

Dengue: the disease and epidemiology



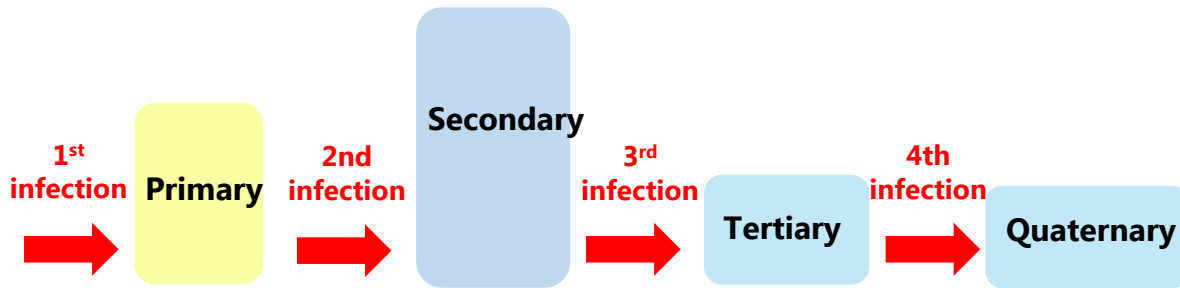
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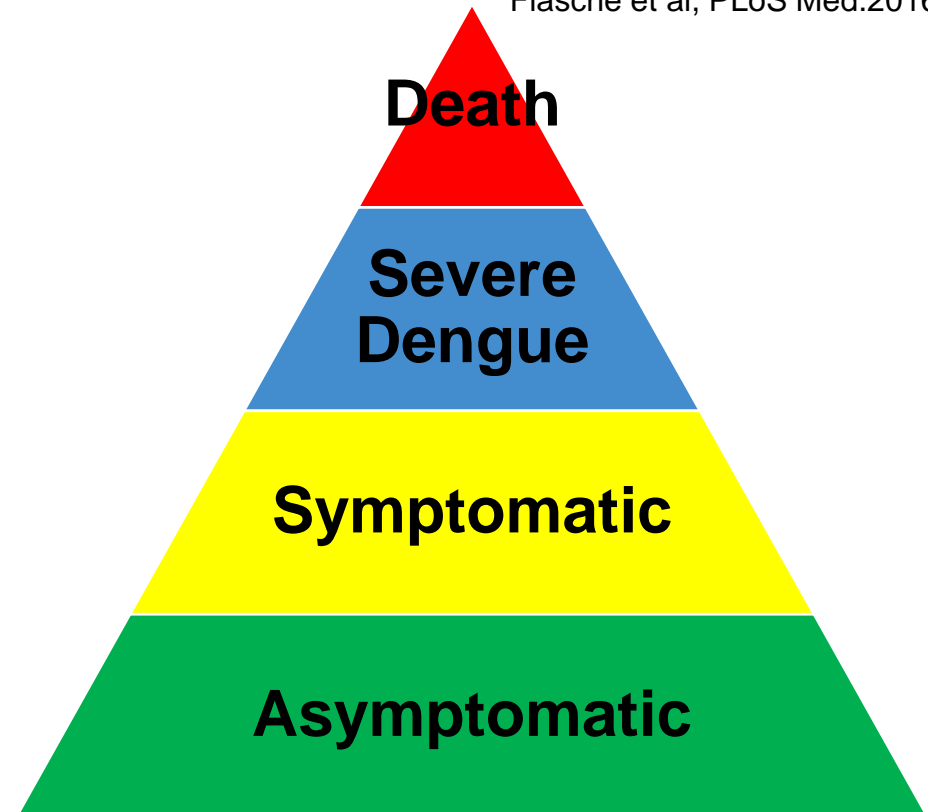
Dengue

