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Outpatient dengue management

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Overview

- Spectrum of dengue illness
  - Mild → ambulatory care
- Clinical versus laboratory diagnosis
- Triage for outpatient management
- Outpatient management

Underrecognized Mildly Symptomatic Viremic Dengue Virus Infections in Rural Thai Schools and Villages

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In-Kyu Yoon,[1] Alan L. Rothman,[2] Darunee Tannitisupawong,[1] Anon Srikiatkhachorn,[3] Richard G. Jarman,[1] Jared Aldstadt,[4] Ananda Nisalak,[1] Mammen P. Mammen Jr,[1] Suwich Thammapalo,[5] Sharone Green,[3] Daniel H. Libraty,[3] Robert V. Gibbons,[1] Arthur Getis,[6] Timothy Endy,[7] James W. Jones,[8] Constantianus J. M. Koenraadt,[9] Amy C. Morrison,[10] Thanyalak Fansiri,[8] Chusak Pimgate,[1] and Thomas W. Scott[10,11]

Journal of Infectious Diseases 2012;206:389–98

	Year				
Description	2004	2005	2006	2007	Total
Cohort size (at start/end of surveillance season)	2078/2023	2088/2021	2086/2039	2060/2007	…
Median age, y (range)	9.0 (4–15)	9.0 (4–15)	9.0 (4–15)	10.0 (4–15)	9.0 (4–15)
Sex					
Female (%)	998 (48)	1005 (48)	994 (48)	964 (47)	5011 (48)
Male (%)	1080 (52)	1083 (52)	1092 (52)	1096 (53)	5476 (52)
School absences (no. of episodes)	1747	1737	1837	1782	7103
Fever history (no. of episodes)	663	764	871	757	3055
Phlebotomized (% of febrile illnesses)	504 (76)	715 (94)	779 (89)	640 (85)	2638 (86)
Dengue EIA positive (% of phlebotomized cases)	33 (6.5)	27 (3.8)	90 (11.6)	39 (6.1)	189 (7.2)
Serological category					
Acute primary (% of dengue EIA-positive)	6 (18.2)	2 (7.4)	5 (5.6)	0 (0)	13 (6.9)
Acute secondary (% of dengue EIA-positive)	27 (81.8)	24 (88.9)	80 (88.9)	38 (97.4)	169 (89.4)
Recent (% of dengue EIA-positive)	0 (0)	1 (3.7)	5 (5.6)	1 (2.6)	7 (3.7)
Seasonal incidence by EIA (%)	1.6	1.3	4.4	1.9	2.3
Dengue PCR positive (% of dengue EIA-positive)	28 (85)	20 (74)	68 (76)	31 (79)	147 (78)
Serotype					
DENV-1	0	2	46	21	69
DENV-2	9	2	1	8	20
DENV-3	3	1	0	0	4
DENV-4	16	15	21	2	54
All symptomatic DENV infections	33	27	90	39	189
Symptomatic category					
Outpatient symptomatic DENV infections	27	22	67	33	149
Hospitalized dengue fever	3	3	19	6	31
DHF	3	2	4	0	9
Inapparent dengue	81	77	103	85	346
Unclassified dengue	6	2	8	4	20
Inapparent-to-symptomatic ratio	2.5:1	2.9:1	1.1:1	2.2:1	1.8:1
Combined inapparent, symptomatic and unclassified DENV infections	120	106	201	128	554
Combined inapparent, symptomatic and unclassified dengue seasonal incidence (%)	5.9	5.2	9.9	6.4	6.8

Symptomatic 189
Outpatient 149
Hospitalised DF 31
DHF 9
Inapparent 346

Early Dengue Infection and Outcome Study (EDEN) – Study Design and Preliminary Findings

Jenny GH Low,[1] *MBBS, MRCP (UK), MMed (Int Med)*, Eng-Eong Ooi,[2] *MBBS, PhD*, Thomas Tolfvenstam,[3] *MD, PhD*, Yee-Sin Leo,[1] *MBBS, MMed (Int Med), MRCP (UK)*, Martin L Hibberd,[4] *BSc (Hons), PhD*, Lee-Ching Ng,[5] *PhD*, Yee-Ling Lai,[5] Grace SL Yap,[5] *BSc (Veterinary Science), BSc (Biology)*, Chenny SC Li,[5] *BSc*, Subhash G Vasudevan,[6] *PhD (ANU)*, Adrian Ong,[1] *MD, MPH*

Ann Acad Med Singapore 2006;35:783-9

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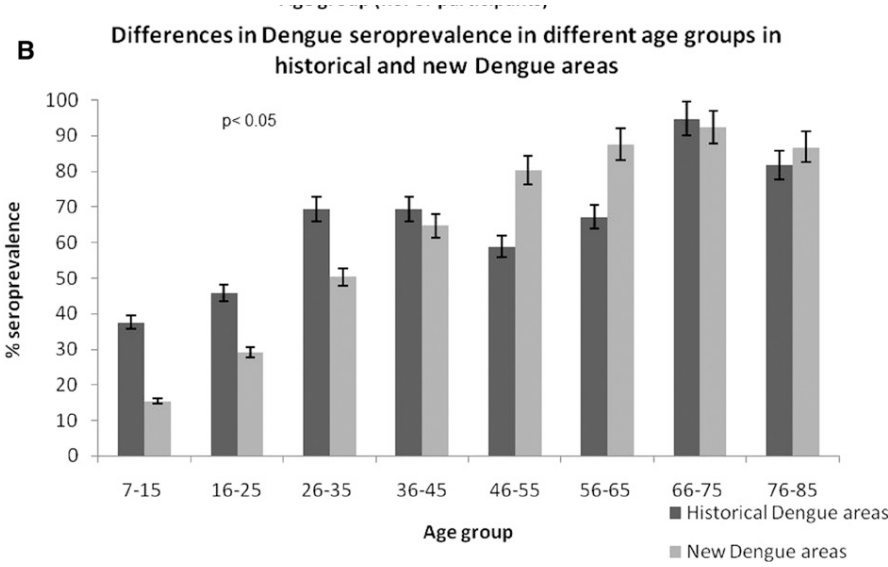
- Over 8 months, 454 patients acute febrile illness
- 133 dengue RT PCR positive
- 58 dengue IgG positive
- 75 hospitalised
- 2 DHF

Inapparent and symptomatic dengue, Singapore and Southern China

- AJTMH 2013;88:1065
  - 2007 outbreak
  - 3939 blood samples → 6.8% ELISA IgM positive (RF removed) → 78% no illness (88% >=45 years vs. 63% <45 years,p=0.005)
  - 22% symptomatic → 5 (8%) saw doctor → 1 diagnosed dengue



- PLOS NTD 2015, in press
  - 2013 outbreak, Zhongshan, Guangdong
  - 77 index cases and 887 contacts
  - 41 (4.6%) dengue positive, 1 secondary dengue, 13 symptomatic, 28 inapparent, I:S ratio 2.2

Age and Clinical Dengue Illness

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Joseph R. Egger* and Paul G. Coleman*

924 Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 6, June 2007

Clinical dengue

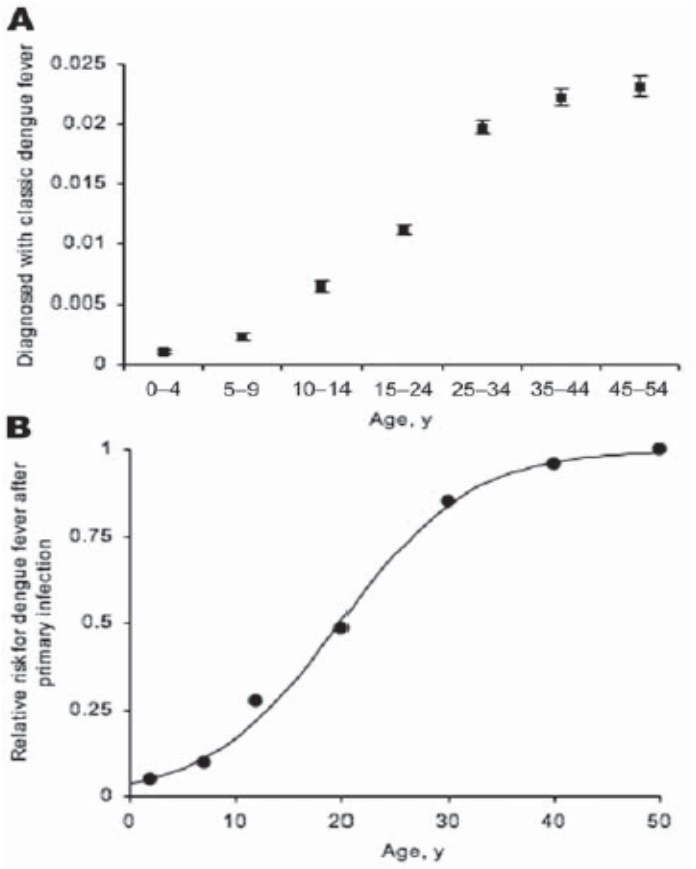

Figure. Estimated minimum proportion of the population, by age, with laboratory-confirmed classical dengue, showing exact 95% binomial confidence intervals. A) Fitting a logistic regression model (not shown) to the absolute proportion produced a significant age estimate: McFadden $R^2 = 0.762$, $\chi^2 = 5{,}196.13$, df = 1, $p<0.001$. B) Relative risk, by age, of having classical dengue after primary infection. Black circles, observed; line, model fit. See text for details of statistical analysis.

More likely to manifest clinical illness with increasing age in primary infection (Brazil)

Age-Specificity of Clinical Dengue during Primary and Secondary Infections

Khoa T. D. Thai[1,2]*, Hiroshi Nishiura[3,4], Phuong Lan Hoang[5], Nga Thanh Thi Tran[6], Giao Trong Phan[5], Hung Quoc Le[5], Binh Quang Tran[5], Nam Van Nguyen[7], Peter J. de Vries[1,2]

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PLOS NTD 2011;5:e1180

Abstract

Background: This study aims to estimate the age-specific risks of clinical dengue attack (i.e., the risk of symptomatic dengue among the total number of dengue virus (DENV) infections) during primary and secondary infections.

Methods: We analyzed two pieces of epidemiological information in Binh Thuan province, southern Vietnam, i.e., age-specific seroprevalence and a community-wide longitudinal study of clinical dengue attack. The latter data set stratified febrile patients with DENV infection by age as well as infection parity. A simple modeling approach was employed to estimate the age-specific risks of clinical dengue attack during primary and secondary infections.

Results: Using the seroprevalence data, the force of infection was estimated to be 11.7% (95% confidence intervals (CI): 10.8–12.7) per year. Median age (and the 25–75 percentiles) of dengue fever patients during primary and secondary infections were 12 (9–20) and 20 (14–31) years, respectively. The estimated age-specific risk of clinical dengue increases as a function of age for both primary and secondary infections; the estimated proportion of symptomatic patients among the total number of infected individuals was estimated to be <7% for those aged <10 years for both primary and secondary infections, but increased as patients become older, reaching to 8–11% by the age of 20 years.

Conclusions/Significance: For both primary and secondary infections, higher age at DENV infection was shown to result in higher risk of clinical attack. Age as an important modulator of clinical dengue explains recent increase in dengue notifications in ageing countries in Southeast Asia, and moreover, poses a paradoxical problem of an increase in adult patients resulting from a decline in the force of infection, which may be caused by various factors including time-dependent variations in epidemiological, ecological and demographic dynamics.

