Systematic Literature Review of Herpes Zoster Disease Burden in Southeast Asia

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SUPPLEMENTARY MATERIALS

Supplementary Table 1. Keywords used in the search strategy

Database	**Strategy**
PubMed	Main terms: (Herpes zoster OR shingles OR zoster* OR postherp* OR herpes zoster ophthalmicus OR disseminated herpes zoster) AND Combined terms: ((Epidem* OR incidence* OR prevalence OR morbidity rate OR mortality rate OR hospitalization OR rate OR ratio OR "burden of disease" OR surveillance OR case-fatality) OR ("clinical pathway" OR "patient pathway" OR "natural history" OR diagnosis OR treatment OR guideline OR management OR "quality of life" OR "quality adjusted life years" OR QALY) OR ("health care resource utilization" OR antiviral* OR cost* OR economic* OR "hospital resources" OR "hospital*" OR "general practitioner" OR acyclovir OR acyclovir OR valaciclovir OR valacyclovir OR famciclovir OR famcyclovir OR penciclovir OR pencyclovir OR desciclovir OR descyclovir OR "medical savings*" OR "treatment cost" OR "health economics" OR "healthcare financing")) AND Location: ("southeast asia*" OR malaysia* OR Indonesia* OR philippines OR filipino OR singapore* OR thai OR thailand OR Vietnam* OR "Viet Nam")
Embase	Main terms: *add field: ab,ti('herpes zoster':ab,ti OR shingles:ab,ti OR zoster*:ab,ti OR postherp*:ab,ti OR 'herpes zoster ophthalmicus':ab,ti OR 'disseminated herpes zoster':ab,ti) AND Combined terms:

	('clinical pathway':ab,ti OR 'patient pathway':ab,ti OR 'natural history':ab,ti OR diagnosis:ab,ti OR treatment:ab,ti OR guideline:ab,ti OR management:ab,ti OR 'quality of life':ab,ti OR 'quality adjusted life years':ab,ti OR qaly:ab,ti OR epidem*:ab,ti OR incidence*:ab,ti OR prevalence:ab,ti OR 'morbidity rate':ab,ti OR 'mortality rate':ab,ti OR hospitalization:ab,ti OR rate:ab,ti OR ratio:ab,ti OR 'burden of disease':ab,ti OR surveillance:ab,ti OR 'health care resource utilization':ab,ti OR 'antiviral*':ab,ti OR cost*:ab,ti OR economic*:ab,ti OR 'or hospital resources':ab,ti OR 'hospital*':ab,ti OR 'general practitioner':ab,ti OR acyclovir:ab,ti OR valaciclovir:ab,ti OR valacyclovir:ab,ti OR famciclovir:ab,ti OR famcyclovir:ab,ti OR penciclovir:ab,ti OR pencyclovir:ab,ti OR desciclovir:ab,ti OR descyclovir:ab,ti OR 'medical savings*':ab,ti OR 'treatment cost':ab,ti OR 'health economics':ab,ti OR 'healthcare financing':ab,ti) <u>AND Location:</u> ('southeast asia*':ab,ti OR malaysia*:ab,ti OR indonesia*:ab,ti OR philippines:ab,ti OR filipino:ab,ti OR singapore*:ab,ti OR thai:ab,ti OR thailand:ab,ti OR vietnam*:ab,ti OR 'viet nam':ab,ti)
Scopus	<u>Main terms:</u> ALL (zoster OR shingles OR postherp*) <u>AND Location</u> ALL ('southeast AND asia*' OR malaysia* OR indonesia* OR philippines OR filipino OR singapore* OR thai OR thailand OR vietnam* OR 'viet AND nam')

