BAYESIALAB

The webinar will start at:

13:00:00

The current time is:

13:01:13

Central Daylight Time
UTC-5

ARE TESTS OVERRATED?

Optimizing Health Policies

Malaria and Pneumonia in Sub-Saharan Africa

Introduction

Your Hosts Today

- Stefan Conrady
  stefan.conrady@bayesia.us

- Stacey Blodgett
  stacey.blodgett@bayesia.us

Today's Objectives

Methodological Objective

- Bayesian networks as a framework for reasoning about health policies under uncertainty.

Substantive Research Objective

- Establish optimal policies for malaria and pneumonia diagnosis and treatment, i.e., "Test & Treat" vs. Presumptive Treatment.

Today's Agenda

Motivation & Background

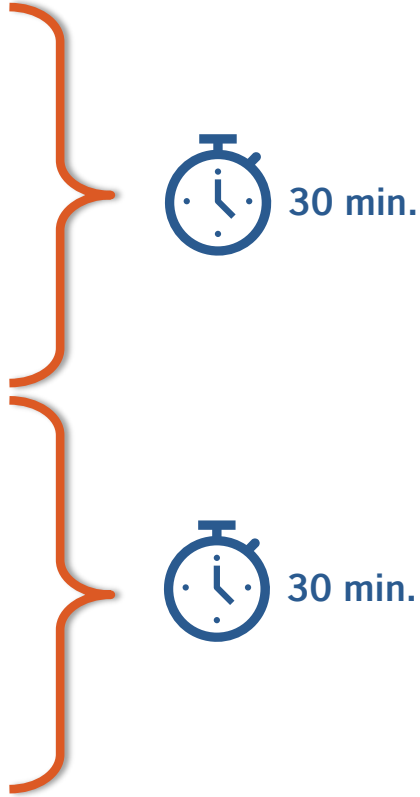
- Over- and Undertreatment Malaria and Pneumonia
- Testing Innovations & WHO Guidelines

Methodology

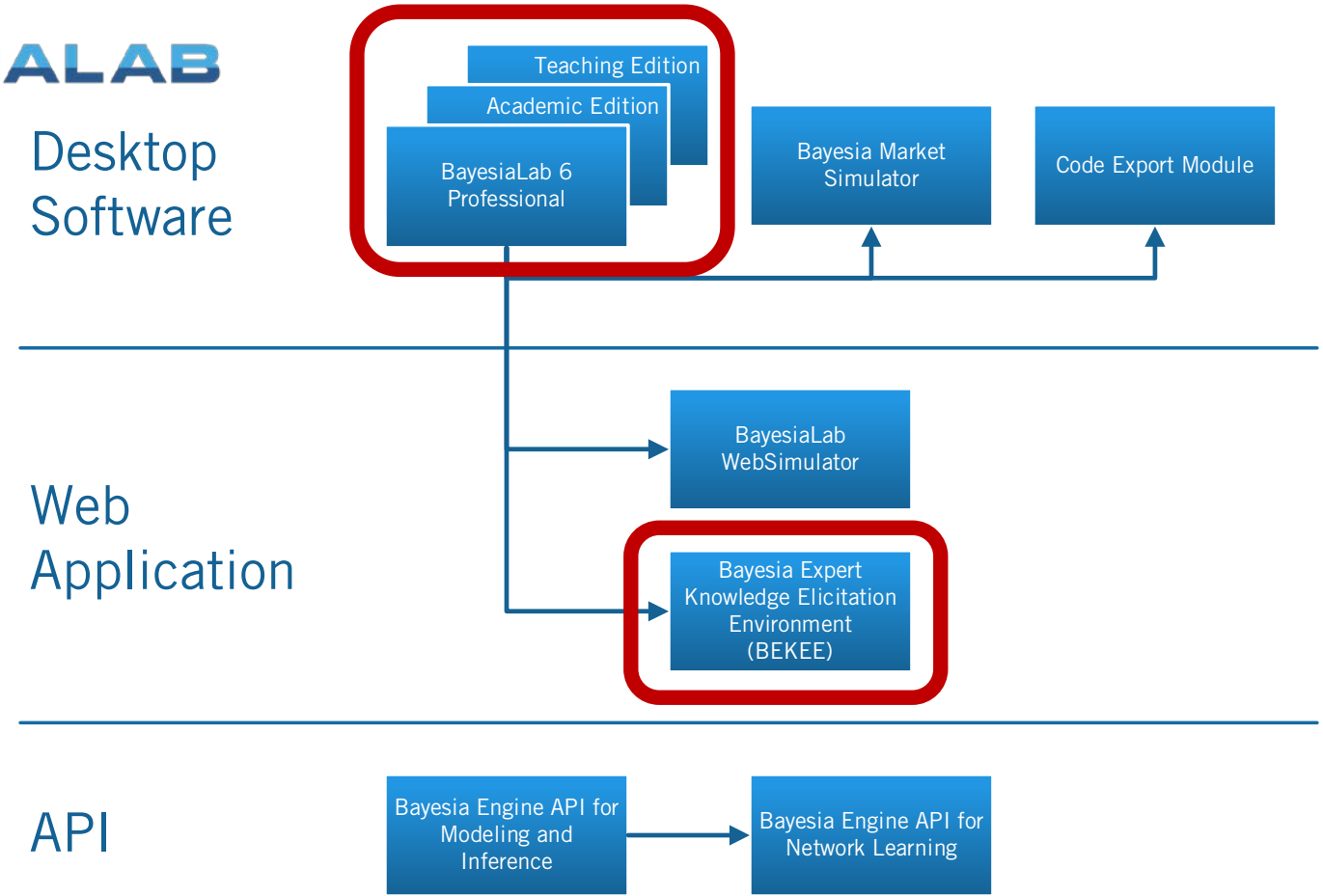
- Knowledge Modeling & Reasoning with Bayesian Networks

