Mahidol University
Faculty of Tropical Medicine

Bayesian Network Decision Model for Supporting Dengue Diagnosis

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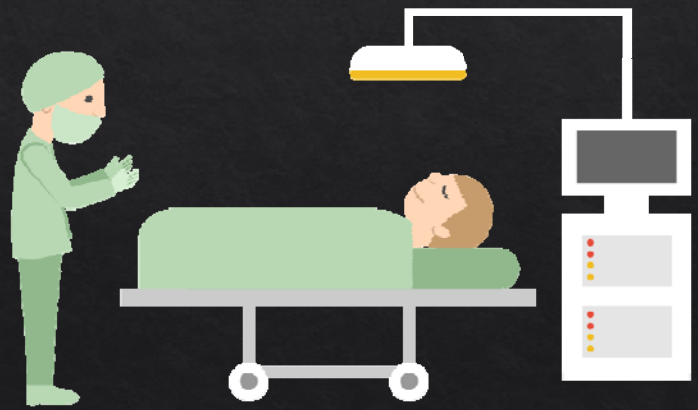
Doctor making diagnosis

History Taking

Physical Examination

Basic Laboratory tests



Confirmed Laboratory tests

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Making Diagnosis decision is a complex process

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Dengue Diagnosis

Require physician's knowledge, skills, and experience

Day of fever

Stay in/travel to endemic area

Other tests, etc

Acute fever + Nausea + Vomiting + muscle pain
Tourniquet test- negative
Hct – 34%, Platelet 180,000

Not Dengue?