Decreasing dengue hospitalisation

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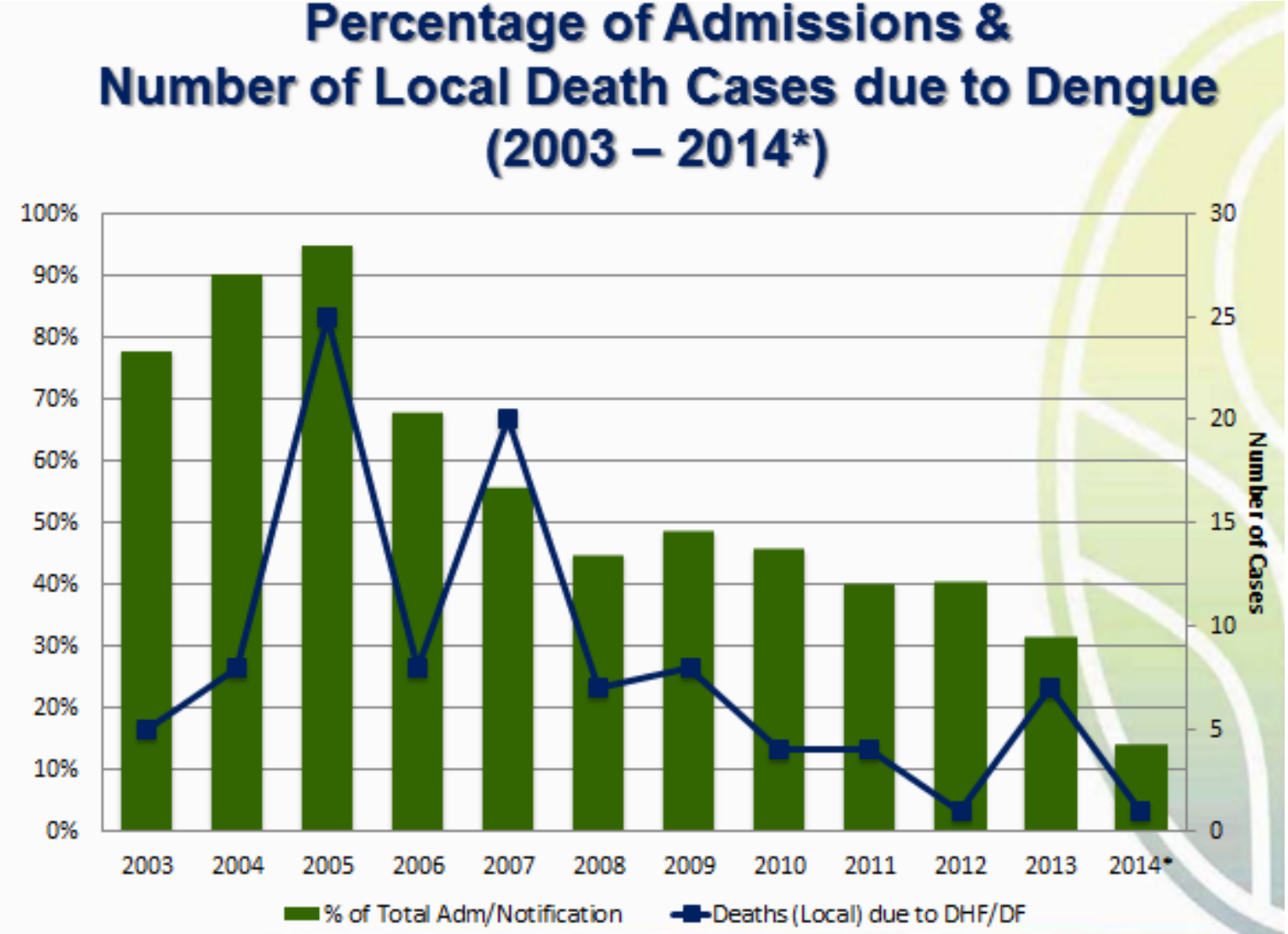
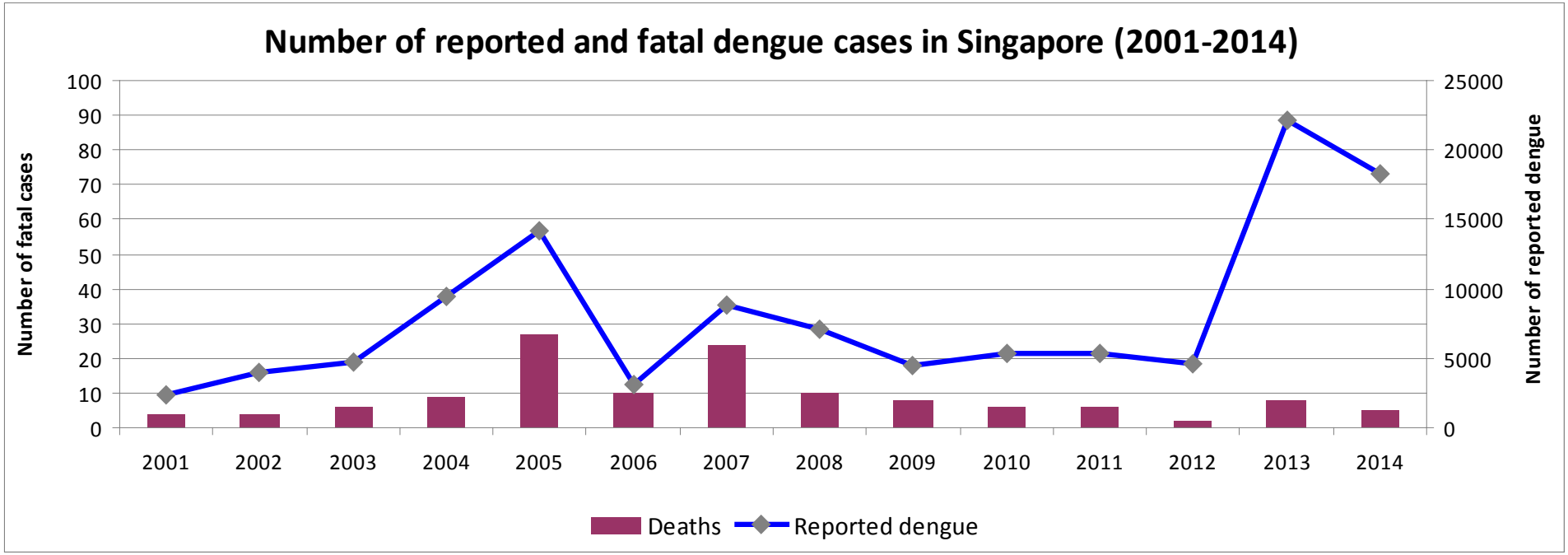


Rising dengue
Less hospitalisation
No increased dengue death



Implications

- Questions for Hong Kong
  - What is the receptive mosquito population?
    - *A aegypti* vs. *A albopictus*?
  - What is overall population seroprevalence?
  - What is age dependent seroprevalence?

Accurate diagnosis
Clinical versus laboratory

Predicting dengue diagnosis

Clinical diagnosis

- WHO 1997 Probable dengue fever
  - Acute fever with ≥2 of headache, eye pain, myalgia, arthralgia, rash, bleeding and leukopenia, AND
  - Supportive serology OR occurrence same location and time as confirmed dengue
- WHO 2009 Probable dengue
  - Live in or travel to dengue endemic area
  - Fever and 2 of nausea/vomit, rash, aches/pains, Tourniquet's test +ve, leukopenia, any warning sign

Dengue warning signs

- Abdominal pain/tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleeding
- Lethargy and restlessness
- Hepatomegaly >2cm
- Haematocrit rise AND rapid platelet drop

The Early Clinical Features of Dengue in Adults: Challenges for Early Clinical Diagnosis

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titute of Infectious Diseases
l Epidemiology

Jenny G. H. Low[1], Adrian Ong[1], Li Kiang Tan[2], Shera Chaterji[3], Angelia Chow[3], Wen Yan Lim[3], Koon Wui Lee[4], Robert Chua[3], Choon Rong Chua[2], Sharon W. S. Tan[2], Yin Bun Cheung[3,5], Martin L. Hibberd[6], Subhash G. Vasudevan[3], Lee-Ching Ng[2], Yee Sin Leo[1], Eng Eong Ooi[3,4]*

PLOS NTD 2011;5:e1191

Table 8. Age-specific features of probable dengue diagnosis using the WHO 1997 or 2009 classification schemes.

WHO 1997	18–25 (dengue n = 49; OFI n = 553)	26–35 (dengue n = 60; OFI n = 499)	36–45 (dengue n = 60; OFI n = 327)	46–55 (dengue n = 43; OFI n–287)	56+ (dengue n = 38; OFI n = 212)
Sensitivity %	95.9 (86.0–99.5	98.3 (91.1–99.9)	95.0 (86.1–99.0)	95.4 (84.2–99.4)	73.7 (56.9–86.6)
Specificity %	32.0 (28.1–36.1)	29.1 (25.1–33.3)	26.3 (21.6–31.4)	35.2 (29.7–41.0)	44.8 (38.0–51.8)
PPV %	11.1 (8.3–14.5)	14.3 (11.1–18.0)	19.1 (14.8–24.1)	18.1 (13.3–23.7)	19.3 (13.2–26.7)
NPV %	98.9 (96.0–99.9)	99.3 (96.3–99.9)	96.6 (90.5–99.3)	98.0 (93.2–99.8)	90.5 (83.2–95.3)
WHO 2009					
Sensitivity %	95.9 (86.0–99.5)	96.7 (88.5–99.6)	96.7 (88.5–99.6)	100 (91.8–100)	81.6 (65.7–92.3)
Specificity %	23.0 (19.5–26.7)	19.9 (16.5–23.7)	19.0 (14.9–23.6)	22.7 (17.9–27.9)	34.9 (28.5–41.7)
PPV %	9.9 (7.4–13.0)	12.7 (9.8–16.1)	18.0 (13.9–22.6)	16.2 (12.0–21.2)	18.3 (12.8–25.0)
NPV %	98.5 (94.5–99.8)	98.0 (93.0–99.8)	96.7 (89.2–99.6)	100 (94.5–100)	91.4 (83.0–96.5)

WHO 1997 Sn 95-98.3% Sp 26.3-35.2%
WHO 2009 Sn 95.9-100% Sp 10-23%
Sensitivity decreased in >55 years
Clinical diagnosis not specific → need laboratory confirmation

Distinguishing dengue fever from other infections on the basis of simple clinical and laboratory features: Application of logistic regression analysis

David Chadwick [a,b,*], Barbara Arch [c], Annelies Wilder-Smith [a], Nicholas Paton [a]

Journal of Clinical Virology 35 (2006) 147–153

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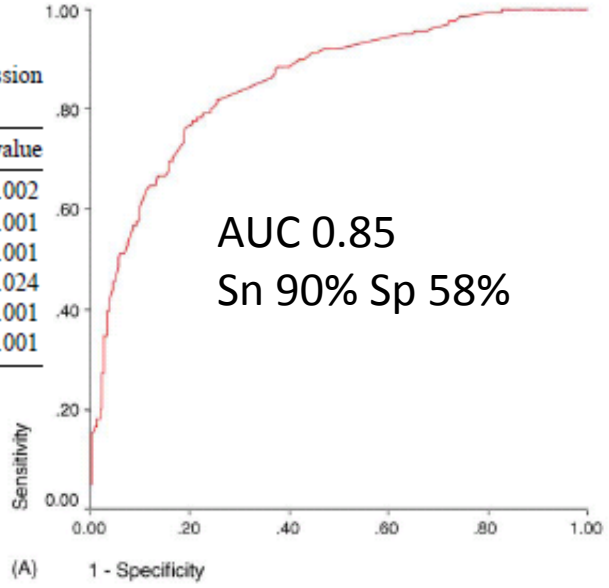
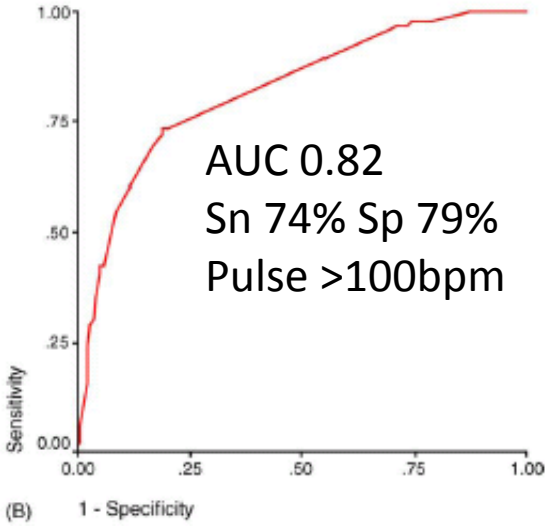
Results of chosen clinical features alone model using logistic regression analysis (omitting age and gender)

Covariate	OR	95% CI	*p* value
Myalgia	2.82	(1.47, 5.41)	0.002
Pharyngeal injection	0.22	(0.09, 0.53)	<0.001
Skin flushing	4.55	(2.34, 8.82)	<0.001
Macular or maculopapular rash	2.64	(1.13, 6.16)	0.024
Scattered petechiae	7.62	(3.20, 18.13)	<0.001
Pulse rate[a]	0.53	(0.43, 0.67)	<0.001