Supplementary Table 2. Inclusion and exclusion criteria

	Inclusion Criteria	Exclusion Criteria
Abstract	• Available	• Not available
Scope	• Research focus on HZ	• Research unrelated to HZ, outside the scope of the study endpoints, or with no clear case definition for HZ
Location	• South East Asia (Indonesia, Malaysia, Philippines, Singapore, Thailand, Vietnam)	• Outside the geographical scope of Southeast Asia
Population	• Immunocompetent ≥50 years (no age limit for seroprevalence studies) • Immunocompromised ≥18 years	• Pediatric population (<18 years old)
Study type	• Peer-reviewed observational, cross-sectional, ecological, systematic review (with new unreported data), meta-analysis, survey, supranational report, case series, and case report studies • Qualitative or quantitative	• Study type not within scope (e.g., clinical trials, interventional studies, editorials, commentaries, and systematic literature reviews [without new data included]) • Non-human or preclinical studies
Language	• English or English translated abstract for local publications	• Abstract and full-text presented in non-English

HZ: herpes zoster.

Supplementary Table 3. Results of quality assessment for observational studies (n=44)

Study Details			Major Criteria			Minor Criteria		Overall Assessment	
Reference	**Design**	**Sampling**	**Methods for selecting study participants**	**Methods for measuring exposure and outcome variables**	**Methods to control confounding**	**Design-specific sources of bias**	**Statistical methods**	**Risk of Bias**	**Quality**
Aunhachoke et al. 2011 [1]	Prospective cohort	Non-Probabilistic	Low	Moderate	Low	Moderate	Low	Moderate	Moderate
Adinda et al. 2015 [2]	Cross-sectional	Non-Probabilistic	Moderate	Moderate	High	High	Low	High	Low
Chayangsu et al. 2016 [3]	Cross-sectional	Non-Probabilistic	Moderate	High	Low	High	Low	High	Low
Chen et al. 2015 [4]	Retrospective cohort	Non-Probabilistic	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Chitasombat and Watcharananan 2016 [5]	Retrospective cohort	Non-Probabilistic	Low	Low	Moderate	Moderate	Low	Moderate	Moderate
Chow 1998 [6]	Cross-sectional	Non-Probabilistic	High	Moderate	Low	Low	Low	High	Low
Chuanchaiyakul 2022 [7]	Nested case-control study	Non-Probabilistic	Low	Low	Moderate	Moderate	Low	Moderate	Moderate
Dashraath et al. 2007 [8]	Cross-sectional	Non-Probabilistic	Moderate	Low	Low	Low	Low	Moderate	Moderate
Dela Cruz-Tan 2017 [9]	Retrospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Dilly et al. 2016 [10]	Cross-sectional	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Dwiyana et al. 2009 [11]	Cross-sectional	Non-Probabilistic	Low	Low	Moderate	Moderate	Low	Moderate	Moderate
Fatha et al. 2014 [12]	Cross-sectional	Non-Probabilistic	Low	Moderate	Low	Low	Moderate	Moderate	Moderate
Follézou et al 1999 [13]	Cross-sectional	Non-Probabilistic	Low	Low	Low	Moderate	Moderate	Moderate	Moderate
Hidayati 2017 [14]	Cross-sectional	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Hoài 2012 [15]	Cross-sectional	Non-Probabilistic	Low	Low	Moderate	Moderate	Low	Moderate	Moderate
Jara and Roa 2010 [16]	Cross-sectional	Non-Probabilistic	Moderate	Low	Low	Low	Low	Moderate	Moderate
Juffrie et al. 2000 [17]	Cross-sectional	Non-Probabilistic	Moderate	Low	Low	Low	Low	Moderate	Moderate