- Rapidly expanding arboviral disease transmitted by *Aedes* mosquitoes

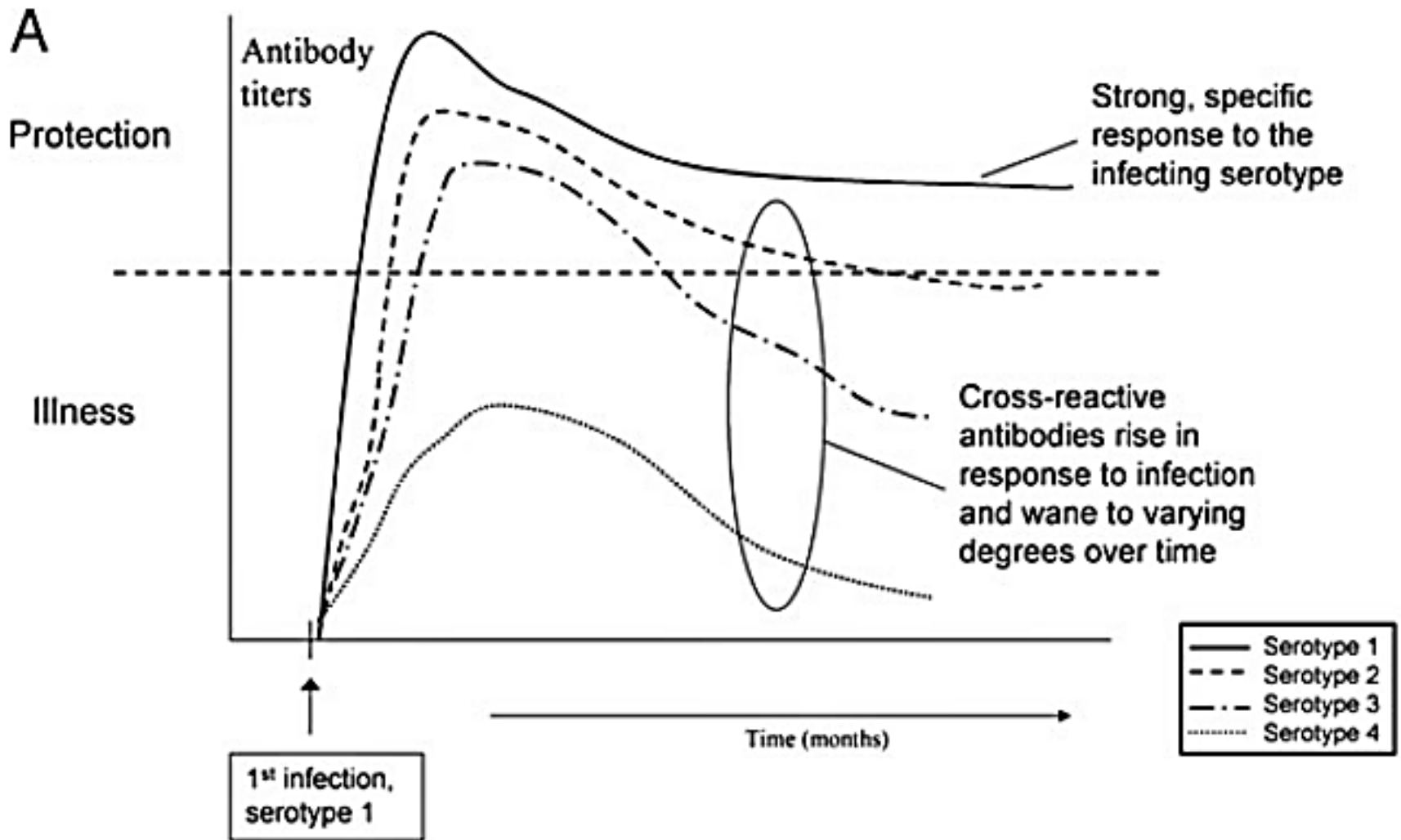


- 50 fold increase in past 50 years
- Four antigenically distinct serotypes (DENV1-4)
- Clinical spectrum:
 - 80% asymptomatic
 - Self-limiting febrile illness
 - Severe dengue (~2-4% of symptomatic)
 - Secondary infections are associated with higher risk of more severe dengue
 - CFR 0.1—1%

Flasche et al, PLoS Med.2016



Homotypic and heterotypic immunity



Anderson et al, A Shorter Time Interval Between First and Second Dengue Infections Is Associated With Protection From Clinical Illness in a School-based Cohort in Thailand. J Inf Dis. 2014