Research Workflow

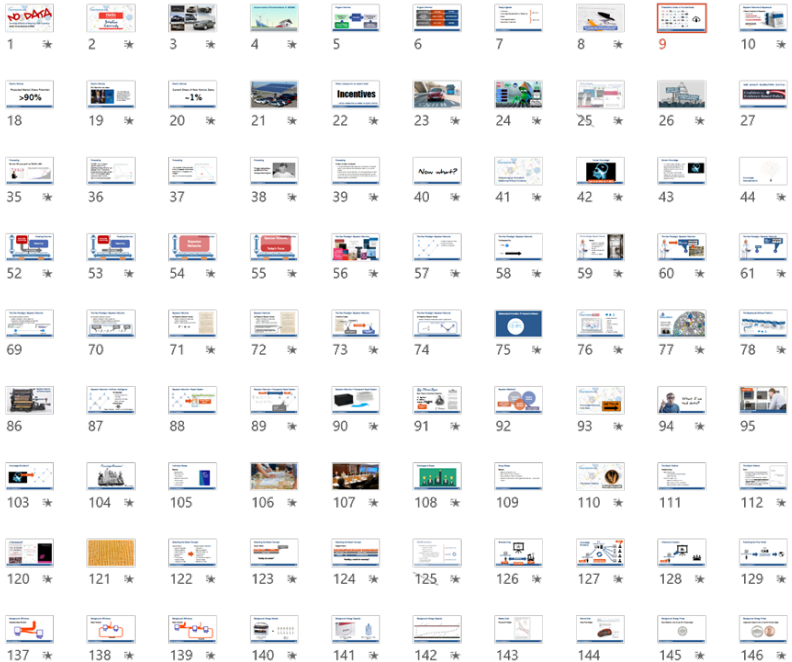
- Encode Domain Knowledge in Bayesian Network
- Elicit Probabilities
- Assess Costs and Utilities
- Search for Optimal Policies



BAYESIALAB


Desktop Software
Teaching Edition
Academic Edition
BayesiaLab 6 Professional
Bayesia Market Simulator
Code Export Module
Web Application
BayesiaLab WebSimulator
Bayesia Expert Knowledge Elicitation Environment (BEKEE)
API
Bayesia Engine API for Modeling and Inference
Bayesia Engine API for Network Learning

Webinar Slides & Recording Available



Motivation & Background

Graz *et al. Malaria Journal* 2011, **10**:136
http://www.malariajournal.com/content/10/1/136

MALARIA JOURNAL

COMMENTARY Open Access

"Test and treat" or presumptive treatment for malaria in high transmission situations? A reflection on the latest WHO guidelines

Bertrand Graz[1*], Merlin Willcox[2], Thomas Szeless[1] and André Rougemont[1]

Abstract

Recent WHO guidelines recommend a universal "test and treat" strategy for malaria, mainly by use of rapid diagnostic test (RDT) in all areas. The evidence for this approach is questioned here as there is a risk of over-reliance on parasitological diagnosis in high transmission situations, which still exist. In such areas, when a patient has fever or other malaria symptoms, the presence of *Plasmodium* spp neither reliably confirms malaria as the cause of the fever, nor excludes the possibility of other diseases. This is because the patient may be an asymptomatic carrier of malaria parasites and suffer from another disease.