Myalgia, rash, petechiae
Bradycardia



AUC 0.85
Sn 90% Sp 58%

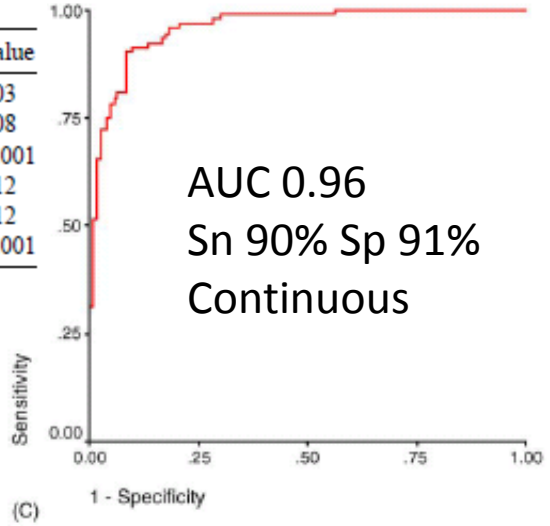


AUC 0.82
Sn 74% Sp 79%
Pulse >100bpm

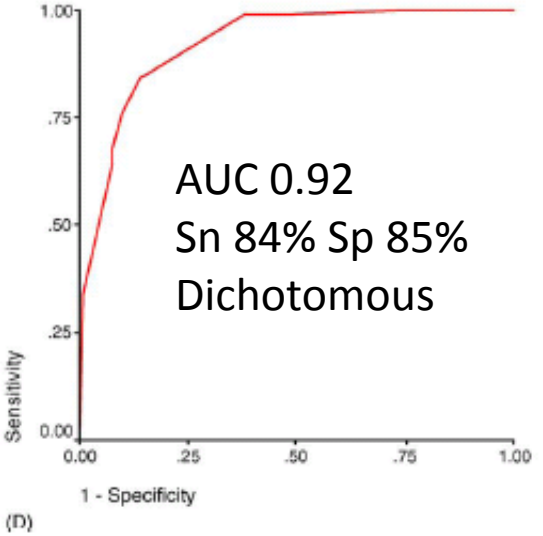
Chosen logistic regression model results using both clinical and laboratory data (clinical and laboratory features model)

Covariate	OR	95% CI	*p*-value
Rash[a]	9.13	(2.14, 38.94)	0.003
Haemaglobin	1.52	(1.11, 2.06)	0.008
White cell count	0.43	(0.31, 0.59)	< 0.001
Creatinine[b]	0.73	(0.57, 0.93)	0.012
Bilirubin[c]	0.74	(0.59, 0.94)	0.012
Prothrombin time	0.44	(0.30, 0.65)	< 0.001

Rash, raised HCT
Low WCC



AUC 0.96
Sn 90% Sp 91%
Continuous



AUC 0.92
Sn 84% Sp 85%
Dichotomous

Decision Tree Algorithms Predict the Diagnosis and Outcome of Dengue Fever in the Early Phase of Illness

Lukas Tanner[1,3], Mark Schreiber[1,3], Jenny G. H. Low[2], Adrian Ong[2], Thomas Tolfvenstam[3], Yee Ling Lai[4], Lee Ching Ng[4], Yee Sin Leo[2], Le Thi Puong[5], Subhash G. Vasudevan[1], Cameron P. Simmons[6], Martin L. Hibberd[3], Eng Eong Ooi[7]*

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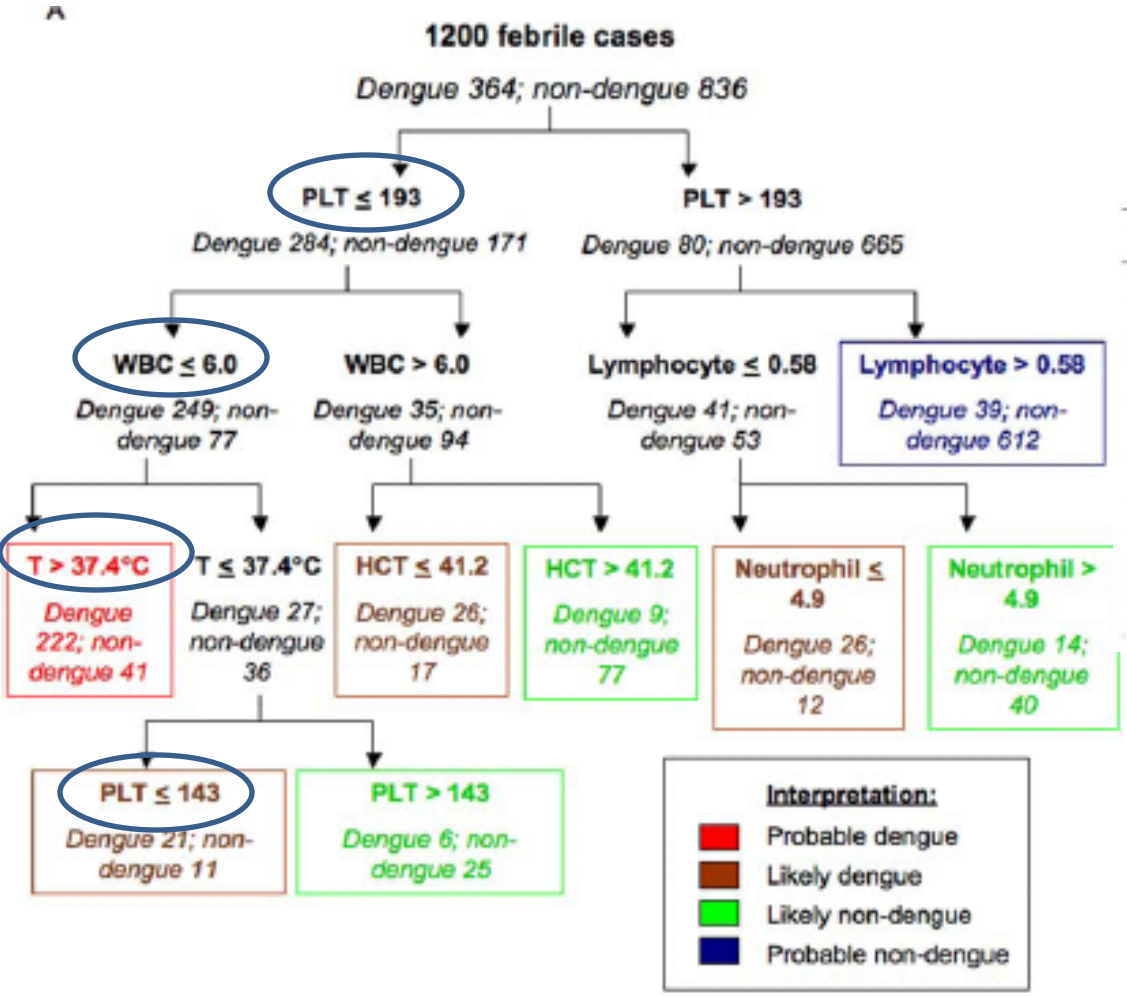
PLOS NTD 2008;2:e196



Decision Node Feature	OR	95% CI (OR)	p value
Platelet count ≤ 193 X 1000/mm^3	13.8	13.6, 14.1	<0.0001
White cell count ≤ 6.0 x 1000 cells/mm^3	8.7	8.3, 9.1	< 0.0001
Body temperature > 37.4°C	7.2	6.6, 7.8	< 0.001
Platelet < 143 x 1000/mm^3	8.0	5.7, 11.3	< 0.01
Hematocrit ≤ 41.2	13.1	11.3, 15.2	< 0.001
Lymphocyte count ≤ 0.58 x 1000 cells/mm^3	12.1	11.6, 12.6	<0.001
Neutrophil count < 4.9 x 1000 cells/mm^3	5.9	4.6, 7.5	<0.01

Sn 71.2% Sp 90.1%

Pitfalls of dengue laboratory diagnosis

Dengue: a continuing global threat

Maria G. Guzman, Scott B. Halstead‡, Harvey Artsob§, Philippe Buchy‖, Jeremy Farrar¶, Duane J. Gubler#, Elizabeth Hunsperger**, Axel Kroeger‡‡, Harold S. Margolis**, Eric Martínez*, Michael B. Nathan§§, Jose Luis Pelegrino*, Cameron Simmons¶, Sutee Yoksan¶¶ and Rosanna W. Peeling‡‡,##*

Nat Rev Microbiol 2010;8:S7

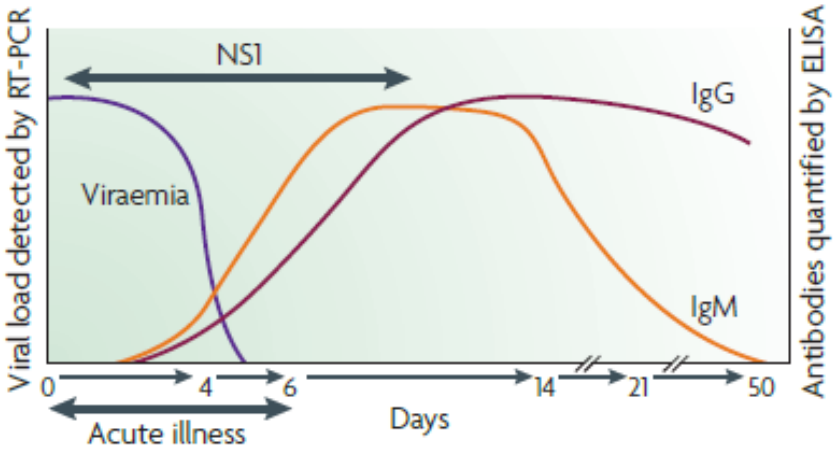
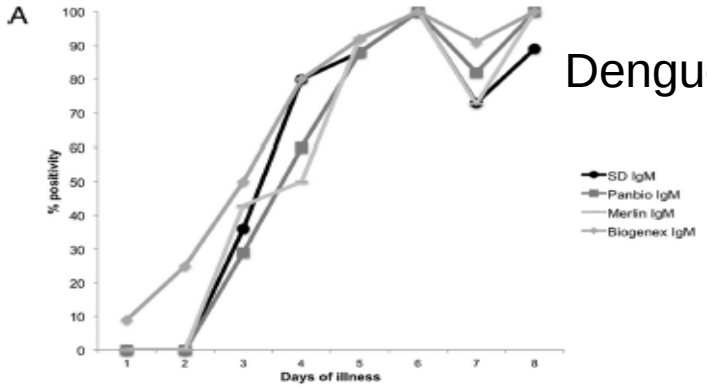


Figure 4 | **Dengue virus, antigen and antibody responses used in diagnosis.** Ig, immunoglobulin; NS, non-structural.

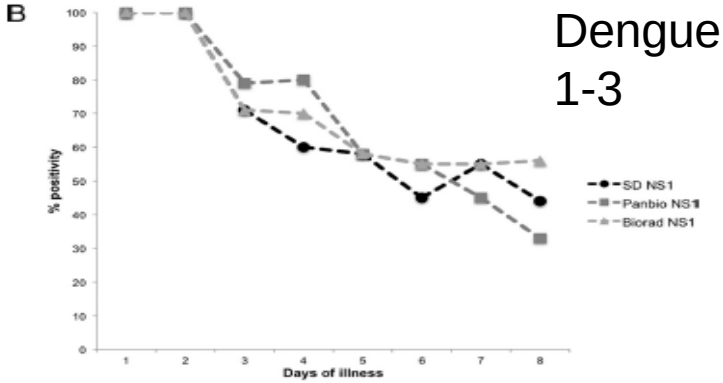
Evaluation of Six Commercial Point-of-Care Tests for Diagnosis of Acute Dengue Infections: the Need for Combining NS1 Antigen and IgM/IgG Antibody Detection To Achieve Acceptable Levels of Accuracy▽†

Stuart D. Blacksell,[1,2]* Richard G. Jarman,[3] Mark S. Bailey,[4] Ampai Tanganuchitcharnchai,[1] Kemajittra Jenjaroen,[1] Robert V. Gibbons,[3] Daniel H. Paris,[1,2] Ranjan Premaratna,[5] H. Janaka de Silva,[5] David G. Lalloo,[6] and Nicholas P. J. Day[1,2]

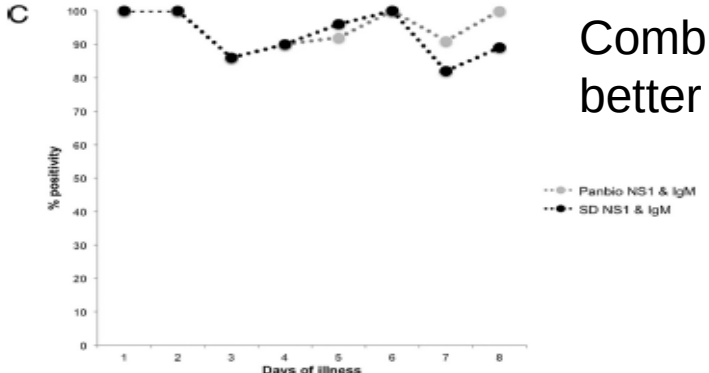
CLINICAL AND VACCINE IMMUNOLOGY, Dec. 2011, p. 2095–2101



Dengue IgM day 5



Dengue NS1 days 1-3



Combined → better

Evaluation of Six Commercial Point-of-Care Tests for Diagnosis of Acute Dengue Infections: the Need for Combining NS1 Antigen and IgM/IgG Antibody Detection To Achieve Acceptable Levels of Accuracy▽†