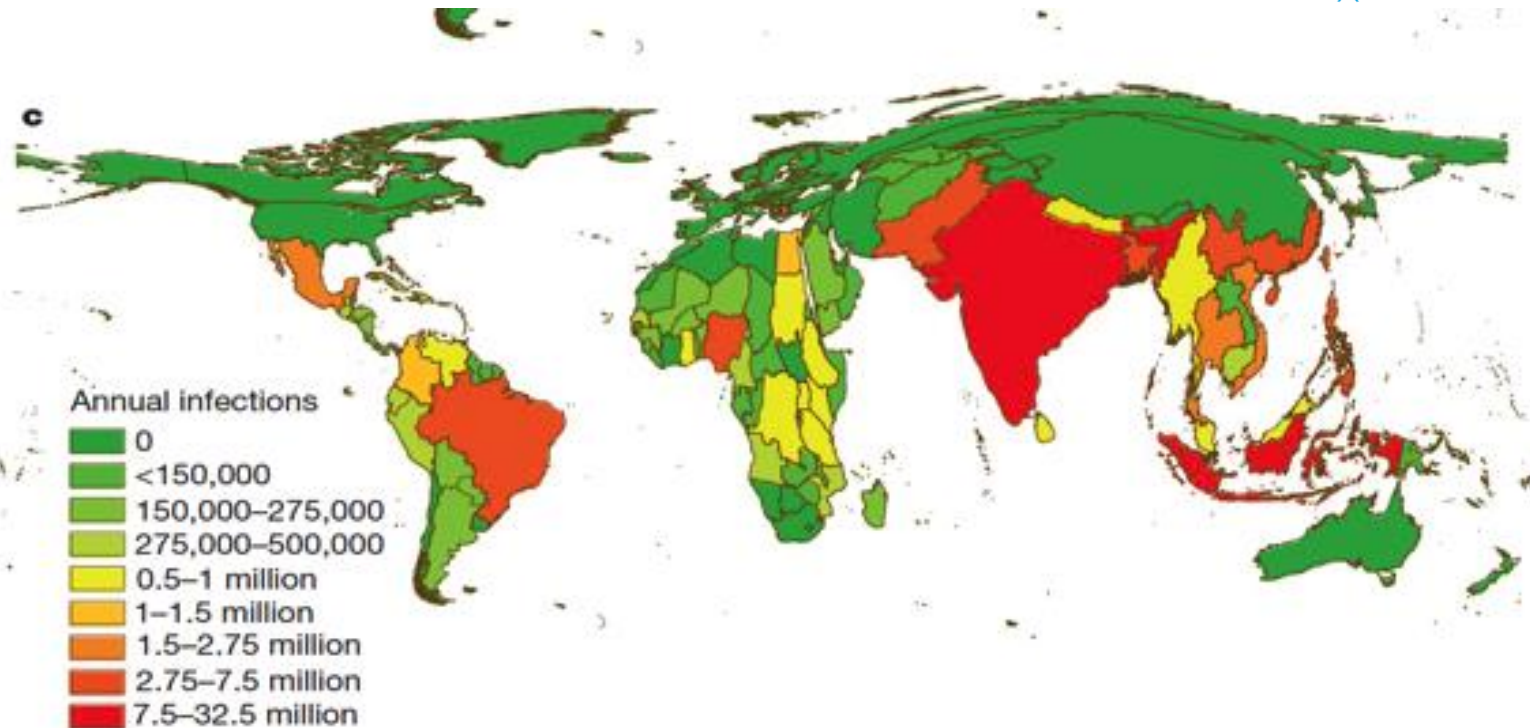
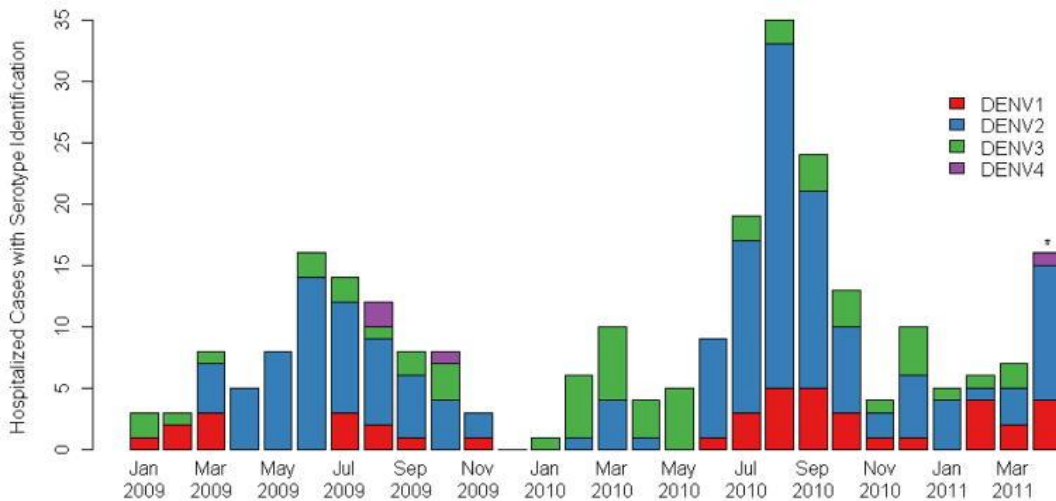