To allow clinicians to perform their work adequately, local epidemiologic data are necessary. One size all. If parasite prevalence in the population is low, a diagnostic test is relevant; if the prevalence is does not provide information of any clinical usefulness, as happens with any test in medicine w of the tested characteristic is high in the healthy population. It should also be remembered that, anti-malarials are prescribed to parasite-negative patients, this will not increase selection pressure fo resistance, because the parasite is not there.

In high transmission situations at least, other diagnoses should be sought in all patients, irrespective of th presence of malaria parasites. For this, clinical skills (but not necessarily physicians) are irreplaceable, in order differentiate malaria from other causes of acute fever, such as benign viral infection or potentially dangerous conditions, which can all be present with the parasite co-existing only as a "commensal" or silent undesirable guest.

Background

The latest WHO guidelines on the treatment of malaria state that, whenever possible, "*in all settings, clinical suspicion of malaria should be confirmed with a parasitological diagnosis*" [1,2]. This is a significant change

settings, which still exist. Basically, the « level of transmission » in malarial areas is an entomological concept. In most cases, the so-called transmission level is derived from the proportion of infected people in the general population. For practical purposes, it is consid-

Ghai *et al. Malar J (2016) 15:460*
DOI 10.1186/s12936-016-1502-4

Malaria Journal

RESEARCH Open Access

CrossMark

Multi-method assessment of patients with febrile illness reveals over-diagnosis of malaria in rural Uganda

Ria R. Ghai[1,2*], Mary I. Thurber[3], Azza El Bakry[4], Colin A. Chapman[5,6,7] and Tony L. Goldberg[6,8]

Abstract

Background: Health clinics in rural Africa are typically resource-limited. As a result, many patients presenting with fever are treated with anti-malarial drugs based only on clinical presentation. This is a considerable issue in Uganda, where malaria is routinely over-diagnosed and over-treated, constituting a wastage of resources and an elevated risk mortality in wrongly diagnosed patients. However, rapid diagnostic tests (RDTs) for malaria are increasingly being health facilities. Being fast, easy and inexpensive, RDTs offer the opportunity for feasible diagnostic capacity in limited areas. This study evaluated the rate of malaria misdiagnosis and the accuracy of RDTs in rural Uganda, presumptive diagnosis still predominates. Specifically, the diagnostic accuracy of "gold standard" methods, PCR, were compared to the most feasible method, RDTs.

presenting with fever at one of two health clinics in the Kabarole District of Uganda were enrolled d was collected by finger prick and used to administer RDTs, make blood smears for microscopy, man FTA cards for DNA extraction, polymerase chain reaction (PCR) amplification, and sequencing. The RDTs and microscopy were assessed relative to PCR, considered the new standard of malaria diagnosis.

s: A total of 78 patients were enrolled, and 31 were diagnosed with *Plasmodium* infection by at least one hod. Comparing diagnostic pairs determined that RDTs and microscopy performed similarly, being 92.6 and 2.0 % sensitive and 95.5 and 94.4 % specific, respectively. Combining both methods resulted in a sensitivity of 96.0 % and specificity of 100 %. However, both RDTs and microscopy missed one case of non-falciparum malaria (*Plasmodium malariae*) that was identified and characterized by PCR and sequencing. In total, based on PCR, 62.0 % of patients would have been misdiagnosed with malaria if symptomatic diagnosis was used.

Conclusions: Results suggest that diagnosis of malaria based on symptoms alone appears to be highly inaccurate in this setting. Furthermore, RDTs were very effective at diagnosing malaria, performing as well or better than microscopy. However, only PCR and DNA sequencing detected non-*P. falciparum* species, which highlights an important limitation of this test and a treatment concern for non-falciparum malaria patients. Nevertheless, RDTs appear the only feasible method in rural or resource-limited areas, and therefore offer the best way forward in malaria management in

?

Optimizing Health Policies

Caveat

- The medical subject matter presented in this webinar is strictly for methodological illustration purposes.
- Today's particular problem domain of infectious disease diagnosis is merely a prototypical example diagnostic inference.
- Also, the subject matter is presented in a highly simplified format. This is by no means an exhaustive treatment of the topic.
- No part of this webinar should be interpreted as medical research or a health policy recommendation.