Kowitdamrong et al. 2005 [18]	Cross-sectional	Non-Probabilistic	Moderate	Low	Low	Low	Low	Moderate	Moderate
Lolekha et al. 2001 [19]	Cross-sectional	Non-Probabilistic	Moderate	Low	Low	Low	Low	Moderate	Moderate
Low et al. 2013 [20]	Retrospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Migasena et al. 1997 [21]	Cross-sectional	Non-Probabilistic	Low	Low	Moderate	Low	Low	Low	High
Mok and Tan 2013 [22]	Retrospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
My 2020 [23]	Prospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
My 2020 [24]	Prospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Oh et al. 1997 [25]	Retrospective cohort	Non-Probabilistic	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Ooi et al. 1992 [26]	Cross-sectional	Non-Probabilistic	Low	Moderate	Low	Low	Low	Moderate	Moderate
Putri Mellaratna et al. 2020 [27]	Cross-sectional	Non-Probabilistic	Low	Low	Moderate	Low	Moderate	Moderate	Moderate
Sam et al. 2008 [28]	Cross-sectional	Non-Probabilistic	High	Moderate	Low	Moderate	Low	High	Low
Sermswan 2010 [29]	Cross-sectional	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Shaharir et al. 2021 [30]	Retrospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Sivayathorn et al. 1995 [31]	Cross-sectional	Non-Probabilistic	Low	Low	Moderate	Low	Moderate	Moderate	Moderate
Soong 2021 [32]	Cross-sectional	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Supanaranond et al. 2001 [33]	Retrospect and prospective cohort	Non-Probabilistic	Low	Moderate	Moderate	Moderate	Low	High	Low
Suwanpakdee et al. 2012 [34]	Cross-sectional	Non-Probabilistic	Moderate	Low	Low	Low	Low	Moderate	Moderate
Tan et al. 2014 [35]	Prospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Tan et al. 2014 [36]	Retrospective cohort	Non-Probabilistic	Low	Low	Moderate	Moderate	Low	Moderate	Moderate
Tan et al. 2013 [37]	Retrospective cohort	Non-Probabilistic	High	Low	Moderate	Moderate	Low	High	Low
Taylor et al. 2012 [38]	Prospective cohort	Non-Probabilistic	Moderate	Moderate	Low	Low	Low	Moderate	Moderate

Tunsuriyawong 2005 [39]	Retrospective cohort	Non-Probabilistic	Low	Moderate	Moderate	Moderate	Low	Moderate	Moderate
Wang et al. 2009 [40]	Retrospective cohort	Non-Probabilistic	Low	Low	Low	Moderate	Low	Low	High
Watcharananan et al. 2012 [41]	Prospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Wijaya 2016 [42]	Prospective cohort	Non-Probabilistic	NA	NA	NA	NA	NA	NA	NA
Wiwanitkit 2004 [43]	Cross-sectional	Non-Probabilistic	Low	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Zamora et al. 2020 [44]	Case control	Non-Probabilistic	Low	Low	Low	Low	Low	Low	High

NA: not applicable.