Stuart D. Blacksell,[1,2]* Richard G. Jarman,[3] Mark S. Bailey,[4] Ampai Tanganuchitcharnchai,[1] Kemajittra Jenjaroen,[1] Robert V. Gibbons,[3] Daniel H. Paris,[1,2] Ranjan Premaratna,[5] H. Janaka de Silva,[5] David G. Lalloo,[6] and Nicholas P. J. Day[1,2]

CLINICAL AND VACCINE IMMUNOLOGY, Dec. 2011, p. 2095–2101

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TABLE 4. Overall diagnostic accuracy and sensitivity[a]

Type of antibodies or antigens	Test	Sensitivity (%)	Specificity (%)	PPV[b]	NPV[c]	Kappa value
IgM antibodies	Merlin	72.7 (62.9–81.2)	73.8 (66.2–80.4)	63.2 (53.6–72.0)	81.4 (74.1–87.4)	0.79
	Biosynex	79.8 (70.5–87.2)	46.3 (38.3–54.3)	49.9 (40.1–55.8)	78.7 (69.1–86.5)	0.57
	Standard Diagnostics	79.2 (70.5–87.2)	89.4 (83.5–93.7)	82.3 (73.2–89.3)	87.7 (81.7–92.3)	0.92
	Panbio	70.7 (60.7–79.4)	80.0 (73.0–85.9)	68.6 (58.7–77.5)	81.5 (74.6–87.3)	0.92
NS1 antigen	Standard Diagnostics	48.5 (38.5–58.7)	99.4 (96.6–100)	98.0 (89.1–100)	75.7 (69.3–81.4)	0.96
	Bio-Rad	58.6 (48.2–68.4)	98.8 (95.6–99.9)	96.7 (88.5–99.6)	79.4 (73.1–84.8)	0.94
	Panbio	58.6 (48.2–68.4)	92.5 (87.3–96.1)	82.9 (72.0–90.8)	78.3 (71.7–84.0)	0.95
IgM antibodies and NS1 antigen	Standard Diagnostics	92.9 (83.9–97.1)	88.8 (82.8–93.2)	83.6 (75.4–90.0)	95.4 (90.6–98.1)	Not applicable
	Panbio	89.9 (82.2–95.0)	75.0 (67.6–81.5)	69.0 (60.3–76.8)	92.3 (86.3–96.2)	Not applicable

Better sensitivity NS1/IgM vs. each
Comparable specificity

False positive dengue IgM and NS1

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TABLE 3. Dengue IgM and IgG seroprevalence and cross-reactivity for each rapid diagnostic test and each analyte in patients with nondengue infections

Disease	Total no. of samples	No. of samples (%; 95% CI) with >15 units of:[a]		No. of samples (%; 95% CI) with cross-reactivity of:						
				IgM antibodies by indicated test				NS1 antigens by indicated test		
		IgM	IgG	Merlin	Biosynex	Standard Diagnostics	Panbio	Standard Diagnostics	Bio-Rad	Panbio
Chikungunya	82	2 (2.4; 1–8)	22 (26.8; 18–37)	25 (59.5; 44–73)	47 (53.4; 43–63)	10 (58.8; 36–78)	15 (46.9; 31–64)	1 (100)		4 (36.4; 15–65)
Leptospirosis	33	1 (3.0; 1–15)	2 (6.1; 2–20)	5 (11.9; 5–25)	16 (18.2; 12–28)	2 (11.8; 3–34)	3 (9.4; 3–24)		1 (50; 9–91)	2 (18.2; 5–48)
Bacteremia	19	0	3 (15.8; 6–38)	3 (7.1; 2–19)	11 (12.5; 7–21)		3 (9.4; 3–24)		1 (50; 9–91)	1 (9.1; 2–4)
Scrub typhus	8	0	2 (25.0; 5–33)	2 (4.8; 1–16)	5 (5.7; 2–13)	1 (5.9; 1–27)	5 (15.6; 7–32)			2 (18.2; 5–48)
Q fever	7	0	1 (14.3; 3–51)	2 (4.8; 1–16)	2 (2.3; 1–8)	1 (5.9; 1–27)	3 (9.4; 3–24)			2 (18.2; 5–48)
Tuberculosis	4	0	0	3 (7.1; 2–19)	3 (3.4; 1–10)	2 (11.8; 3–34)	1 (3.1; 1–16)			
Urinary tract infection	5	0	1 (20.0; 4–62)		2 (2.3; 1–8)					
Malaria	1	1 (100; 21–100)	1 (100; 21–100)	1 (2.4; 0–12)	1 (1.1; 0–6)	1 (5.9; 1–27)	1 (3.1; 1–16)			
Spotted fever	1	0	0	1 (2.4; 0–12)	1 (1.1; 0–6)		1 (3.1; 1–16)			
Total	160	4 (2.5; 0–6)	32 (20; 15–27)	42 (26.3; 10–33)	88 (55.0; 47–63)	17 (10.6; 7–16)	32 (20.0; 15–27)	1 (0.63; 0–33)	2 (1.3; 0–4)	11 (6.9; 4–12)

IgM 10-50%
NS1 1-7%

Diagnosing Dengue at the Point-of-Care: Utility of a Rapid Combined Diagnostic Kit in Singapore

Victor C. Gan[1]*, Li-Kiang Tan[2], David C. Lye[1,3], Kwoon-Yong Pok[2], Shi-Qi Mok[1], Rachel Choon-Rong Chua[2], Yee-Sin Leo[1,3], Lee-Ching Ng[2,4]

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Whole blood
Finger prick

Table 1. Performance of point-of-care strategies for dengue diagnosis against laboratory-based composite reference standards.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Dengue Duo (NS1/IgM/IgG)	138/147, 93.9 (88.8–96.8)	46/50, 92.0 (81.2–96.9)	138/142, 97.2 (93.0–98.9)	46/55, 83.6 (71.7–91.1)
Dengue Duo (NS1/IgM)	135/147, 91.8 (86.3–95.3)	48/50, 96.0 (86.5–98.9)	135/137, 98.5 (94.8–99.6)	48/60, 80.0 (68.2–88.2)
Dengue Duo (NS1 only)	120/147, 81.6 (74.6–87.1)	49/50, 98.0 (89.5–99.7)	120/121, 99.2 (95.5–99.9)	49/76, 64.5 (53.3–74.3)
WHO 1997	141/147, 95.9 (91.4–98.1)	10/50, 20.0 (11.2–33.0)	141/181, 77.9 (71.3–83.3)	10/16, 62.5 (38.6–81.5)
WHO 2009	142/147, 96.6 (92.3–98.5)	13/50, 26.0 (15.9–39.6)	142/179, 79.3 (72.8–84.6)	13/18, 72.2 (49.1–87.5)
WHO 1997 then Dengue Duo (NS1/IgM/IgG)	134/147, 91.2 (85.5–94.8)	47/50, 94.0 (83.8–97.9)	134/137, 97.8 (93.8–99.3)	47/60, 78.3 (66.4–86.9)
WHO 2009 then Dengue Duo (NS1/IgM/IgG)	134/147, 91.2 (85.5–94.8)	47/50, 94.0 (83.8–97.9)	134/137, 97.8 (93.8–99.3)	47/60, 78.3 (66.4–86.9)

Table 2. Sensitivity of SD Dengue Duo in different subpopulations against laboratory-based composite reference standards.

	POCT NS1 OR IgM OR IgG	POCT NS1 OR IgM	POCT NS1
Fever <=5 days (n=50)	45/50, 90.0 (78.6–95.7)	44/50, 88.0 (76.2–94.4)	43/50, 86.0 (73.8–93.1)
Fever >5 days (n=97)	93/97, 95.9 (89.9–98.4)	91/97, 93.8 (87.2–97.1)	77/97, 79.4 (70.3–86.2)
DENV-1 (n=22)	22/22, 100.0 (85.1–100.0)	21/22, 95.5 (78.2–99.2)	19/22, 86.4 (66.7–95.3)
DENV-2 (n=89)	84/89, 94.4 (87.5–97.6)	84/89, 94.4 (87.5–97.6)	78/89, 87.6 (79.2–93.0)

Implications

- Have the right diagnostic assay
- Be readily available
  - Point of care
  - Daily
  - Quick turn-around time

With confirmed dengue, how do we decide on hospitalisation versus outpatient observation?

World Health Organisation 2009

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Textbox E. Admission criteria

Warning signs	Any of the warning signs (Textbox C)
Signs and symptoms related to hypotension (possible plasma leakage)	Dehydrated patient, unable to tolerate oral fluids Giddiness or postural hypotension Profuse perspiration, fainting, prostration during defervescence Hypotension or cold extremities
Bleeding	Spontaneous bleeding, independent of the platelet count
Organ impairment	Renal, hepatic, neurological or cardiac – enlarged, tender liver, although not yet in shock – chest pain or respiratory distress, cyanosis
Findings through further investigations	Rising haematocrit Pleural effusion, ascites or asymptomatic gall-bladder thickening
Co-existing conditions	Pregnancy Co-morbid conditions such as diabetes mellitus, hypertension, peptic ulcer, haemolitic anemias and others Overweight or obese (rapid venous access difficult in emergency) Infancy or old age
Social circumstances	Living alone Living far from health facility Without reliable means of transport

Why?

How much?

US?

Effect of age on outcome of secondary dengue 2 infections

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María G. Guzmán,[1] Gustavo Kouri,[1] Jose Bravo,[1] Luis Valdes,[2] SusanaVazquez,[1] and Scott B. Halstead[3]

Int J Infect Dis 2002; 6: 118–124

Risk of DHF

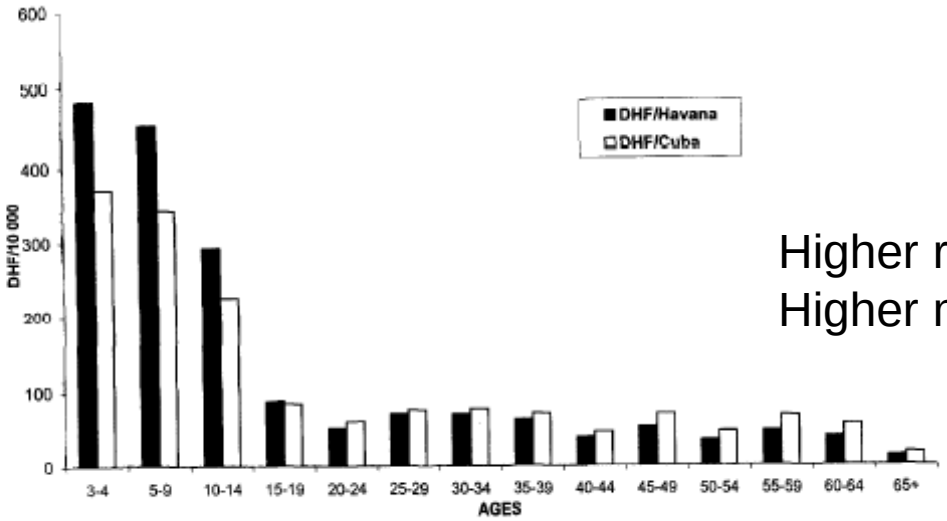

Figure 1. Age-specific DHF/DSS rates per 10 000 secondary dengue 2 infections and case fatality rates in Havana, 1981.

Higher risk of DHF in children
Higher mortality in children but also elderly

Risk of death

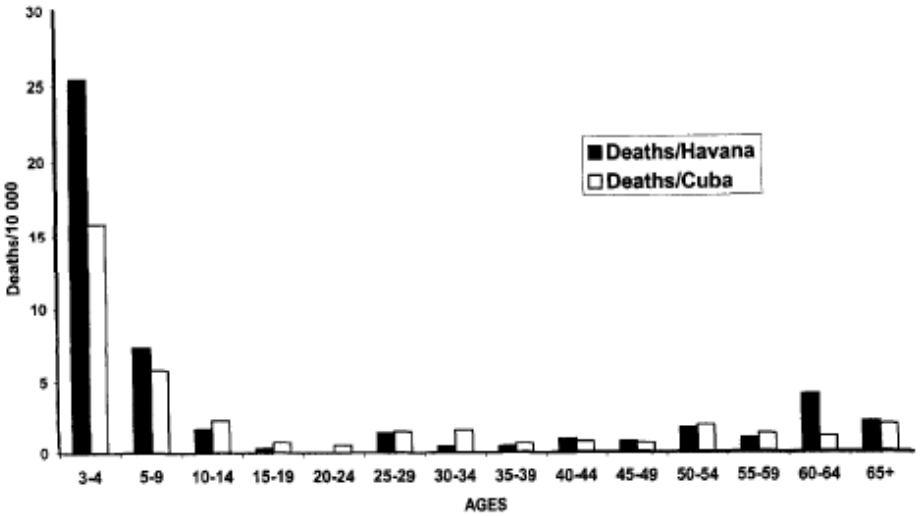

Figure 2. Age-specific DHF/DSS death rates per secondary dengue 2 infections and case fatality rates in Cuba, 1981.