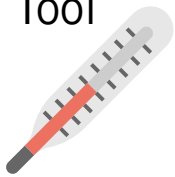
Motivation & Background

Infectious Diseases in Sub-Saharan Africa

- 4.2 million annual child deaths
- Over 1 million due to bacterial pneumonia
- Over 750,000 due to malaria

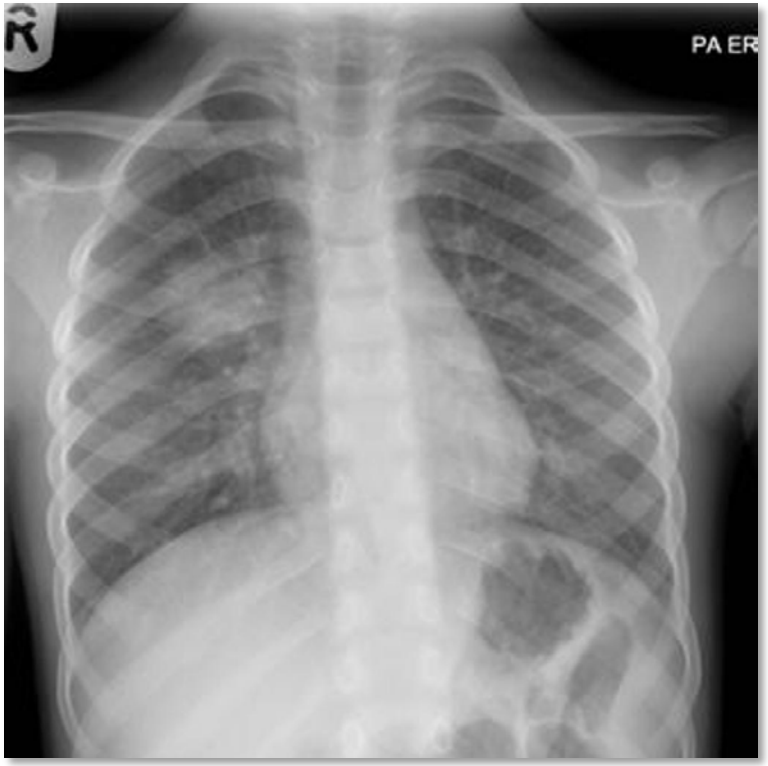
Similar Symptoms

Diagnostic Tool



Economical, efficacious treatments are available:
- Antibiotics for bacterial pneumonia
- Artimisinin-combination therapies (ACT) for malaria

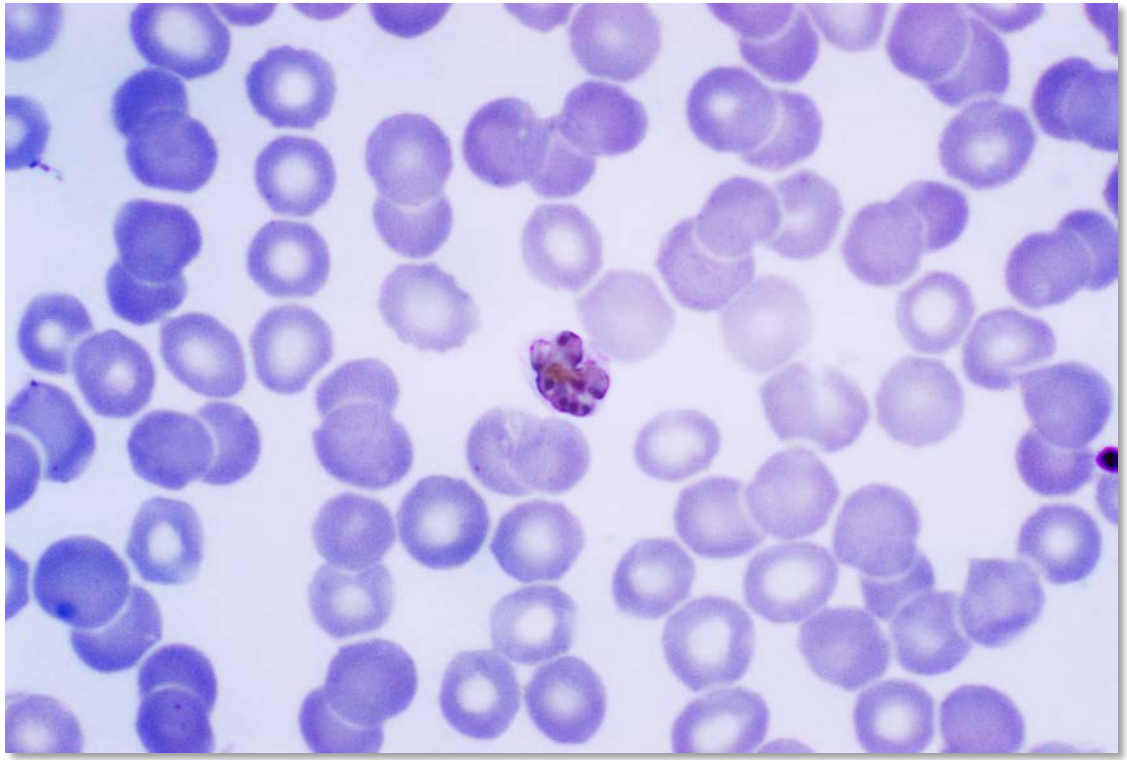
Pneumonia Diagnosis in the Developed World