Supplementary Table 4. Case reports and series involving HZ in Southeast Asia

Country	Reference	Age (Sex)	Risk Factors and Comorbidities	Complication
Singapore	Chiew et al. 2022 [45]	65 (F)	Immunocompromised with poorly controlled diabetes mellitus, antisynthetase syndrome, and mycophenalate treatment	HZO with orbital apex syndrome
Singapore	Goh et al. 2019 [46]	76 (M)	Immunocompromised with ischemic heart disease, diabetes mellitus, hypertension, and dyslipidemia	Syndrome of inappropriate antidiuretic hormone secretion
Singapore	Jun et al. 2018 [47]	67 (M)	Immunocompromised with poorly controlled diabetes mellitus and hypertension, hyperlipidemia, and ischemic heart disease	Orbital apex syndrome
Singapore	Lee et al. 2021 [48]	79 (M)	NR	Asymmetrical oligoarthritis
Singapore	Lim et al. 2005 [49]	41 (M)	Transient decrease in CD4 lymphocyte counts and CD4/CD8 ratio	Progressed from outer retinitis with features of progressive outer retinal necrosis to typical acute retinal necrosis
Singapore	Lim and Tey 2018 [50]	64 (M)	Immunocompromised with arteriovenous malformation resulting to epilepsy	HSV and VZV co-infection
Singapore	Tan et al. 2012 [51]	40 (F)	HIV	Extraocular myositis
Singapore	Tan et al. 2021 [52]	80 (M)	Diabetes mellitus, hypertension, hyperlipidemia, and ischemic heart disease	Abdominal pseudohernia
Singapore	Teo et al. 2016 [53]	74 (M)	Diabetes mellitus, hypertension, and ischemic heart disease	Segmental zoster paresis
Thailand	Amonchaisakda and Leeyaphan 2021 [54]	48 (F)	Immunocompromised with SLE	HZ duplex (after recurrent varicella)
Thailand	Chotmongkol and Phankingthongkum 1992 [55]	54 (F)	NR	HZ myelitis
Thailand	Jiravichitchai et al. 2021 [56]	31 (F)	Immunocompromised	Distal neuropathy
Thailand	Siritho et al. 2015 [57]	43 (F)	NR	HZO affecting the trigeminal tract and brainstem nuclei
Thailand	Siwamogstham et al. 2006[a] [58]	30[b] (2x M and 2x F)	HIV	Osteonecrosis of the jaw and tooth exfoliation
Thailand	Vanikieti et al. 2018 [59]	58 (F)	NR	Optic neuritis

Indonesia	Adiguna et al. 2020 [60]	75 (M)	Malnourishment	HZO
Indonesia	Suwenny and Halim 2021 [61]	43 (F)	COVID-19 infection	NR
Malaysia	Ahmad et al. 2019 [62]	40 (M)	No risk factors noted (immunocompetent)	Neovascular glaucoma
Malaysia	Lim et al. 2018[a] [63]	77 (F) and 65 (M)	Hypertension, diabetes mellitus, and tocilizumab treatment	Orbital apex syndrome
Malaysia	Othman et al. 2017 [64]	59 (F)	Diabetes mellitus	Hyphema and orbital apex syndrome
Malaysia	Suraiya et al. 2003 [65]	25 (F)	Pregnant with SLE	Bilateral optic neuritis
Philippines	Ramos and Robredo-vitas 2020 [66]	32 (M)	HIV and hepatitis B	Disseminated VZV

[a]Case series; [b]Mean age of patients. HIV: human immunodeficiency virus; HSV: herpes simplex virus; HZ: herpes zoster; HZO: HZ ophthalmicus; NR: not reported; PHN: postherpetic neuralgia; SLE: systemic lupus erythematosus; VZV: varicella zoster virus.

Supplementary Table 5. Proportion of prodromal symptoms in patients with HZ in Southeast Asia

Country	Reference	N	Pain	Itching	Paresthesia	Insomnia
Singapore	Chen et al. 2015 [4]	347	81.8%[a]	15.9%[a]	NR	4.3%[a]
Singapore	Goh and Khoo 1997 [67]	164	41%	27%	12%	NR
Thailand	Chayangsu et al. 2016 [68]	118	53.4%	NR	NR	NR
Philippines	Jara and Roa 2010 [16]	221	24%	NR	NR	NR
Vietnam	Haoi 2012 [69]	71	90.14%[b]	NR	NR	NR

Data presented as the proportion of HZ patients unless stated otherwise. [a]Proportion of patients with prodrome; [b]Proportion of hospital inpatients with HZ. HZ: herpes zoster; NR: not reported.