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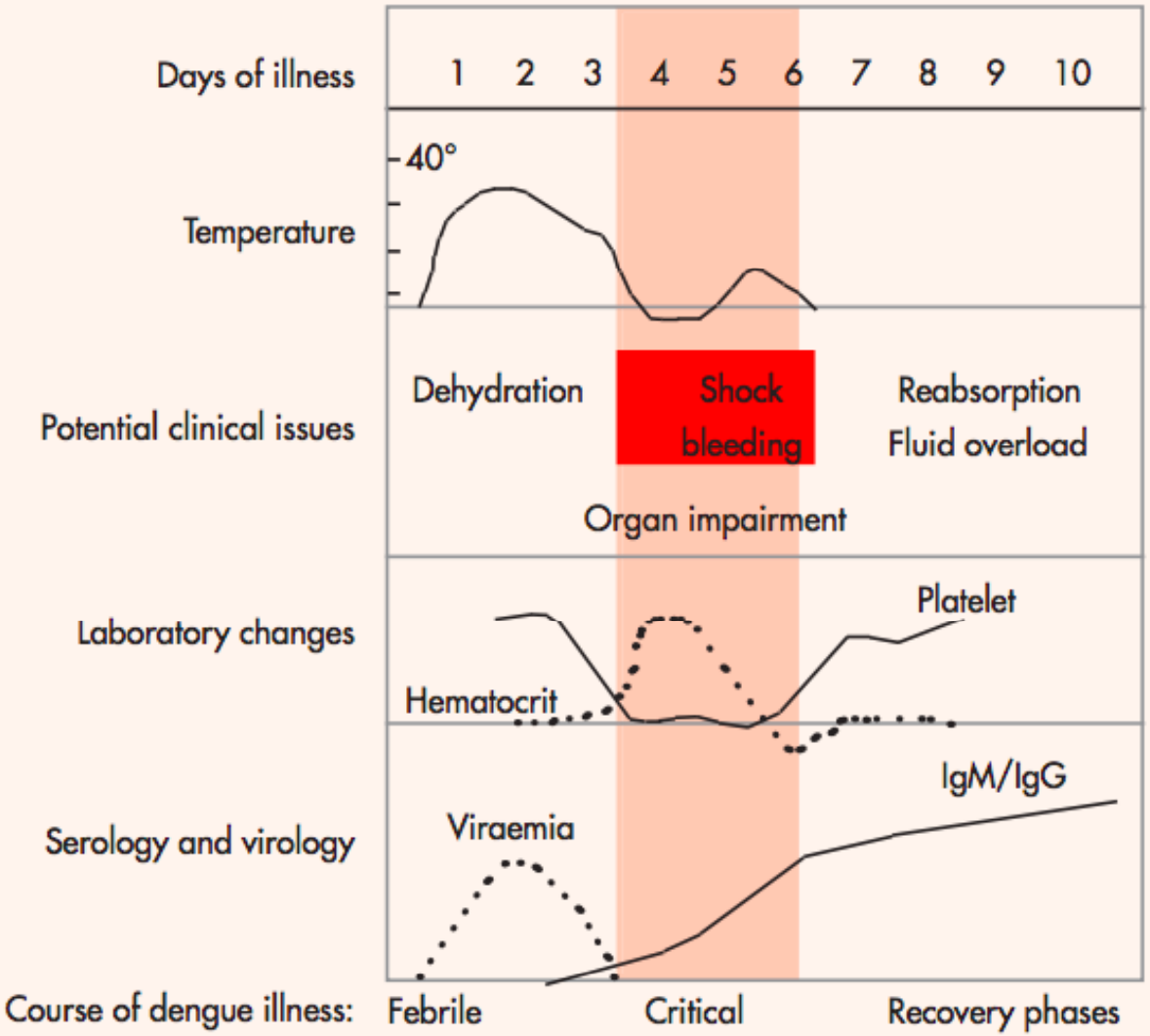
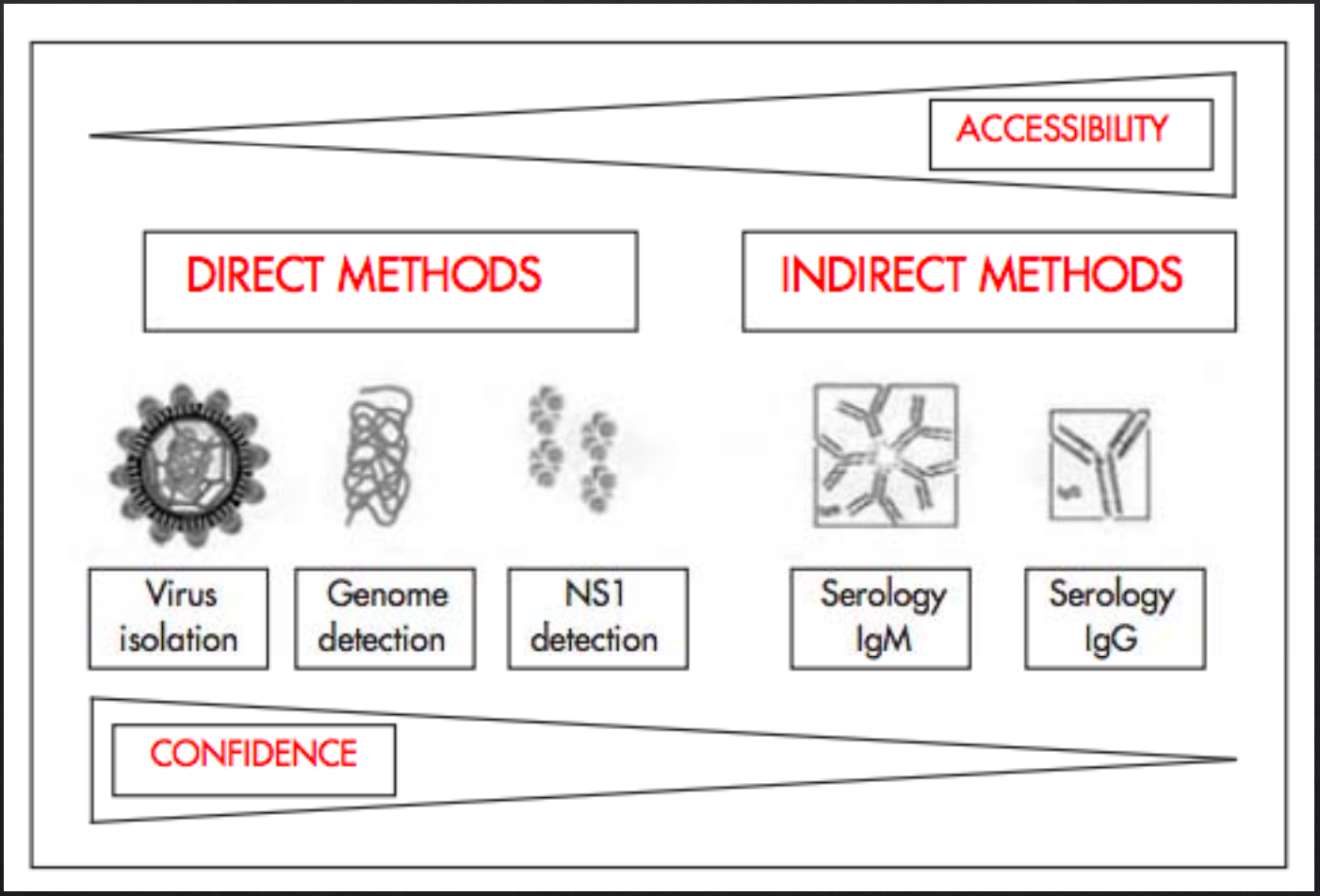