Table 1 | Estimated burden of dengue in 2010, by continent

	Apparent	Inapparent
	Millions (credible interval)	Millions (credible interval)
Africa	15.7 (10.5–22.5)	48.4 (34.3–65.2)
Asia	66.8 (47.0–94.4)	204.4 (151.8–273.0)
Americas	13.3 (9.5–18.5)	40.5 (30.5–53.3)
Oceania	0.18 (0.11–0.28)	0.55 (0.35–0.82)
Global	96 (67.1–135.6)	293.9 (217.0–392.3)

Temporal and spatial heterogeneity of dengue transmission

Spatial heterogeneity at small scale



Salje et al. Dengue diversity across spatial and temporal scales. Science 2017

Yoon et al. Fine scale spatiotemporal clustering of dengue virus transmission in rural Thai villages. PLoS Negl Trop Dis 2012

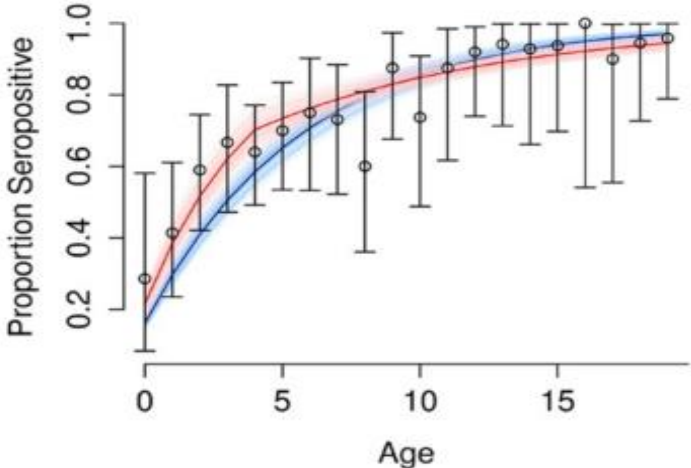
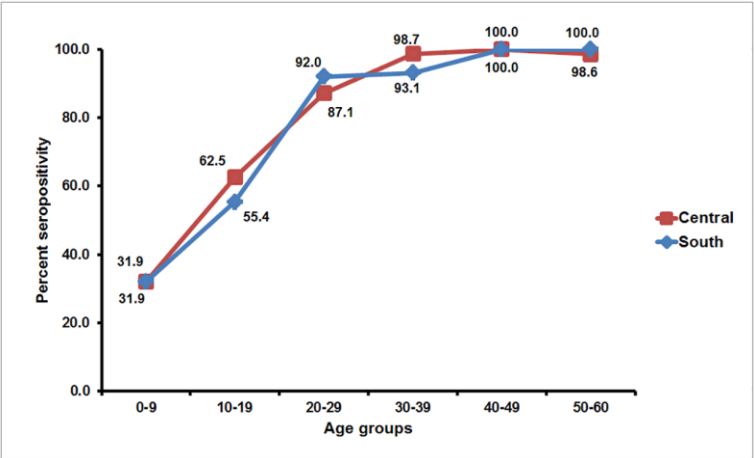
Spatial heterogeneity dependent on socioeconomic factors, population density, ecological factors:

Kamphaeng Phet, Thailand, school based cohort study:

Altstadt et al. **Space-time analysis of dengue in rural Thailand reveals important temporal intervals.** Trop Med Int Health. 2012 Sep; 17(9): 1076–1085.