Supplementary Table 6. Anatomical distribution of HZ skin lesions in Southeast Asian patients

Country	Reference	N	Dermatome with Skin Lesions					
			Thoracic	Lumbar	Cervical	Cranial	Sacral	>1 Dermatome
Singapore	Chen et al. 2015 [4]	347	41.2%	17.3%	16.4%	11% (ophthalmic), 7.5% (maxillary)	6.9%	NR
Singapore	Goh and Khoo 1997 [67]	164	45%	15%	23%	3% (ophthalmic), 9% (maxillary)	6%	NR
Singapore	Oh et al. 1997 [70]	2,262[a]	41.8%	10.4%	23.8%	23.8% (trigeminal)	NR	NR
Singapore	Mok and Tan 2013 [22]	421	46.8%	19.2%	NR	25% (trigeminal)	NR	17.8%
Thailand	Aunhachoke et al. 2011 [71]	180	43.9%	14.4%	22.8%	13.9%	5%	NR
Thailand	Chayangsu et al. 2016 [68]	118	46.2%	15.1%	15.1%	16%	7.6%	NR
Thailand	Tunsuriyawong and Puavilai 2005 [39]	399	64% (trunk)	NR	NR	36% (face)	NR	NR
Philippines	Jara and Roa 2010 [16]	221	52%	23.5%	17.2%	1.81%	2.72%	1.35%
Indonesia	Dilly et al. 2016 [10]	28	46.43%	10.71%	3.57%	28.57% (ophthalmic)	10.71%	NR
Malaysia	Soong et al. 2021 [32]	88	48%	NR	NR	29% (trigeminal)	NR	NR
Vietnam	Haoi 2012 [69]	71	39%	10%	8% (arms)	37%	6% (knees)	NR

[a]Represents all patients admitted to a hospital, not limited to HZ. HZ: herpes zoster; NR: not reported.

Supplementary Table 7. Occurrence of symptoms associated with HZ skin lesions in Southeast Asian patients

Country	Reference	N	Pain	Tenderness	Itching	Fever	Other
Singapore	Chen et al. 2015 [4]	347	85.9%	NR	NR	NR	Insomnia (4%)
Singapore	Mok and Tan 2013 [22]	421	81.7%	NR	NR	NR	NR
Singapore	Goh et al. 1997 [67]	164	90%	NR	NR	12%	Stress (20%), fatigue (7%), depressed (7%)
Singapore	Oh et al. 1997 [70]	2,262[a]	76.1%	1.5% (dysthesia)	9%	25.4%	Headaches (11.9%)
Philippines	Jara and Roa 2010 [16]	221	74.21%	11.76%	30.77%	9.95%	Malaise (3.17%), allodynia (2.71%), myalgia (1.81%), headaches (1.35%), paresthesia (0.45%)
Vietnam	Haoi 2012 [69]	71	100%	NR	NR	8.45%	Lymphadenopathy (63.4%), fatigue (16.9%)

[a]Represents all patients admitted to a hospital, not limited to HZ. HZ: herpes zoster; NR: not reported.

Supplementary Table 8. Therapies used to treat HZ in Southeast Asia

Country	Reference	N	Antiviral Use	Pain Reliever Use	Other Treatments
Singapore	Chen et al. 2015 [4]	347	84.4% (70.9% acyclovir)	55.6% (amitriptyline [25.4%], gabapentin [21.9%], tramadol [16.4%], paracetamol [13.5%], and oral nonsteroidal anti-inflammatory drugs [7.8%])	NR
Singapore	Mok and Tan 2013 [22]	164	NR	No proportion of usage was reported, but analgesia and psychotropic drugs were found to provide pain relief in 71.4%	NR
Thailand	Aunhachoke et al. 2011 [71]	180	85.6% (at first visit)	NR	NR
Thailand	Chayangsu et al. 2016 [68]	118	98.3% (systemic acyclovir)	60.2% (e.g. acetaminophen)	Anxiolytic (78%), Vitamin B complex (50.8%), topical antibiotics (76.3%)
Indonesia	Dilly et al. 2016 [10]	28	85.71% (antiviral alone)	NR	Antiviral and antibiotics (14.29%)
Philippines	Jara and Roa 2010 [16]	221	61.9% (52.6% valaciclovir vs 47.4% acyclovir)	76% (paracetamol and gabapentin most common)	Antihistamine (5.9%), Antibiotics (32.1%)

HZ: herpes zoster; NR: not reported.

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