Dynamic

Non-linear

WHO: Dengue Guideline for Diagnosis, Treatment, Prevention and Control. 2009

Diagnostic Tests for Dengue



- Equipment needed
- Time to results
- Time of specimen collection after onset
- Cost

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WHO: Dengue Guideline for Diagnosis, Treatment, Prevention and Control. 2009

Machine Learning for Medical Diagnosis

- Clinical Profiles
- Tests
- Related data
- Confirmed diagnosis

- Recognize data pattern
- Generate algorithm to understand data

- Prediction
- Probability of disease

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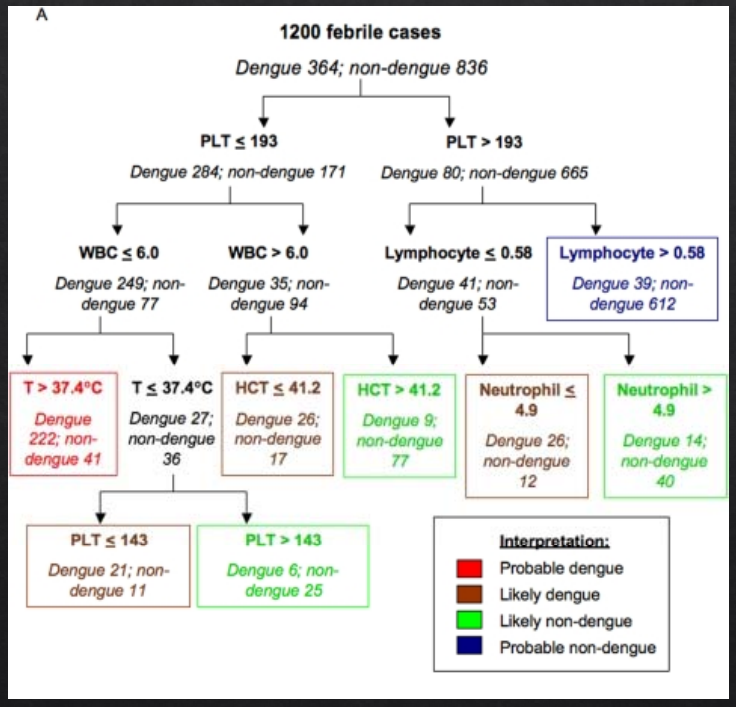
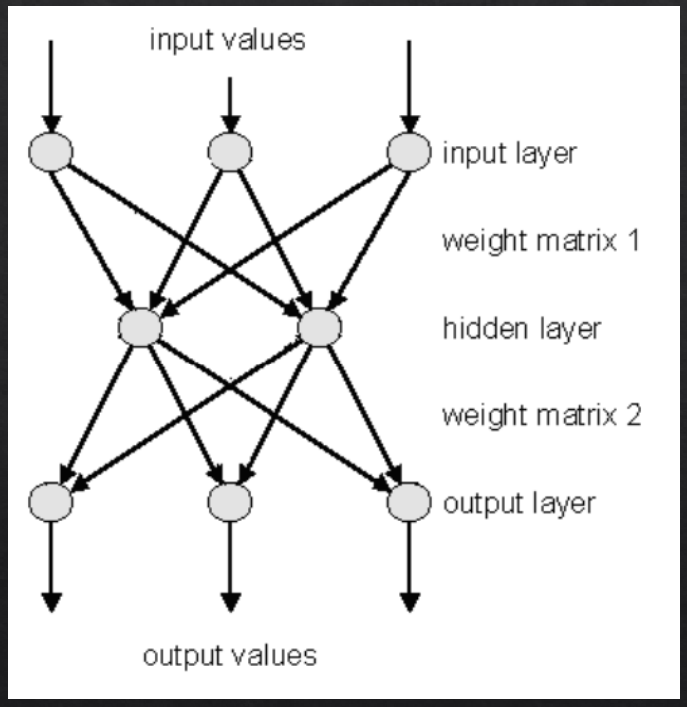
Common Algorithm