Challenges in Dengue Fever in the Elderly: Atypical Presentation and Risk of Severe Dengue and Hospita-Acquired Infection

Emily K. Rowe[1,2*], Yee-Sin Leo[1,2], Joshua G. X. Wong[2], Tun-Linn Thein[2], Victor C. Gan[2], Linda K. Lee[2], David C. Lye[1,2,3]

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Table 2. Outcomes for elderly (≥60) and adult (<60) patients with dengue fever.

Variable	Patient number (%)		P values
	Adults n = 6694	Elderly n = 295	
Dengue severity			
DHF	1431 (21.4)	86 (29.2)	0.002
DHF Grade I–II	1199 (17.9)	80 (27.1)	<0.001
DSS	232 (3.5)	6 (2.0)	0.184
SD	975 (14.6)	60 (20.3)	0.006
SD criteria			
Severe bleeding	401 (41.1)	13 (21.7)	0.003
Severe plasma leakage	332 (34.1)	17 (28.3)	0.363
Severe organ involvement	118 (12.1)	12 (20)	0.100
SB+SPL	67 (6.9)	3 (5.0)	0.792
SB+SOI	14 (1.4)	1 (1.7)	0.594
SPL+SOI	30 (3.1)	10 (16.7)	<0.001
SB+SPL+SOI	13 (1.3)	4 (6.7)	0.014
Outcome			
ICU	13 (0.2)	2 (0.7)	0.130
Death	3 (0.1)	0 (0)	1
HAI			
Any HAI	66 (1.2)	13 (4.9)	<0.001
Pneumonia	36 (0.7)	10 (3.8)	<0.001
UTI	17 (0.3)	5 (1.9)	0.003
Clostridium difficile	1 (0)	0 (0)	1
Bloodstream infection	14 (0.3)	0 (0)	1

Older patients >DHF, severe dengue and nosocomial infections

Table 3. Excess length of hospital stay.

Variable	Adjusted odds ratio*	95% Confidence interval
Elderly (age ≥60)		
No (n = 5774)	Reference	Reference
Yes (n = 296)	2.01	1.37–2.88
Critically ill		
Pitt bacteremia score <4 (n = 6016)	Reference	Reference
Pitt bacteremia score ≥4 (n = 54)	5.13	2.59–9.75
Hospital-acquired infection		
No (n = 5988)	Reference	Reference
Yes (n = 82)	12.06	7.39–19.90
Charlsons co-morbidity score		
≤3 (n = 6054)	Reference	Reference
>3 (n = 16)	6.90	2.02–22.56
^**Dengue Severity**		
Not severe (n = 3840)	Reference	Reference
Severe (n = 2230)	2.24	1.83–2.74

Age, co-morbidity, illness severity and nosocomial infection → longer hospitalisation

Diabetes with Hypertension as Risk Factors for Adult Dengue Hemorrhagic Fever in a Predominantly Dengue Serotype 2 Epidemic: A Case Control Study

Junxiong Pang[1,2*], Agus Salim[2], Vernon J. Lee[2,3], Martin L. Hibberd[1,2], Kee Seng Chia[2], Yee Sin Leo[4,5], David C. Lye[4,5]

PLoS NEGLECTED TROPICAL DISEASES May 2012 | Volume 6 | Issue 5 | e1641

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Table 4. Crude and adjusted odds ratios of the association of DHF with multiple co-morbidities in year 2007–2008 epidemic.

Exposures	Cases	Controls				
	N	N	COR	95% CI	AOR*	95% CI
Diabetes						
No	626	1101	1		1	
Yes	43	40	**1.89**	**1.21–2.94**	**1.78**	**1.06–2.97**
Diabetes, Hypertension						
No diabetes with no hypertension	584	1031	1		1	
No diabetes with hypertension	42	70	1.06	0.71–1.57	0.97	0.62–1.52
Diabetes with no hypertension	10	16	1.1	0.50–2.45	1.26	0.55–2.87
Diabetes with hypertension	33	24	**2.43**	**1.42–4.15**	**2.16**	**1.18–3.96**
Diabetes, Hyperlipidemia						
No diabetes with no hyperlipidemia	597	1048	1		1	
No diabetes with hyperlipidemia	29	53	0.96	0.60–1.53	0.82	0.50–1.37
Diabetes with no hyperlipidemia	15	13	2.03	0.96–4.29	2.03	0.93–4.47
Diabetes with hyperlipidemia	28	27	**1.82**	**1.06–3.12**	1.62	0.90–2.92
Diabetes, Asthma						
No diabetes with no asthma	599	1044	1		1	
No diabetes with asthma	27	57	0.83	0.52–1.32	0.79	0.49–1.27
Diabetes with no asthma	38	38	**1.74**	**1.10–2.76**	**1.68**	**1.02–2.76**
Diabetes with asthma	5	2	4.36	0.84–22.53	4.38	0.80–23.85

Multicentre prospective study on dengue classification in four South-east Asian and three Latin American countries

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Neal Alexander[1#], Angel Balmaseda[2], Ivo C. B. Coelho[3], Efren Dimaano[4], Tran T. Hien[5], Nguyen T. Hung[6], Thomas Jänisch[7], Axel Kroeger[8], Lucy C. S. Lum[9], Eric Martinez[10], Joao B. Siqueira[11], Tran T. Thuy[12], Iris Villalobos[13], Elci Villegas[14] and Bridget Wills[15] on behalf of the European Union, World Health Organization (WHO-TDR) supported DENCO Study Group*

Tropical Medicine and International Health

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Table 2 Characteristics used to define the three intervention categories. Patients were classified daily, and the highest level of intervention required during the illness episode defined the final category

	Category 1 (Standard)	Category 2 (Intermediate)	Category 3 (Major)
Nursing care*	Level 1 and no intervention	Level 2 or 3 and no intervention	
Fluid therapy	No IV fluids	IV fluids (any) for maintenance or rehydration	Shock resuscitation or IV fluids (any) for rehydration with nursing care level 3
Blood products	No blood products	Platelets, fresh frozen plasma or cryoprecipitate† with nursing care level 1 or 2	Platelets, fresh frozen plasma or cryoprecipitate with nursing care level 3 Whole blood, packed red cells or any combination of blood products
Additional interventions	No additional interventions	Oxygen therapy alone	Oxygen therapy with nursing care level 3 Respiratory support (e.g. CPAP)
		Diuretics without other specific intervention	Inotropic support Specific treatment for liver, renal or other organ failure

Outpatient care

*Nursing care levels, customised to reflect differing practices between sites: 1: in- or outpatient, free to walk around, standard observation protocol – e.g. 6 hourly; 2: hospitalised with more stringent observation protocol – e.g. 2–4 hourly; 3: bed rest with ICU level observation protocol (even if managed outside an ICU) – e.g. hourly.

†At some sites, these blood products were given in response to abnormal laboratory results rather than for clinical reasons. We classified such interventions in the intermediate category.

Table 3 Warning signs associated with disease progression.* Crude and adjusted associations between possible risk factors and development of severe dengue disease, defined in terms of requirement for major intervention, are presented. Overall, 79 patients required major intervention between days 4 and 7 of illness and had clinical and laboratory information available for the previous day. Six-hundred and ninety-one patients were available as controls. For each covariate, the number of cases included in the analysis who progressed, versus the number of controls who did not progress, is presented in the table

Predictor	*N* Cases (%) or mean (95% CI)	*N* Controls (%) or mean (95% CI)	Univariate		Multivariate	
			OR (*P*-value)	95% CI	OR (*P*-value)	95% CI
Age group						
<15 years	56 (70.9)	435 (63.0)	Reference		Reference	
≥15 years	23 (29.1)	256 (37.0)	0.70 (0.167)	0.42–1.16	0.34 (0.002)	0.17–0.68
Continent						
SE Asia	67 (84.8)	579 (83.9)	Reference		Reference	
L America	12 (15.2)	112 (1.62)	0.93 (0.816)	0.48–1.77	2.83† (0.013)	1.24–6.47
Day of illness						
4	9 (11.4)	101 (14.8)	Reference		Reference	
5	25 (31.6)	197 (28.9)	1.42 (0.386)	0.64–3.17	1.05 (0.917)	0.45–2.42
6	27 (34.2)	228 (33.5)	1.33 (0.481)	0.60–2.93	0.63 (0.283)	0.27–1.47
7	18 (22.8)	155 (22.8)	1.22 (0.636)	0.53–2.83	0.58 (0.237)	0.23–1.44
Abdominal pain and/or tenderness‡						
Not present	29 (36.7)	528 (76.4)	Reference		Reference	
Present	50 (63.3)	156 (22.6)	5.84 (<0.001)	3.57–9.54	3.53 (<0.001)	2.09–5.96
Lethargy§						
Not present	69 (87.3)	672 (97.2)	Reference		Reference	
Present	10 (12.7)	15 (2.2)	6.49 (<0.001)	2.81–15.01	10.69¶ (<0.001)	3.17–36.09
Mucosal bleeding**						
Not present	58 (73.4)	618 (89.6)	Reference		Reference	
Present	21 (26.6)	72 (10.4)	3.11 (<0.001)	1.78–5.42	2.87 (0.002)	1.49–5.53
Haematocrit increase†† (per 1% increase)	42.3 (40.8–43.7)	41.8 (41.5–42.1)	1.02 (0.561)	0.95–1.10	1.00 (0.983)	0.93–1.07
Platelet decrease‡‡ (per 10 000/μl)	70 000 (57 000–82 000)	104 000 (100 000–109 000)	1.16 (<0.001)	1.07–1.25	1.18 (<0.001)	1.08–1.29

Utilities and Limitations of the World Health Organization 2009 Warning Signs for Adult Dengue Severity

Tun-Linn Thein[1*], Victor C. Gan[1], David C. Lye[1,2], Chee-Fu Yung[1], Yee-Sin Leo[1,2]

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Table 3. Performance of warning signs (WS) for predicting dengue hemorrhagic fever (DHF) (n = 1507).

Warning signs	Sn	Sp	PPV	NPV
Individual WS				
Abdominal pain or tenderness	0.29	0.73	0.17	0.85
Persistent vomiting	0.06	0.93	0.16	0.82
Hepatomegaly	0.01	0.99	0.20	0.81
Hematocrit rise and rapid platelet count drop	0.09	0.92	0.17	0.83
Clinical fluid accumulation	0.02	0.98	0.18	0.83
Mucosal bleeding	0.42	0.88	0.31	0.93
Lethargy[x]	0.33	0.55	0.28	0.61
WS count*				
Any number of seven WS[x]	0.87	0.18	0.30	0.77
Any number of six WS (without lethargy)	0.81	0.57	0.19	0.96
One WS	0.64	0.70	0.18	0.95
Two WS	0.44	0.89	0.25	0.95
Three WS	0.21	0.96	0.27	0.95
Four WS	0.04	0.98	0.14	0.94

Table 4. Performance of warning signs (WS) for predicting severe dengue (SD) (n = 1507).

