective audit of patients identified via viral swabs, ICD-10 coding and pharmacy dispensing records was undertaken for the period of January 2012 to December 2013. The initial antiviral treatment, length of treatment, outcomes and complications were documented. The initial antiviral treatment was compared to treatment recommendations published in the literature. Guidelines were then developed to standardise the treatment of HSK and these were implemented via numerous sources including the Intranet and the Sydney and Sydney Eye Hospital Ophthalmic Pharmacopoeia App.

## Results

A total of 305 eyes from 300 patients were identified as purely HSK and these were included in this review. Of these, 83% (n=254) received treatment dosing of antiviral therapy and 17% (n=51) received prophylactic antiviral therapy.

Treatment options were collated and reviewed with published clinical trials and systematic reviews. We found that 63% of prophylactic dosing and 57% of treatment dosing complied with published literature. Complications and side effects of treatment were seen in approximately 7% of patients on treatment doses and 12% on prophylaxis.

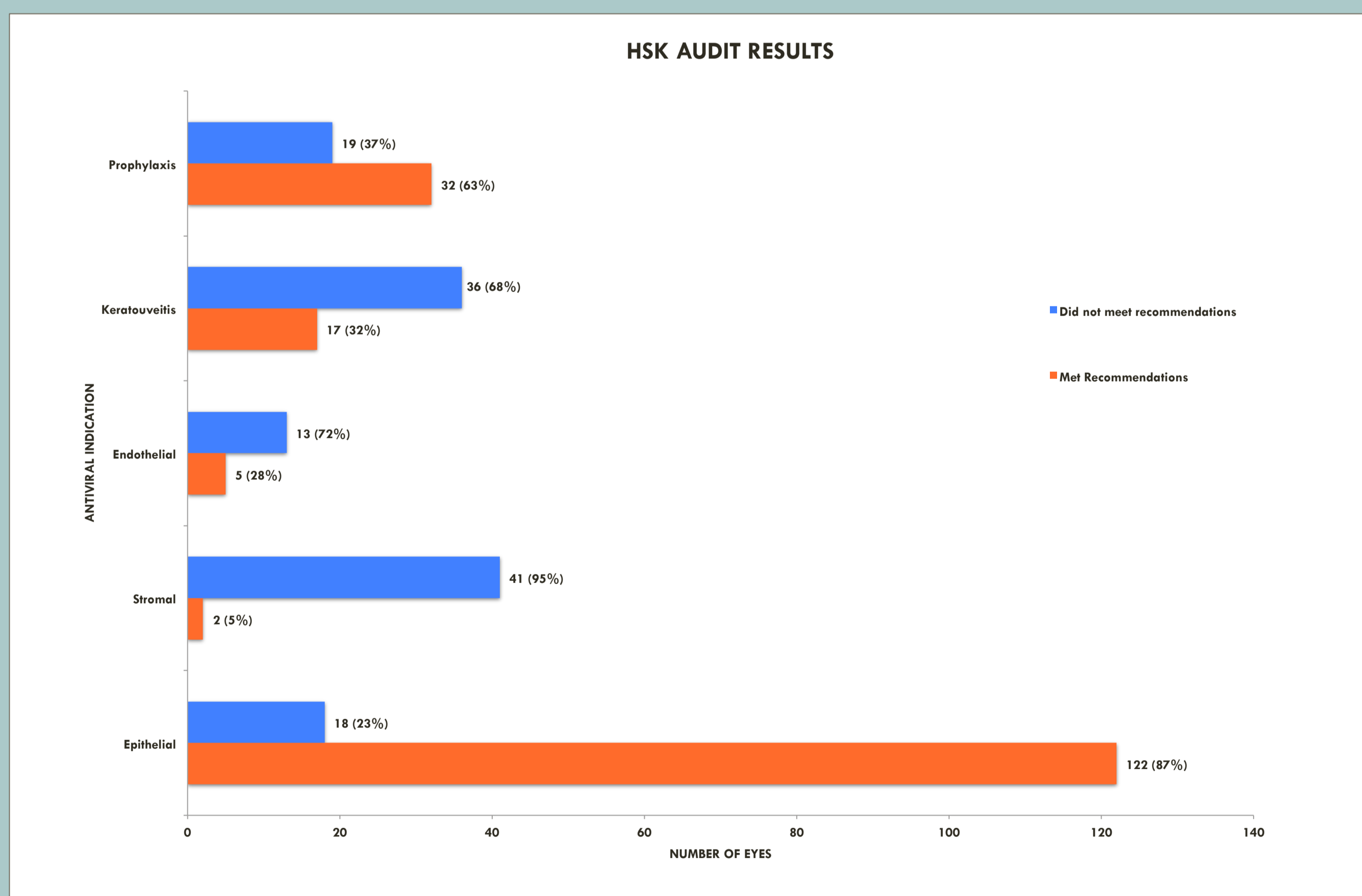
## Guideline Development and Implementation

### Guideline development involved:

1. Extensive literature review
2. Meetings with the corneal and uveitis department
3. Advice from the Pharmacy Department
4. Endorsement by the hospital Drug and Therapeutics Committee

### Implementation included:

1. Education sessions for all ophthalmology registrars
2. Guideline cards printed and laminated for lanyards
3. Laminated A4 versions of the guidelines to be available in all ophthalmology clinic rooms and wards
4. Full guideline document to be included on the hospital Intranet and be uploaded on the Sydney Eye Hospital Ophthalmic Pharmacopoeia App