Decision Trees



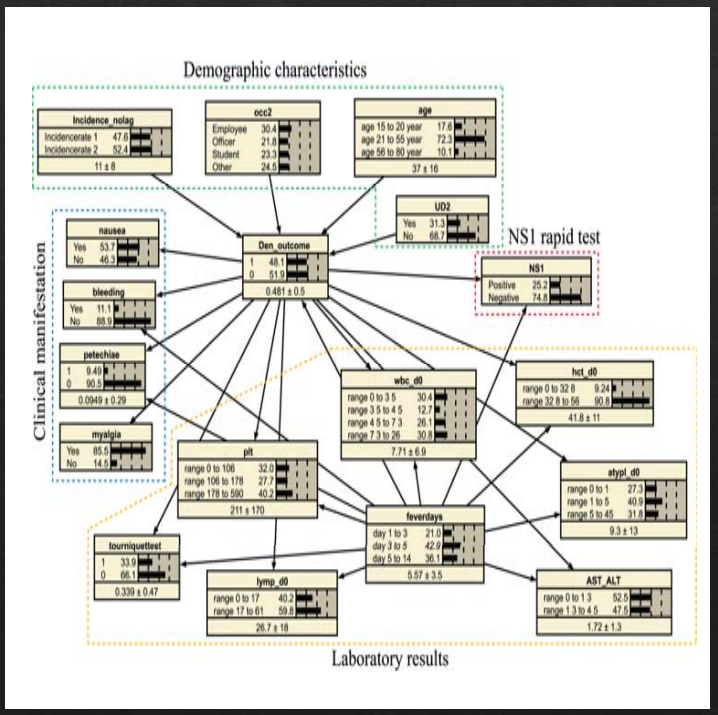
Tanner L., et al. PLoS Negl Trop Dis. 2008

Artificial Neuron Network



Al-Shayea QK. International Journal of Computer Science. 2011

Bayesian Network



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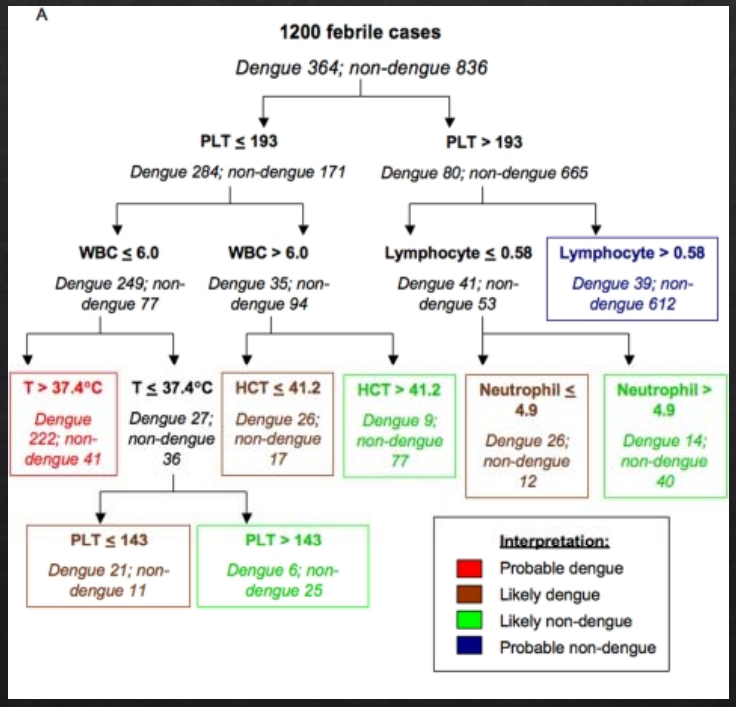
Common Algorithms

Decision Trees



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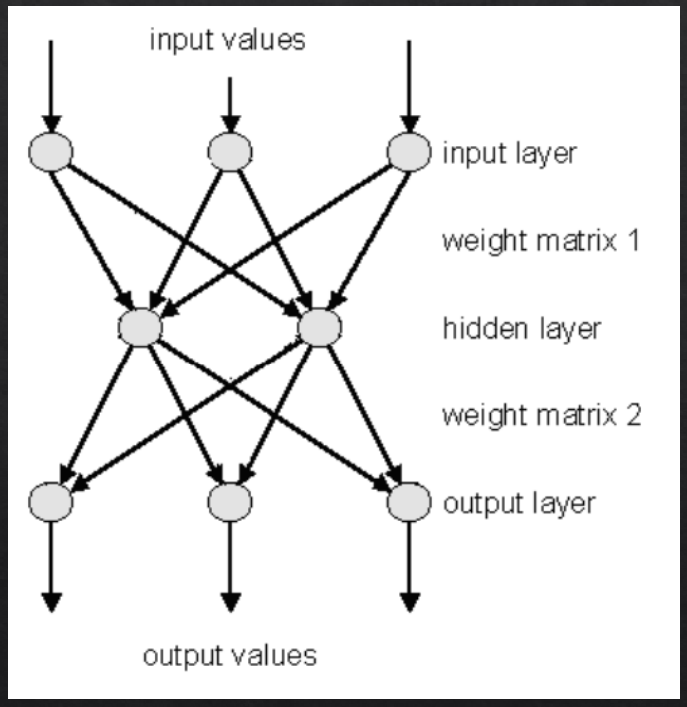