Warning signs	Sn	Sp	PPV	NPV
Individual WS				
Abdominal pain or tenderness	0.21	0.72	0.09	0.87
Persistent vomiting	0.08	0.93	0.18	0.85
Hepatomegaly	0.00	0.99	0.06	0.84
Hematocrit rise and rapid platelet count drop	0.05	0.94	0.09	0.89
Clinical fluid accumulation	0.02	0.98	0.16	0.87
Mucosal bleeding	0.17	0.82	0.10	0.89
Lethargy[x]	0.34	0.56	0.17	0.76
WS count*				
Any number of seven WS[x]	0.96	0.18	0.15	0.96
Any number f six WS (without lethargy)	0.71	0.55	0.10	0.97
One WS	0.58	0.69	0.12	0.96
Two WS	0.32	0.88	0.12	0.96
Three WS	0.15	0.95	0.12	0.96
Four WS	0.04	0.98	0.25	0.96
Five WS	0.02	1.00	0.09	0.96

Specific: persistent vomit, hepatomegaly, haematocrit/platelet, clinical fluid accumulation

Poor sensitivity but good negative predictive value

Utility of warning signs in guiding admission and predicting severe disease in adult dengue

Yee-Sin Leo[1,2,3*], Victor C Gan[1], Ee-Ling Ng[1], Ying Hao[1], Lee-Ching Ng[4], Kwoon-Yong Pok[4], Frederico Dimatatac[1], Chi-Jong Go[1] and David C Lye[1,3]

BMC Infectious Diseases 2013, 13:498

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Table 4 Performance of individual warning signs in predicting DHF and SD in outpatients

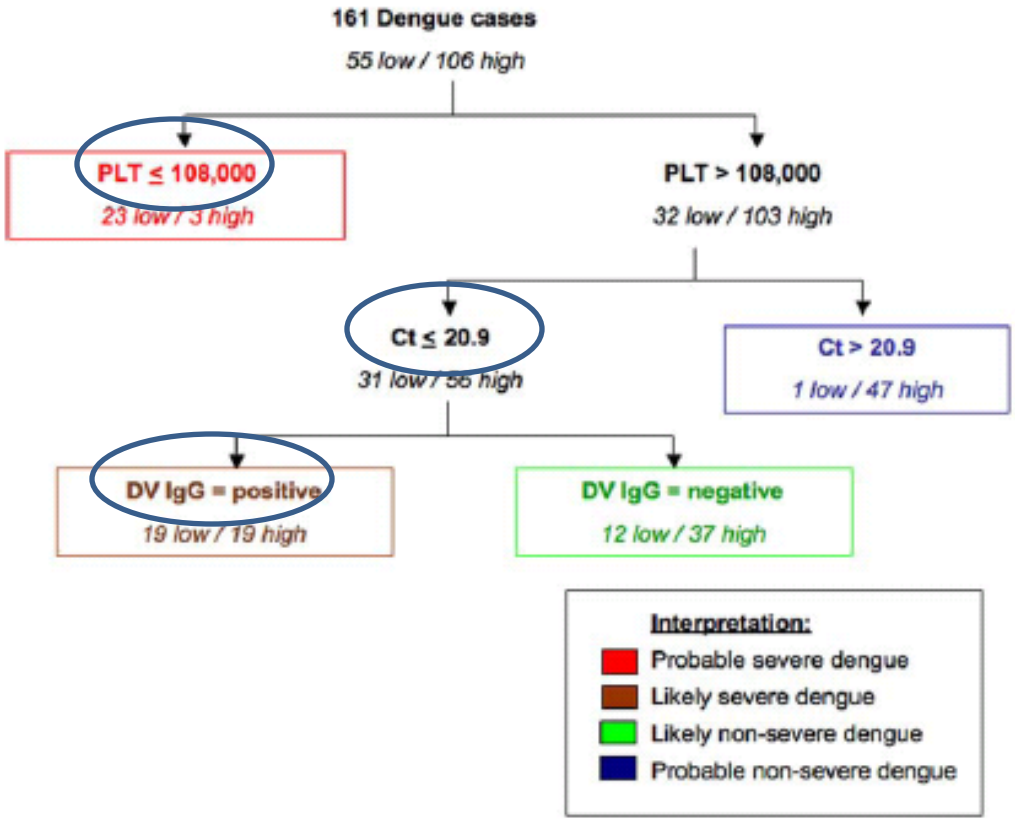
Warning sign	DHF I-IV (N = 70)				DHF II-IV (N = 43)				SD (N = 13)			
	Sn	Sp	PPV	NPV	Sn	Sp	PPV	NPV	Sn	Sp	PPV	NPV
Abdominal pain (N = 88)	31	78	25	83	37	78	18	91	38	77	6	97
Persistent vomiting (N = 16)	7	96	31	82	9	96	25	89	23	96	19	97
Clinical fluid accumulation (N = 1)	1	100	100	82	0	100	0	89	0	100	0	97
Mucosal bleeding (N = 154)	61	64	28	88	100	67	28	100	62	60	5	98
Hepatomegaly (> 2 cm) (N = 2)	1	100	50	82	0	99	0	89	0	99	0	97
↑ in hematocrit; rapid ↓ of platelet (N = 10)	14	100	100	84	9	98	40	89	31	98	40	98
Any warning sign (N = 203)	79	52	27	91	100	52	21	100	100	48	6	100
Two warning signs (N = 61)	33	88	38	85	47	88	33	93	46	85	10	98
Three warning signs (N = 7)	6	99	57	82	9	99	57	89	8	98	14	97

Specific: persistent vomit, clinical fluid accumulation, hepatomegaly, haematocrit/platelet

Poor sensitivity but high negative predictive value

Other predictive algorithms for dengue severity

Predicting dengue severity



Tanner PLOS NTD 2008;2:e196

Singapore adults

Vietnamese children and adults

Decision Node Feature	OR	95% CI (OR)	p value
Platelet count ≤ 108,000/mm^3	24.7	20.9, 29.2	< 0.001
Ct ≤ 20.9	26.0	18.0, 37.5	< 0.001
DV IgG = positive	3.1	2.0, 4.8	< 0.05

Marker of severity: platelet <50,000

Sn 78.2% Sp 80.2%

Predicting dengue severity

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Potts PLOS NTD 2010;4:e769

Thai children

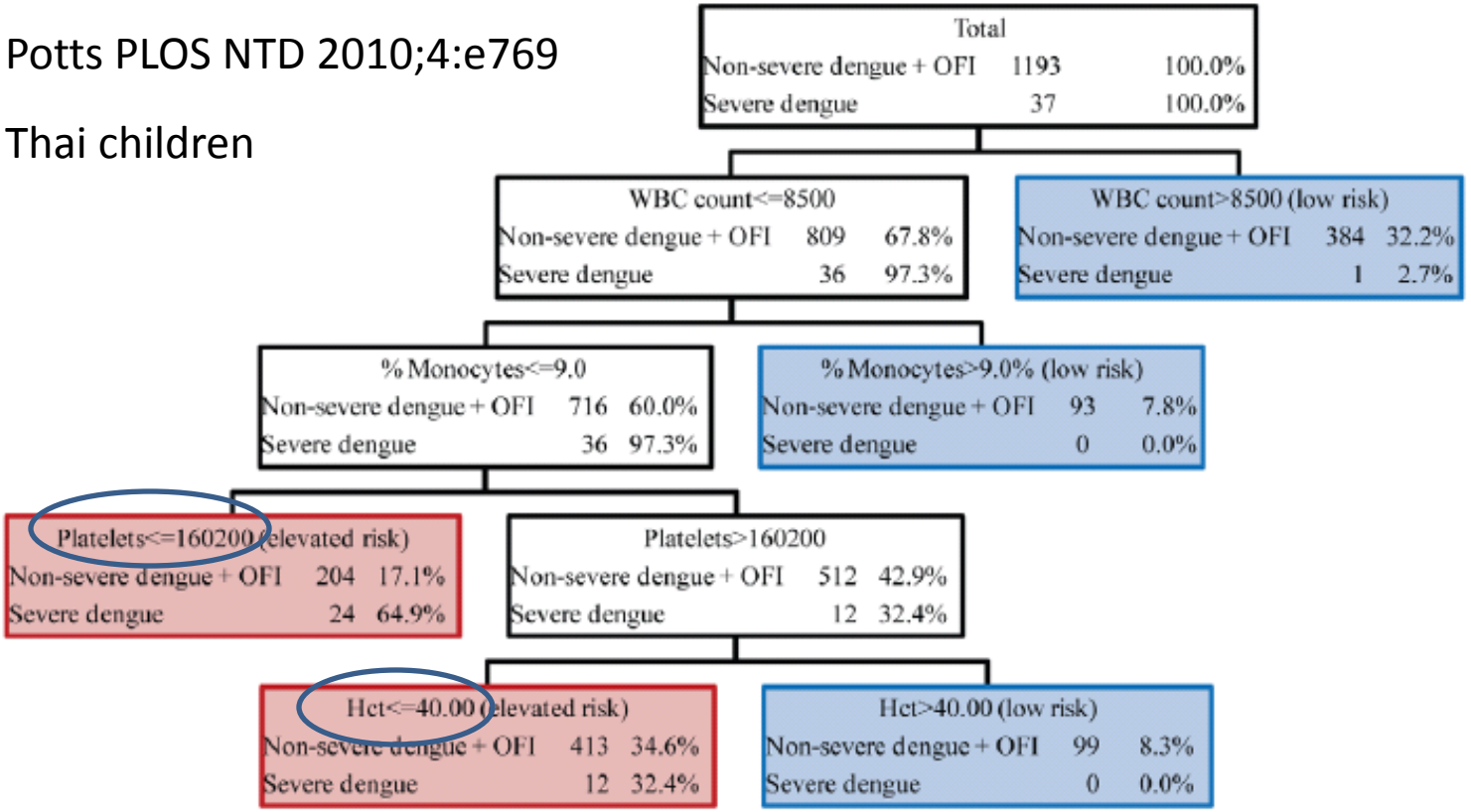

Figure 1. CART algorithm #1 for identifying patients who subsequently developed severe dengue (defined as WHO criteria for dengue shock syndrome, DSS) using dinical laboratory data obtained within the first three days of illness. Each node is shown with the selected splitting variable, the number of patients with severe/non-severe or OFI, and the proportion of each from the parent node. Terminal nodes are marked as 'elevated risk' of severe dengue illness, outlined in red, and 'low risk' of severe dengue, outlined in blue.

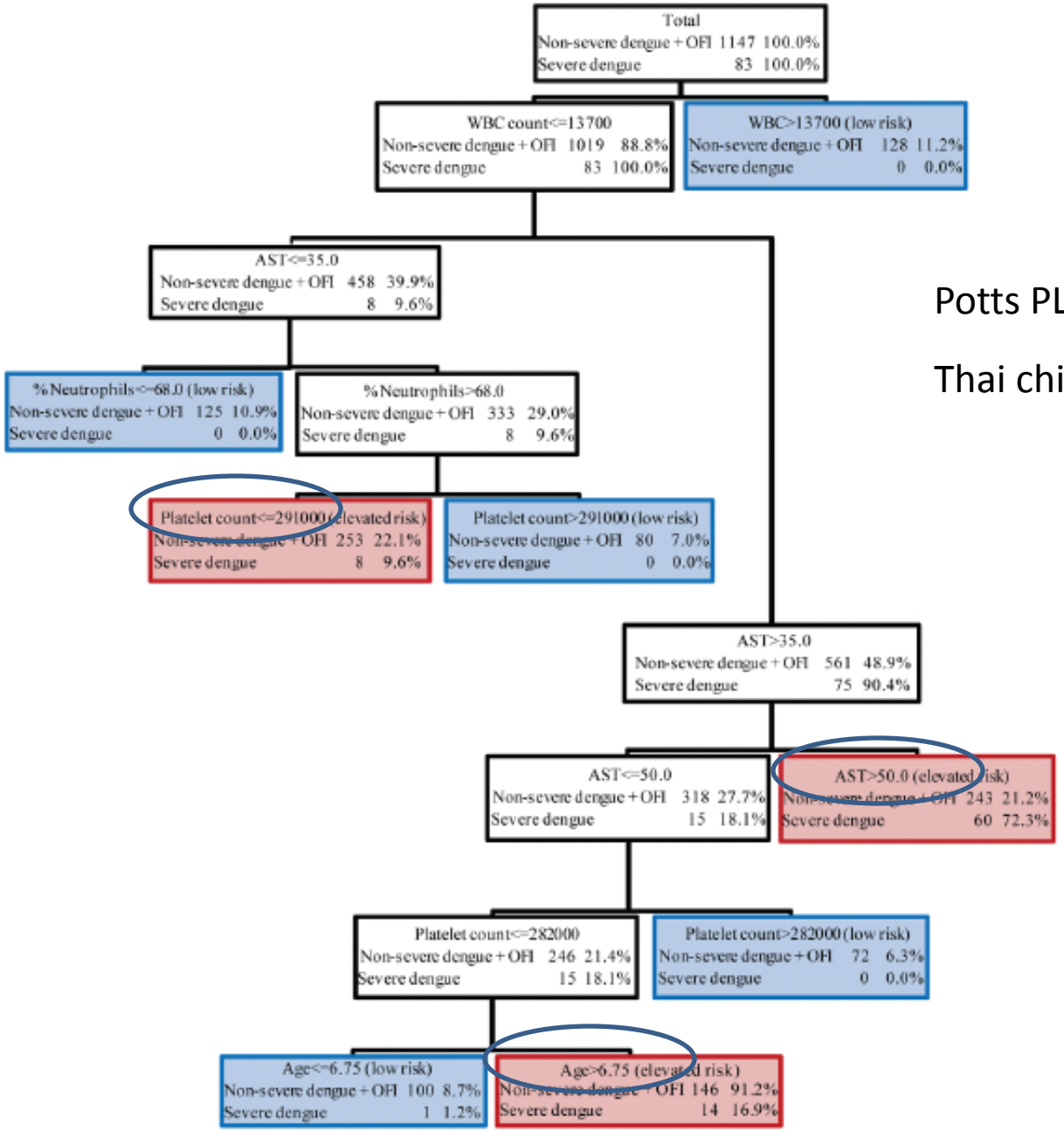

Figure 2. CART algorithm #2 for identifying patients who subsequently developed severe dengue (defined as WHO criteria for dengue shock syndrome, DSS, or dengue with significant pleural effusion) using clinical laboratory data obtained within the first three days of illness. Pleural effusion index (PEI)>15 was used as the criterion for significant pleural effusion. Each node is shown with the selected splitting variable, the number of patients with severe/non-severe or OFI, and the proportion of each from the parent node. Terminal nodes are marked as 'elevated risk' of severe dengue illness, outlined in red, and 'low risk' of severe dengue, outlined in blue.