Herpes Simplex Keratitis (HSK) Treatment Guidelines		
ADULTS		
Epithelial	Local treatment: Topical aciclovir 5 times a day for 14 days	Systemic treatment: • Immunocompromised patients • Non-compliance, inability to use or tolerate, or ocular toxicity from topical aciclovir Valaciclovir 500 mg BD for 7 days
	Without epithelial ulcers: Valaciclovir 500 mg ONCE a day during topical steroid use PLUS Prednefrin Forte eye drops 4-6 times a day tapered over > 10 weeks	With epithelial ulcers: Valaciclovir 1 g TDS for 7-10 days * PLUS Prednefrin Forte eye drops BD tapered slowly as disease comes under control
Stromal	Without epithelial ulcers: Valaciclovir 500 mg ONCE a day during topical steroid use PLUS Prednefrin Forte eye drops 4-6 times a day tapered over > 10 weeks	With epithelial ulcers: Valaciclovir 1 g TDS for 7-10 days * PLUS Prednefrin Forte eye drops BD tapered slowly as disease comes under control
Endothelial	PLUS Prednefrin Forte eye drops 4-6 times a day tapered over > 10 weeks	
Keratouveitis	Valaciclovir 1 g TDS for 7-10 days * PLUS Prednefrin Forte eye drops 4-6 times a day tapered over > 10 weeks	Refer patient to cornea/uveitis clinic, respectively depending on degree of cornea or uveal involvement
	Indications: • Multiple recurrences of any type of HSK, especially stromal HSK • Patients with a history of ocular HSV: - following any ocular surgery, including penetrating keratoplasty - during immunosuppressive treatment	
Prophylaxis	Aciclovir 400 mg BD OR Valaciclovir 500 mg ONCE a day	
	* Reduce Valaciclovir to prophylactic dose after 7-10 days and maintain for as long as frequent topical steroids are in use	
Adult Renal Dosing for oral antivirals		
CrCl (mL/min)	Dose	Frequency
<30	Normal dosage Valaciclovir 500 mg ONCE a day	
	500 mg	Every 48 hours
<30	Normal dosage Valaciclovir 500 mg BD	
	500 mg	Every 24 hours
30-49	Normal dosage Valaciclovir 1 g TDS	
	1 g	Every 12 hours
10-29	1 g	Every 24 hours
<10	500 mg	Every 24 hours
0-10	Normal dosage Aciclovir 400 mg BD	
	200 mg	Every 12 hours

Use in Pregnancy	
Aciclovir – Preferred due to more clinical experience. Category B3. Valaciclovir – Limited data do not suggest an increased risk of congenital malformations. May be used from 36 weeks of pregnancy. Category B3.	
PAEDIATRIC	
• Aciclovir is the drug of choice • Valaciclovir must only be used in children >12 years old	
Local treatment	
3 months to 18 years	Epithelial HSK: Topical aciclovir 5 times a day for 14 days <sup>1,2</sup> or for at least 3 days after healing, whichever is shorter
Systemic treatment	
Indications: • Stromal HSK • Skin involvement • Coexistent systemic disease • Non-compliance, inability to use or tolerate, or ocular toxicity from topical aciclovir • Immunocompromised patients – seek advice from a Paediatric Infection Diseases Physician	
Birth (at term) to 3 months	Seek advice from a Paediatric Infection Diseases Physician
3 months to 12 years	Oral aciclovir 10 mg/kg (max 400 mg) 5 times a day for 5-7 days <sup>1</sup> or until there are no new lesions PLUS Prednefrin Forte eye drops BD-QID a day. (For severe inflammation, consider hourly dosing for 1-2 days <sup>1</sup> )
12 years to 18 years	Oral aciclovir 10 mg/kg (max 400 mg) 5 times a day for 5-7 days <sup>1</sup> or until there are no new lesions OR Valaciclovir 500 mg BD for 5 days <sup>2</sup> if first episode (longer if new lesions appear during treatment or healing is incomplete) Valaciclovir 500 mg BD for 3-5 days <sup>2</sup> if recurrent episode PLUS Prednefrin Forte eye drops BD-QID a day. (For severe inflammation, consider hourly dosing for 1-2 days <sup>1</sup> )
<sup>1</sup> Dosages taken from Australian Medical Handbook Children's Dosing Companion <sup>2</sup> Dosages taken from British National Formulary for children	
Lanyard produced by the Save Sight Institute, Sydney Eye Hospital and SESLHD Sponsored by a grant from the Sydney Eye Hospital Foundation	

## Conclusion

Herpes Simplex Keratitis (HSK) is a common ophthalmic presentation at Sydney and Sydney Eye Hospital. Our audit results identified the need for standardisation of the treatment and management of HSK. Collaboration with ophthalmologists in the corneal and uveitis units led to the development and implementation of accessible, easy to follow, standardised guidelines for the treatment and management of HSK at Sydney and Sydney Eye Hospital.

## References

1. Cochrane review: Kirk R. Wilhelmus, 2011
2. Systematic review: Guess et al, Evidence-based treatment of herpes simplex keratitis: A systematic review. Ocul Surf 2007;5,240
3. Herpetic Eye Disease Study (HEDS):HEDS I: Arch Ophthal 1997;115:703-12
4. HEDS II: Ophthal 1994;101:1883-96 HEDS III: Ophthal 1994;101:1871-82
5. HEDS IV: Arch Ophthal 1996;114:1035-72, HEDS V: Arch Ophthal 2000;118:1030-36
6. American Academy Ophthalmology: White ML, Chodosh J. Herpes Simplex Keratitis: a treatment guideline. 2014

## Acknowledgements

Save Sight Institute of NSW  
Sydney Eye Hospital Foundation  
Corneal and Uveitis Units, Sydney and Sydney Eye Hospital



Sydney Hospital and  
Sydney Eye Hospital