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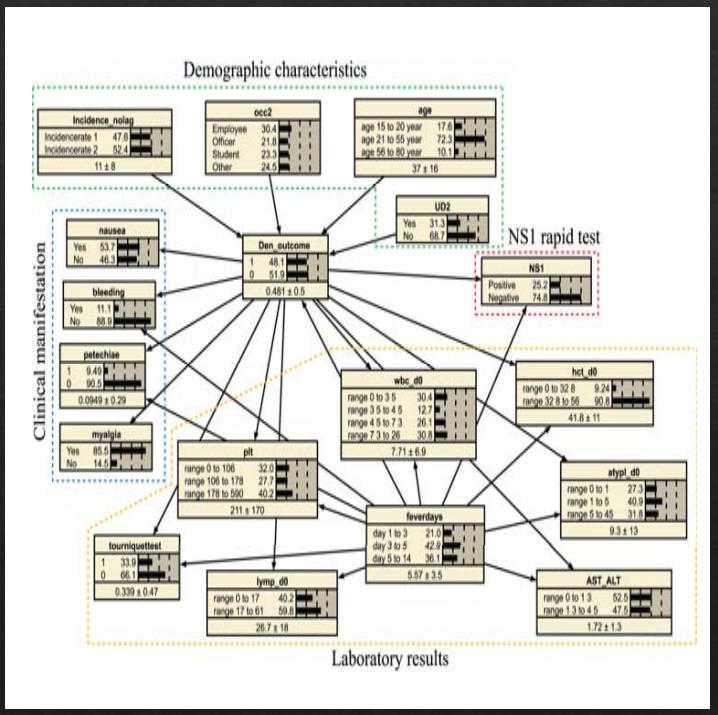

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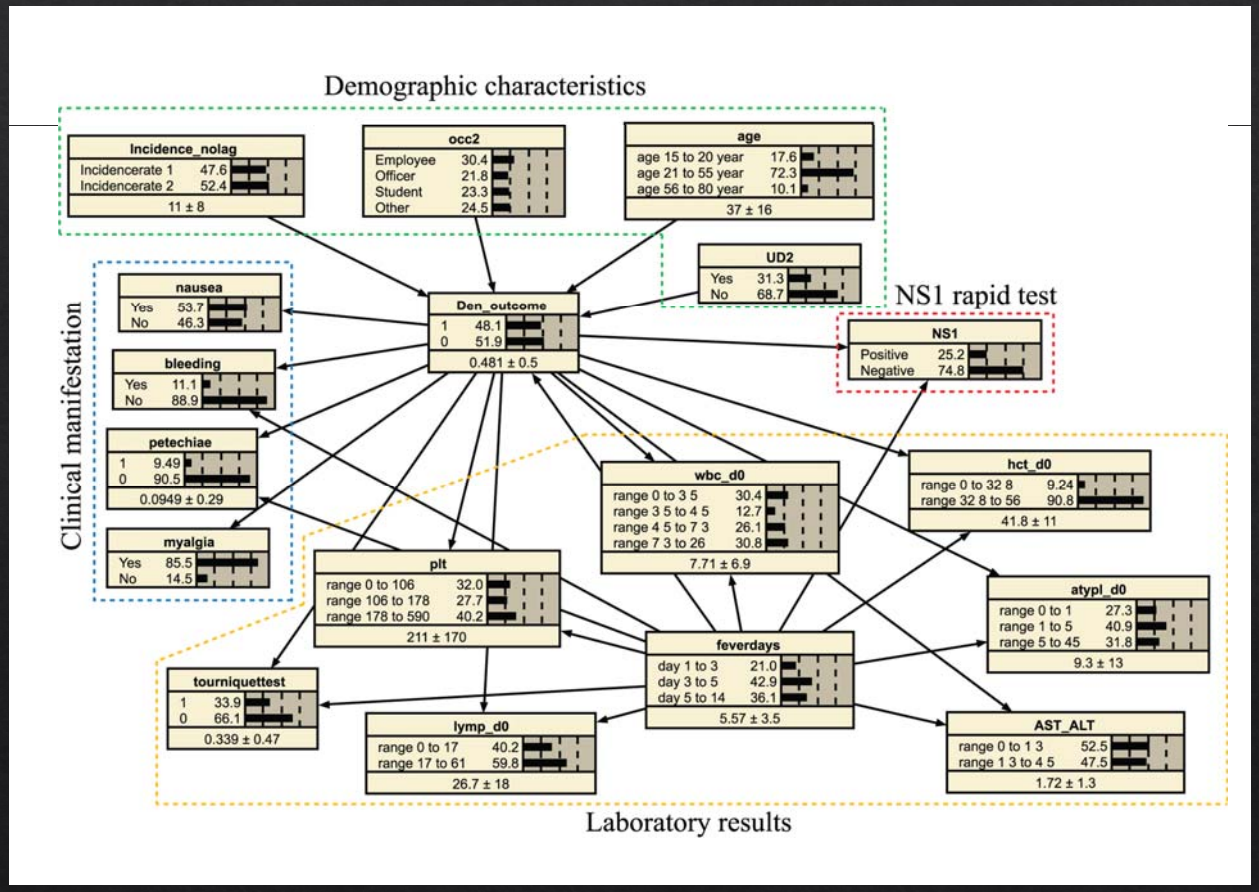
Bayesian Network Diagnosis Decision Model