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Potts PLOS NTD 2010;4:e769

Thai children

Predictive value of simple clinical and laboratory variables for dengue hemorrhagic fever in adults

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Journal of Clinical Virology 42 (2008) 34–39

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1973 dengue patients at TTSH, 2004, 118 had DHF, 82 developed DHF after admission

Variables	Univariate factors		Multivariate factors	
	Odds ratio	95% CI	Odds ratio	95% CI
Presence of bleeding	40.8	24.0, 69.2	237.6	51.9, 1087.1
Rash	1.61	1.03, 2.53		
Pulse pressure (mmHg)	0.98	0.95, 0.99		
Lymphocyte proportion (%)	0.98	0.96, 0.99	0.94	0.89, 0.99
Platelets ($\times 10^3/\mu L$)	0.99	0.98, 0.99		
Urea (mmol/L)	1.10	1.01, 1.22	1.31	1.12, 1.55
Total protein (g/L)	0.89	0.85, 0.93	0.79	0.71, 0.87
Alanine transaminase (IU/L)	1.001	1.001, 1.003		
Aspartate transaminase (IU/L)	1.001	1.001, 1.002		
Gamma glutamyl transpeptidase (IU/L)	1.002	1.001, 1.003		

Utility of investigational laboratory markers predictive of DHF compared with the predictive probability equation utilizing clinical and laboratory predictors in this study

Variable	Sensitivity (%)	Specificity (%)	PPV[a] (%)	NPV[a] (%)
sTNFR80[b] cut-off 1.6 ng/mL 2 days before fever abates (25)	67	80	66	69
Dengue viral load >5.7 log on day fever abates (24)	–	–	88	95
Free secreted NS1[c] >600 ng/mL (26)	72	79	81	69
Platelet-associated IgM >20 ng/10^7 platelets (27)	49	92	–	–
sTNFR75[d] >55 pg/mL predicted DHF with shock vs. no shock (28)	93	34	27	95
Outcome of predictive probability equation, $\ln\frac{p_i}{1-p_i} \geq -2.9$	83	84	18	99
Outcome of predictive probability equation, $\ln\frac{p_i}{1-p_i} \geq -5.1$	98	60	10	>99

Decision tree algorithm in deciding hospitalization for adult patients with dengue haemorrhagic fever in Singapore

V. J. Lee[1], D. C. Lye[2], Y. Sun[3] and Y. S. Leo[2]

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Tropical Medicine and International Health

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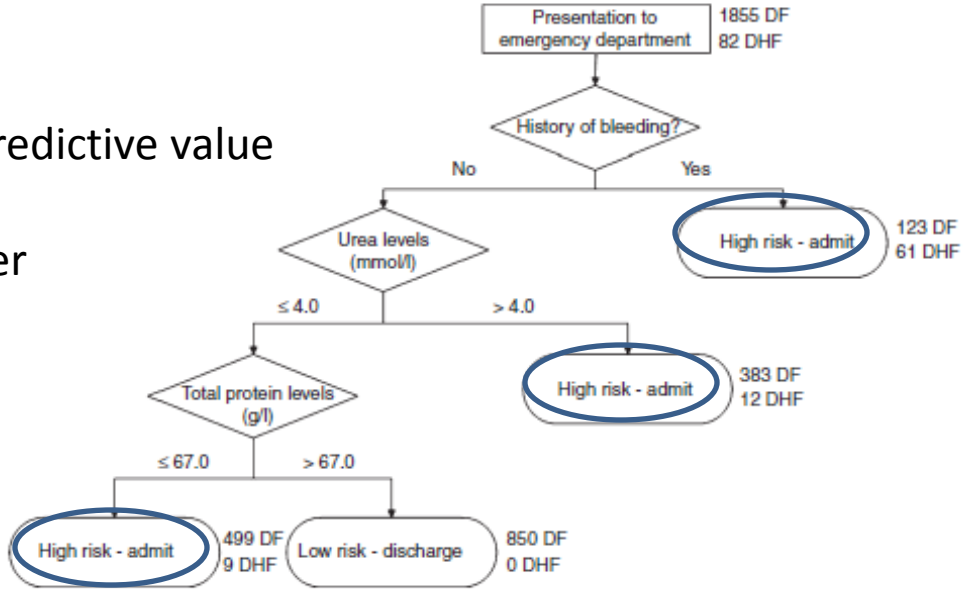
Sensitivity and negative predictive value preserved
Specificity marginally lower



Variable	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall accuracy (%)
Decision tree	100	46	8	100	48
Outcome of predictive probability equation >-2.9 (Lee *et al.* 2008)	83	84	18	99	84
Outcome of predictive probability equation >-5.1 (Lee *et al.* 2008)	98	60	10	>99	62

Validation of Probability Equation and Decision Tree in Predicting Subsequent Dengue Hemorrhagic Fever in Adult Dengue Inpatients in Singapore

Tun L. Thein,* Yee-Sin Leo, Vernon J. Lee, Yan Sun, and David C. Lye

Am. J. Trop. Med. Hyg., 85(5), 2011, pp. 942–945

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Validation of the probability equation and decision tree in the 2007 cohort for predicting progression to dengue hemorrhagic fever

	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Probability equation				
2004* Cohort	98	60	10	99
2007† (the whole cohort)	94	17	16	94
2007 (PCR positive only)	97	14	22	94
2007 (serology positive only)	92	17	13	94
Decision tree				
2004* Cohort	100	46	8	100
2007† (the whole cohort)	99	12	16	99
2007 (PCR positive only)	100	10	22	100
2007 (serology positive only)	99	13	13	99

2004 cohort: n=1973, DHF 118
2007 cohort: n=1017, DHF 215

Sensitivity and negative predictive value remain good
Specificity lower

Safety and cost savings of reducing adult dengue hospitalization in a tertiary care hospital in Singapore

Linda K. Lee[a,*], Arul Earnest[b], Luis R. Carrasco[c], Tun L. Thein[a], Victor C. Gan[a], Vernon J. Lee[d], David C. Lye[a,d] and Yee-Sin Leo[a,d]

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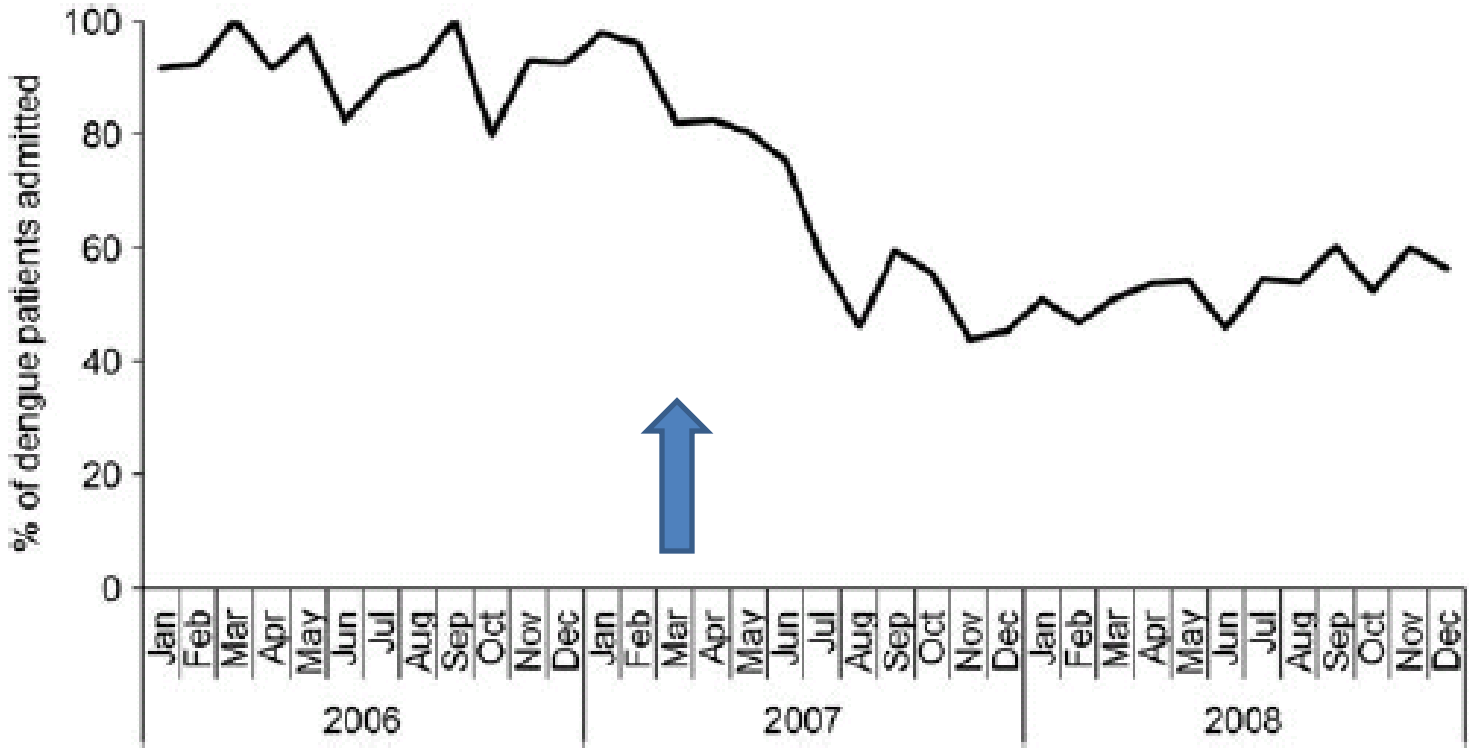
Trans R Soc Trop Med Hyg 2013; **107**: 37–42



Monthly proportion of dengue patients admitted to Tan Tock Seng Hospital, Singapore, January 2006–December 2008

Safety and cost savings of reducing adult dengue hospitalization in a tertiary care hospital in Singapore

Linda K. Lee[a,*], Arul Earnest[b], Luis R. Carrasco[c], Tun L. Thein[a], Victor C. Gan[a], Vernon J. Lee[d], David C. Lye[a,d] and Yee-Sin Leo[a,d]

Trans R Soc Trop Med Hyg 2013; **107**: 37–42

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Table 1. Demographic and clinical characteristics of dengue inpatients at Tan Tock Seng Hospital, Singapore, 2006–2008

	2006 (n = 468)	2007 (n = 1005)	2008 (n = 793)	p-value
Demographics				
Age (years) [median (IQR)]	34 (27–42)	35 (27–45)	35 (26–45)	0.045
Male gender	327 (69.9)	657 (65.4)	536 (67.6)	NS
Charlson score ≥3	8 (1.7)	13 (1.3)	4 (0.5)	NS
WHO 1997 classification				
Dengue fever	292 (62.4)	578 (57.5)	498 (62.8)	0.045
Dengue hemorrhagic fever	122 (26.1)	332 (33.0)	239 (30.1)	0.025
Dengue shock syndrome	26 (5.6)	64 (6.4)	34 (4.3)	NS
WHO 2009 classification				
Dengue without warning signs	80 (17.1)	214 (21.3)	130 (16.4)	0.018
Dengue with warning signs	282 (60.3)	574 (57.1)	512 (64.6)	0.006
Severe dengue	100 (21.4)	207 (20.6)	144 (18.2)	NS
Treatment				
Intravenous fluids ever given	432 (92.3)	902 (89.8)	696 (87.8)	0.038
Blood ever given	5 (1.1)	8 (0.8)	3 (0.4)	NS
Platelet ever given	53 (11.3)	85 (8.5)	62 (7.8)	NS
Outcome				
Length of stay, days[a] (IQR)	4.2 (3–5)	3.8 (3–5)	3.8 (3–5)	<0.001
Intensive care unit admission	2 (0.4)	6 (0.6)	0	0.051
Death	2 (0.4)	3 (0.3)	0	NS

Cost saving USD1.4million in 2008

Predictive Tools for Severe Dengue Conforming to World Health Organization 2009 Criteria

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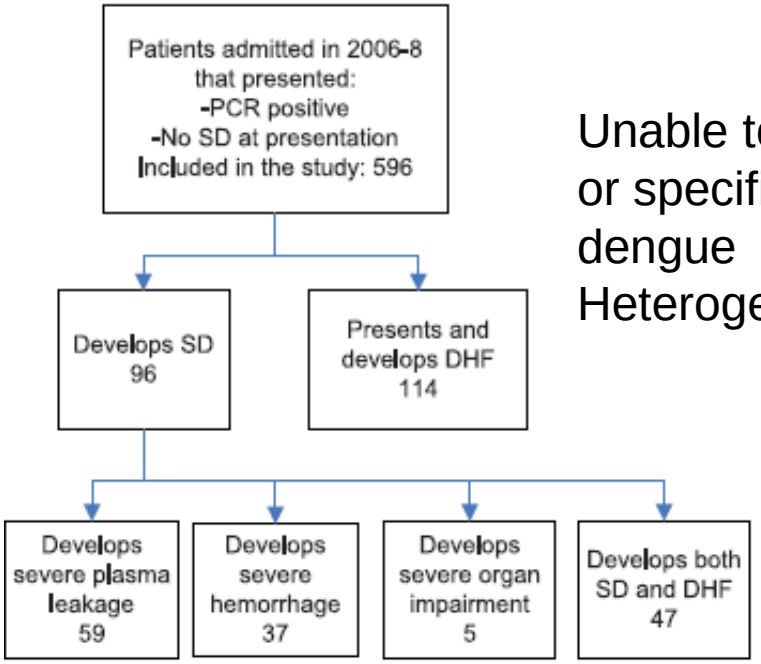
Luis R. Carrasco[1], Yee Sin Leo[2,3*], Alex R. Cook[3,4,5], Vernon J. Lee[3,5,6], Tun L. Thein[2], Chi Jong Go[2], David C. Lye[2,7]

PLOS | NEGLECTED TROPICAL DISEASES
July 2014 | Volume 8 | Issue 7 | e2972



Unable to derive highly sensitive or specific predictors for severe dengue

Heterogeneous groups?