Seroprevalence differences within 5-10km: 1255 children, aged 9: **67 to 92%**.
For all school children: 46 to 94%
(Tim Endy, Katie Anderson, personal communication)

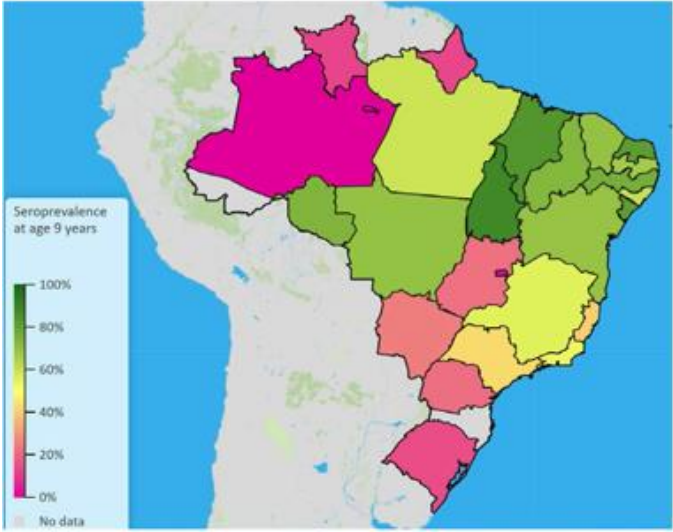
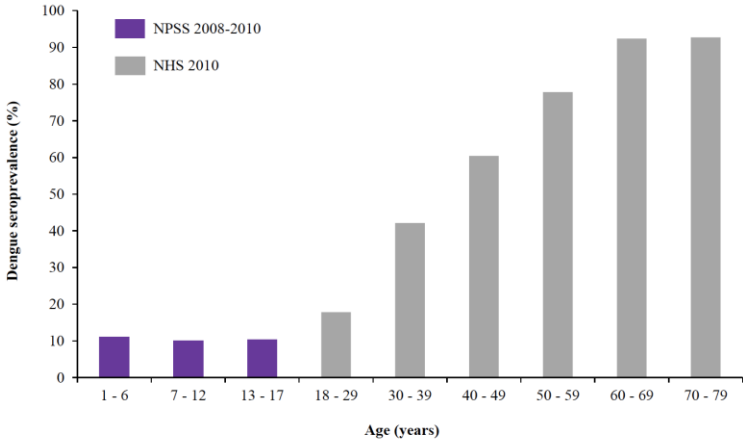
Heterogeneity of seroprevalence between and within countries



Thailand. Vongpunswad et al. PLoS ONE 2017

Philippines. L'Azou M, et al. *N Engl J Med* 2016

Figure 9
Age-specific prevalence (%) of past DENV infection among children and adolescents aged 1-17 years and adults aged 18-79 years



Singapore Ang et al, Epi News Bulletin 2014

https://mrcdata.dide.ic.ac.uk/_dengue/dengue.php

Dengue Vaccine



(http://www.who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/)



DPIV
GlaxoSmithKline,
Biomanguinhos,
WRAIR

DEN-80E
Merck

TVDV
Naval Medical
Research Center

TLAV-TPIV
WRAIR

TV003/TV005
US National
Institutes of Health¹
Butantan

DENVax
Takeda

CYD-TDV
Dengvaxia™
Sanofi Pasteur



YFV 17D-204	5'	C	prM	E	NS1	NS2A	NS2B	NS3	NS4A	NS4B	NS5	3'
DENV1	5'	C	prM	E	NS1	NS2A	NS2B	NS3	NS4A	NS4B	NS5	3'
DENV2	5'	C	prM	E	NS1	NS2A	NS2B	NS3	NS4A	NS4B	NS5	3'
DENV3	5'	C	prM	E	NS1	NS2A	NS2B	NS3	NS4A	NS4B	NS5	3'
DENV4	5'	C	prM	E	NS1	NS2A	NS2B	NS3	NS4A	NS4B	NS5	3'