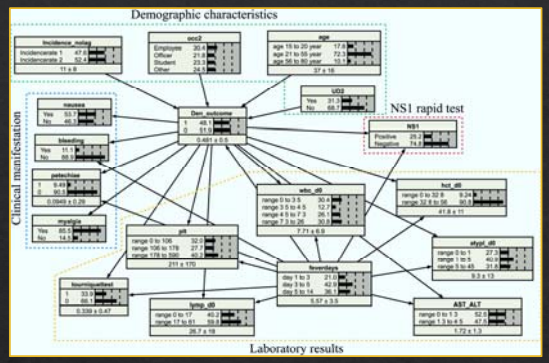
Assuming conditional independence among variables

Transparency of diagnostic knowledge

Solve the task in a similar way as human

Kononenko I. Machine learning for medical diagnosis: history, state of the art and prospective. Artificial Intelligence in Medicine. 2001

Objectives



Develop Bayesian Network model for Dengue Diagnosis using clinical and basic laboratory tests

Compare diagnostic performance between models with and without NS1 rapid test result

Compare diagnostic performance between the models and physicians decision

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Data Source

Previous cohort study on acute undifferentiated febrile illness

March 2013-February 2014

397 AUFI patients

- Aged >15 years
- Body Temp >= 37.8 C
- No specific organ infection

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Data Source

Monthly Dengue incidence in Bangkok from the national surveillance system, MOPH

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Patient's information

- Demographic information
- History taking

- Physical examination
- Tourniquet Test

Basic Laboratory tests

- CBC, UA
- Blood Chemistry
- NS1-IgM/IgG rapid test

Confirmed laboratory tests

- Dengue (Serology & PCR)
- Leptospirosis (Serology & PCR)
- Murine typhus (Serology & PCR)
- Scrub typhus (Serology & PCR)
- Influenza (Serology)
- Blood culture

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Confirmed Dengue Infection

Positive PCR for dengue virus

OR

Fourfold or greater increase in IgG antibody titer in paired serum

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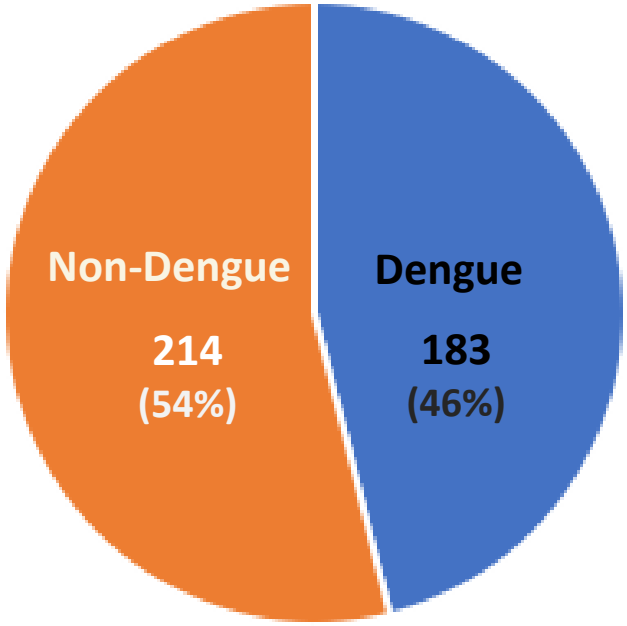
Final Diagnosis