Table 2. Sensitivity and specificity of the GLMs for the prediction of SD using only PCR-positive dengue.

Setting compatibility	Data	Response variable	Specificity (Sens = 1)	Specificity (Sens = 0.95)	Specificity (Sens = 0.9)
resourced	PCR	Any SD	0.01 (0)	0.26 (0.21)	0.41 (0.29)
resource-limited	PCR	Any SD	0.05 (0)	0.21 (0.15)	0.37 (0.27)
resourced	PCR and serology	Any SD	0.08 (0)	0.30 (0.25)	0.40 (0.30)
resource-limited	PCR and serology	Any SD	0.10 (0)	0.36 (0.30)	0.40 (0.30)
resourced	PCR	SH	0.27 (0)	0.42 (0.35)	0.66 (0.47)
resourced	PCR	SPL	0.13 (0)	0.20 (0.14)	0.30 (0.20)

Outpatient dengue management

Dengue management: practical and safe hospital-based outpatient care

Paul R. Ingram[a,b], Malcolm Mahadevan[b,c], Dale A. Fisher[a,b,*]

Trans R Soc Trop Med Hyg (2008), doi:10.1016

Criteria for outpatient care: <60 years, not immunocompromised, no co-morbidity, good social support, able to drink, able to attend daily clinic review, platelet >50,000, no haemoconcentration, confusion, severe abdominal pain, bleeding or shock

Table 1 Comparison of demographics, laboratory findings, disease severity and outcomes of those patients who received hospital-based care

	Hospital-based outpatients	Inpatients	*P*-value
No. of patients	118	221	
Age (years) (mean ± SD)	35 ± 13	44 ± 15	<0.001
Male (*n*) (%)	81 (69%)	114 (52%)	0.003
Platelet count on admission ($\times 10^9$/l) (median [IQR])	82 (68–104)	51 (33–81)	<0.001
Platelet count nadir ($\times 10^9$/l) (median [IQR])	72 (58–84)	35 (18–61)	<0.001
Disease severity (%)			
DF	118 (100%)	181 (82%)	<0.001
DHF/DSS	0	40 (18%)	
Length of stay in clinic/ward (days) (mean ± SD)	1.8 ± 1.3	3.8 ± 2.5	<0.001
Died (*n*) (%)	0	2 (1%)	0.042

IQR: interquartile range; DF: dengue fever; DHF: dengue haemorrhagic fever; DSS: dengue shock syndrome.

Simple Clinical and Laboratory Predictors of Chikungunya versus Dengue Infections in Adults

Vernon J. Lee[1,2*], Angela Chow[1], Xiaohui Zheng[3], Luis R. Carrasco[3,4], Alex R. Cook[2,3,5], David C. Lye[6], Lee-Ching Ng[7], Yee-Sin Leo[6]

PLOS | NEGLECTED TROPICAL DISEASES September 2012 | Volume 6 | Issue 9 | e1786

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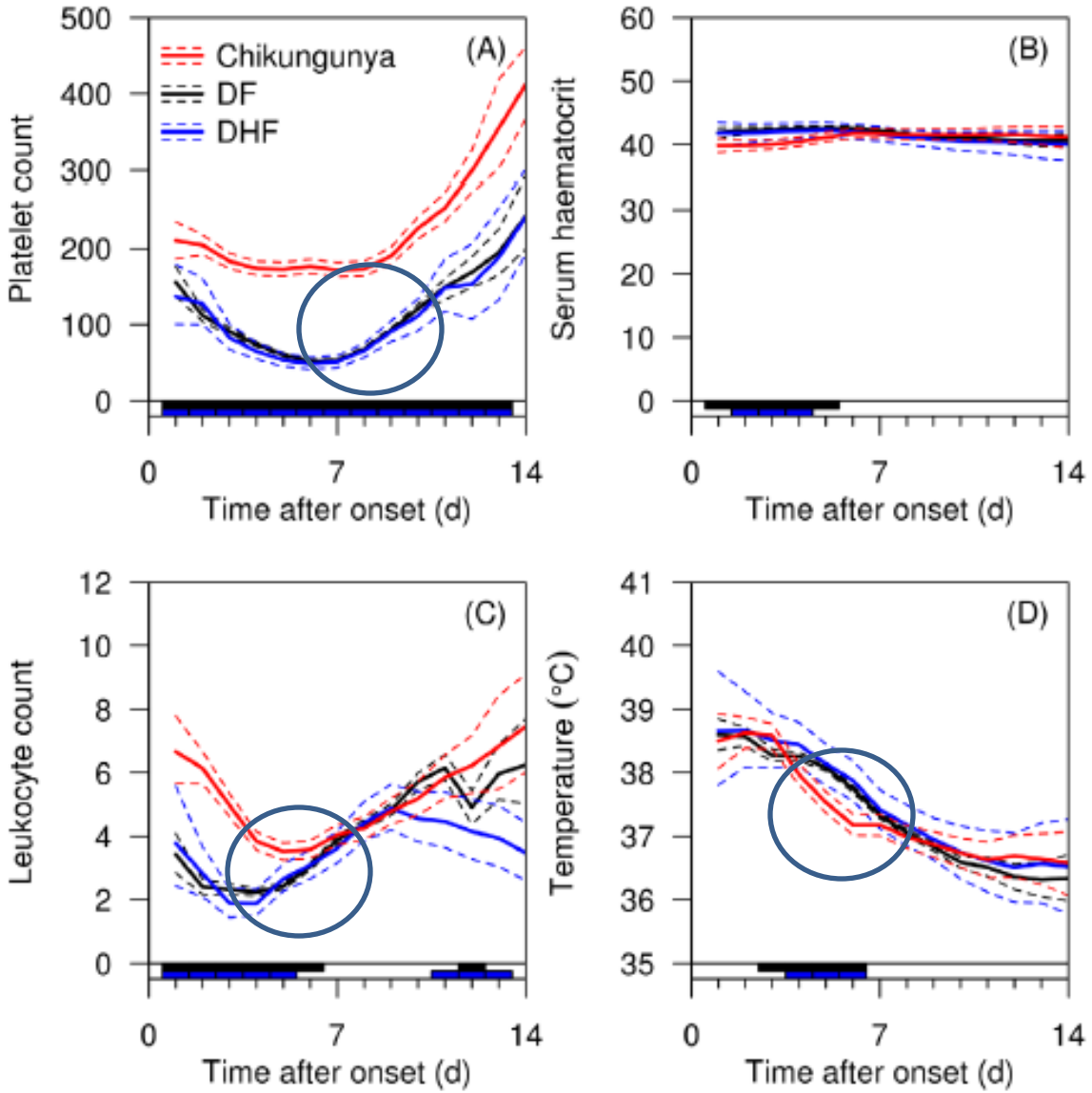

Monitor FBC and BP daily
Postural BP
Symptom relief
No NSAID
Medical leave

Look for haematocrit rise
Threshold 20%

Beware drop in haematocrit
Occult bleeding
Haemodynamic instability

To predict convalescence
Defervescence
WCC rises before PLT

Fluid Intake and Decreased Risk for Hospitalization for Dengue Fever, Nicaragua

Eva Harris,* Leonel Pérez,† Christina R. Phares,* Maria de los Angeles Pérez,‡ Wendy Idiaquez,‡ Julio Rocha,§ Ricardo Cuadra,§ Emelina Hernandez,¶ Luisa Amanda Campos,† Alcides Gonzalez,† Juan Jose Amador,† and Angel Balmaseda†

EID 2003:9:1003

Encourage oral fluid >5 glasses a day

Table 2. Crude and adjusted odds ratios and 95% confidence intervals for factors potentially associated with hospitalization for classic dengue fever or dengue fever with hemorrhagic manifestations

	Children (<15 years of age)[a]			Older adolescents and adults (≥15 years of age)[a]		
Characteristic	No. of patients[b]	OR (95% CI)[c] Crude	OR (95% CI)[c] Adjusted[d]	No. of patients[b]	OR (95% CI)[c] Crude	OR (95% CI)[c] Adjusted[f]
Fluid intake during 24-h period before presentation	587			405		
For each additional glass		0.68 (0.62 to 0.75)	0.74 (0.66 to 0.83)		0.67 (0.5 to 0.79)	0.71 (0.59 to 0.85)
>5 glasses		0.14 (0.08 to 0.25)	0.19 (0.09 to 0.39)[e]		0.16 (0.06 to 0.43)	0.20 (0.07 to 0.57)[g]
Age	719		—[h]	464		—
For each additional year		0.93 (0.8 to 0.97)			0.98 (0.96 to 1.00)	
Sex	718			464		
Male	395	1.43 (1.06 to 1.94)		291	1.27 (0.74 to 2.17)	
Female	323			173		
Distance from healthcare facility	701			460		
For each additional 5 km		2.13 (1.68 to 2.69)	1.46 (1.12 to 1.91)		1.16 (0.92 to 1.46)	—
Date of onset of symptoms	709			455		
For each additional month		1.26 (1.16 to 1.37)	1.51 (1.26 to 1.81)		1.87 (1.53 to 2.29)	2.08 (1.53 to 2.83)
Days between onset of symptoms and being seen at facility	713			457		
For each additional day		1.04 (1.0 to 1.07)	—		0.98 (0.93 to 1.03)	—
Thrombocytopenia	499			227		
Yes	189	6.5 (4.25 to 9.96)	6.16 (3.57 to 10.64)	33	3.31 (1.53 to 7.15)	3.62 (1.24 to 10.52)
No	310			194		
Stomach pain	681			439		
Yes	370	0.94 (0.69 to 1.28)	—	216	1.50 (0.89 to 2.56)	—
No	311			223		

Comparison of the effects of oral hydration and intravenous fluid replacement in adult patients with non-shock dengue hemorrhagic fever in Taiwan

Ing-Kit Lee[a], Wen-Huei Lee[b], Kuender D. Yang[c,d], Jien-Wei Liu[a,*]

Transactions of the Royal Society of Tropical Medicine and Hygiene 104 (2010) 541–545

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The level of plasma leakage is mild to moderate in patients with non-shock dengue hemorrhagic fever (DHF grade I and grade II), and the necessity of intravenous fluid replacement for these patients remains controversial. We conducted an observational study in adult patients (>18 years) with non-shock DHF admitted to a medical centre in southern Taiwan comparing the effects of oral hydration [group 1 (n = 19); age (mean ± SD) 54.6 ± 15.5 years] and intravenous fluid replacement, with a volume of >40 ml/kg/day in the first 72 h of hospitalization [group 2 (n = 30); age 55.9 ± 11.6 years]. No significant difference was found in demographics, clinical manifestations, and mean peak level of hematocrit between the two groups. Patients in group 2 had a significantly longer hospital stay compared to those in group 1 (P = 0.007), and there was a trend suggesting patients in group 2 were prone to develop pleural effusion and/or pulmonary edema. No difference was found in daily mean pulse pressure, mean hematocrit level, and mean platelet count between the groups for the duration of the 7 days in hospital. All 49 patients survived. Our data suggest that oral hydration may be as effective as intravenous fluid replacement for adults with non-shock DHF and this warrants investigation in a larger series of patients.

Mild DHF can be managed with oral fluid

TTSH outpatient dengue care path

Summary

- Identify mild illness and low risk for complications for outpatient follow-up
- Resources:
  - Primary care
  - Dengue diagnosis confirmation
  - Daily review with FBC and BP
  - Encourage oral fluid
  - Symptomatic treatment (avoid NSAID)

Thank you for your attention

Questions?

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