AUFI	147
Murine typhus	21
Leptospirosis	16
Influenza	15
Bacteremia	4
Scrub typhus	4
Enteric fever	2
Murine + Influenza	2
Bacteremia + Influenza	1
Lepto + Influenza	1
Lepto + Scrub	1



Single infection	154
Dengue + Lepto	9
Dengue + Influenza	8
Dengue + Murine	7
Dengue + Scrub	2
Dengue + Typhoid	1
Dengue + Lepto + Murine	1
Dengue + Hep A	1

No statistical difference between single and co-infection

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Potential Factors for Dengue Diagnosis

Demographic characteristics	Clinical manifestation	Laboratory indicators
• Age	• Nausea	• Platelet
• Occupation	• Vomiting	• Hematocrit
• Underlying diseases	• Rash	• White Blood Cell
	• Bleeding	• %Lymphocyte
Monthly incidence report in Bangkok	• Petechial	• %Neutrophil
	• Myalgia	• %Atypical lymphocyte
	• Tourniquet test	• AST / ALT ratio
	• Dehydration	• NS1 rapid test
	• Diarrhea	
	• Day of fever	

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Based on expert opinion, literature review, and univariate analysis

Dengue Rapid Test

	Total N	Dengue infection N (%)	Non-Dengue N (%)
NS1 antigen test			
Positive	101	99 (54)	2 (1)
Negative	296	84 (46)	212 (99)
NS1 + IgM/IgG (Dual test)			
Positive	118	108 (59)	10 (5)
Negative	279	75 (41)	204 (95)

80% of patients came to the clinic within 5 days

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Software


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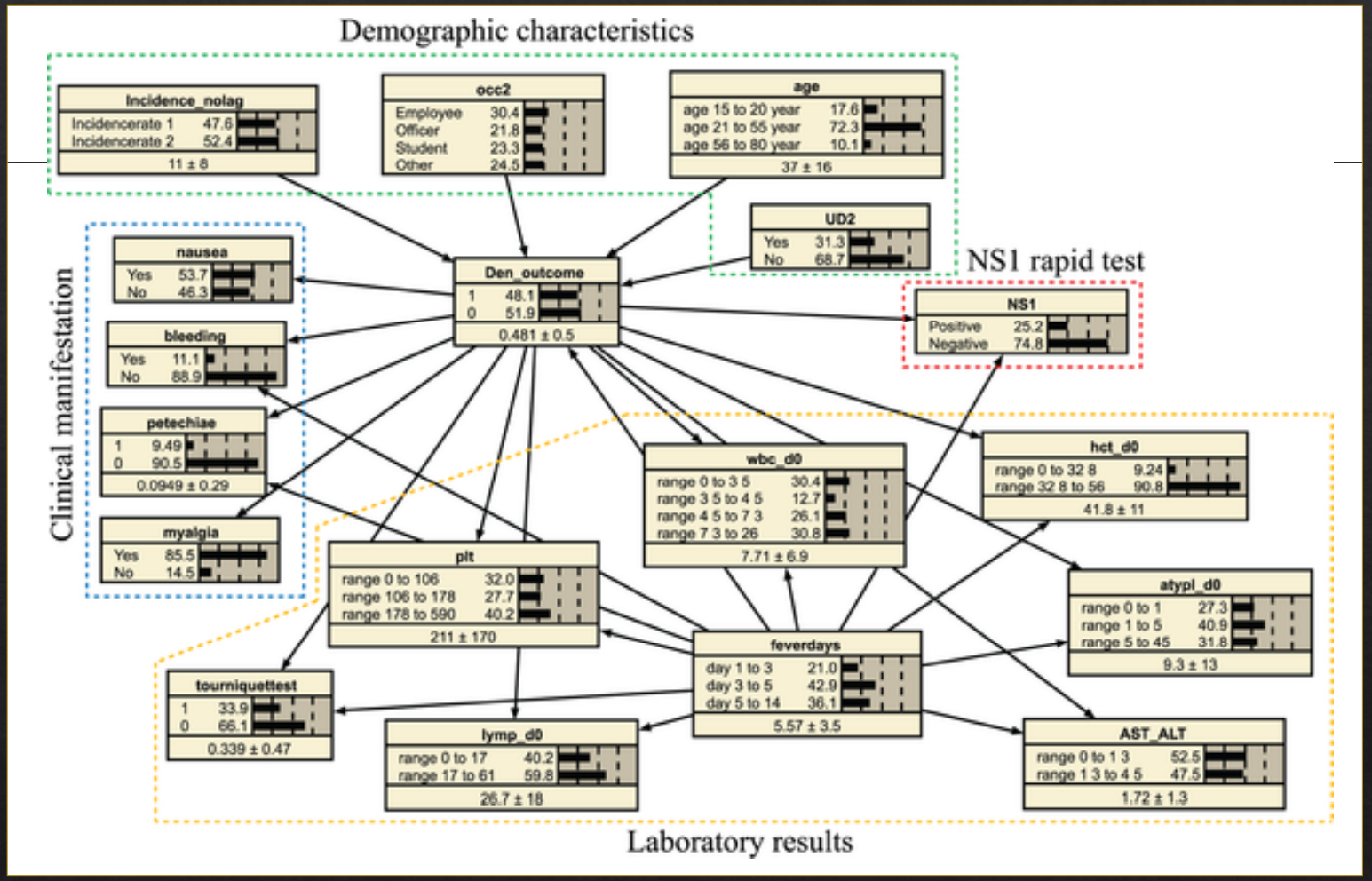
Bayesian Network Model



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Performance of BN dengue diagnosis model

Model	1	2	3	4	5	6	7
Demographic characteristics	✓			✓	✓	✓	✓
Clinical manifestations		✓		✓	✓	✓	✓
Laboratory indicators			✓	✓	✓	✓	✓
NS1 antigen test					✓		✓
Incidence rate						✓	✓
AUC	0.65	0.72	0.87	0.88	0.92	0.92	0.94

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Accuracy of BN dengue diagnosis model

10-fold cross-validation method

Training dataset Testing dataset

1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.76	0.87
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.63	0.73
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.81	0.87
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.75	0.79
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.71	0.81
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.81	0.89
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.62	0.72
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.75	0.86
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.69	0.81
1-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-397	0.96	0.97
									Mean AUC (SD)	0.75 (0.09)	0.83 (0.07)

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Physician's diagnosis

2 infectious diseases fellowships independently review patient's information (with and without NS1 test results)

3rd infectious diseases fellowship review for disagreement decision

Agreement between the two physicians

Kappa coefficient

- With NS1 test = 0.59
- Without NS1 test = 0.5

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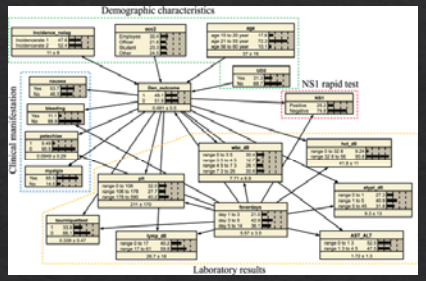
Overall Diagnostic Performance



Sensitivity	With NS1	73.2 (66.9-79.5)	73.5 (66.7-83.7)
	Without NS1	76.3 (68.9-83.7)	73.5 (62.5-84.5)
Specificity	With NS1	79.4 (72.2-86.1)	78.8 (69-88.4)
	Without NS1	71.9 (65.6-78.2)	66 (57.5-74.5)

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Limitations

Training dataset

- From one hospital, specialized in Tropical Medicine
- Small sample size

Did not include background immunity of patients

- History of dengue infection
- History of immunization with dengue vaccine

Dengue incidence data

- Included only data in Bangkok

Physician's decision made from only 2-3 physicians

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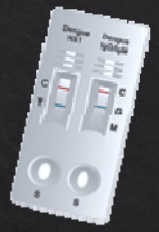
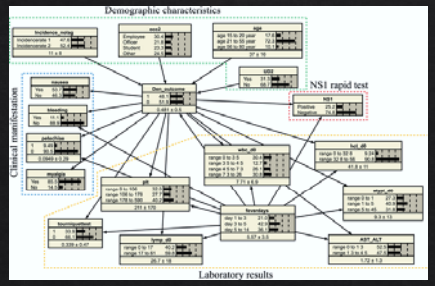
Conclusion

- Accuracy and reliability of clinical dengue diagnosis vary and depend on experience and condition of physicians
- Low reliability when confirmed laboratory not available



- Improve specificity for dengue diagnosis with loosing relatively small sensitivity
- Must incorporate clinical information when making decision



- Promising technique to assist dengue diagnosis
- Helpful in low-resource settings (inexperienced physicians, no confirmation lab)

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Take Home Messages

- Machine learning is a tool, not a magic wand
- Machine learning provides decision support, not replace human
- Machine learning will not automatically discover solutions without guidance
- Selection of machine learning methods/algorithm will affect accuracy of models
- Selection of training data will affect accuracy of models

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