Radiography

Case courtesy of Dr Jeremy Jones, Radiopaedia.org, rID: 20012

Malaria Diagnosis in the Developed World



Microscopic Diagnosis

Past Practice in Developing Nations

Diagnostic Approach:

- Fever → Malaria
  "Presumptive Treatment"
- Result:
  - Overtreatment of malaria
  - Undertreatment of bacterial infections, e.g. pneumonia

Rapid Diagnostic Test for Malaria

- "…in all settings, clinical suspicion of malaria should be confirmed with a parasitological diagnosis"
  Source: WHO: Guidelines for the treatment of malaria (2e). Geneva: World Health Organisation, 2010.
- Result:
  - 200,000 Rapid Diagnostic Tests (RDT) distributed in 2005
  - 50 million in 2010

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Rapid diagnostic tests linked to improved targeting of antimalarial drugs, but more antibiotic prescriptions

8 August 2017

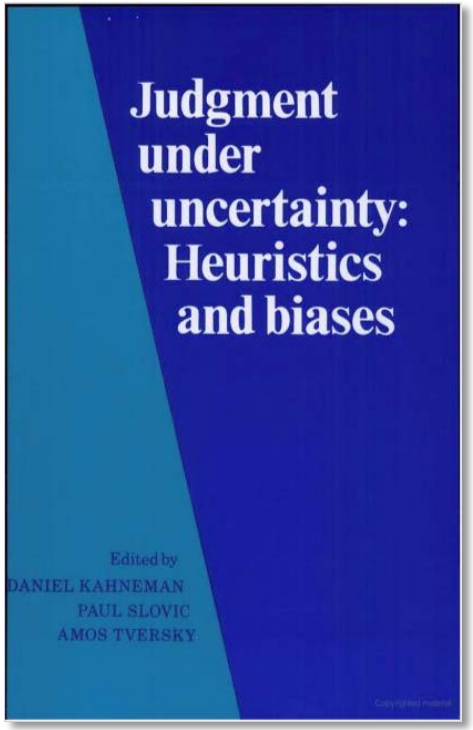
Unintended Consequences

- "The researchers found that after the rapid diagnostic test ruled out malaria, many patients were prescribed antibiotics — in effect, **trading the overuse of anti-malarial drugs for the overuse of antibiotics**."
- "'If you're in a remote area and you don't have a lot of other options — you've got a sick child or a sick patient in front of you, that person may have come from even up to 20 kilometers away with expensive transport or even walking — you want to do something,' Hopkins says. 'And if you don't feel like you should give an anti-malarial — the test is negative — your alternative, in some cases, is an antibiotic.'"

  Source: PRI Interview, October 15, 2017, https://www.pri.org/stories/2017-10-15/quick-and-easy-malaria-tests-some-unexpected-drawbacks

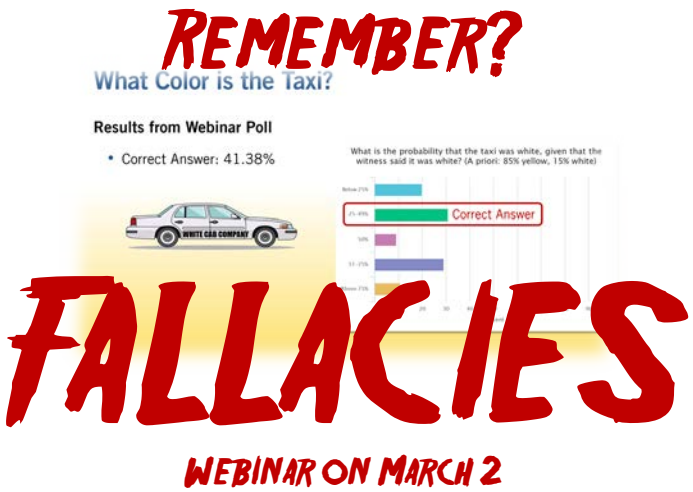
Probabilistic Reasoning

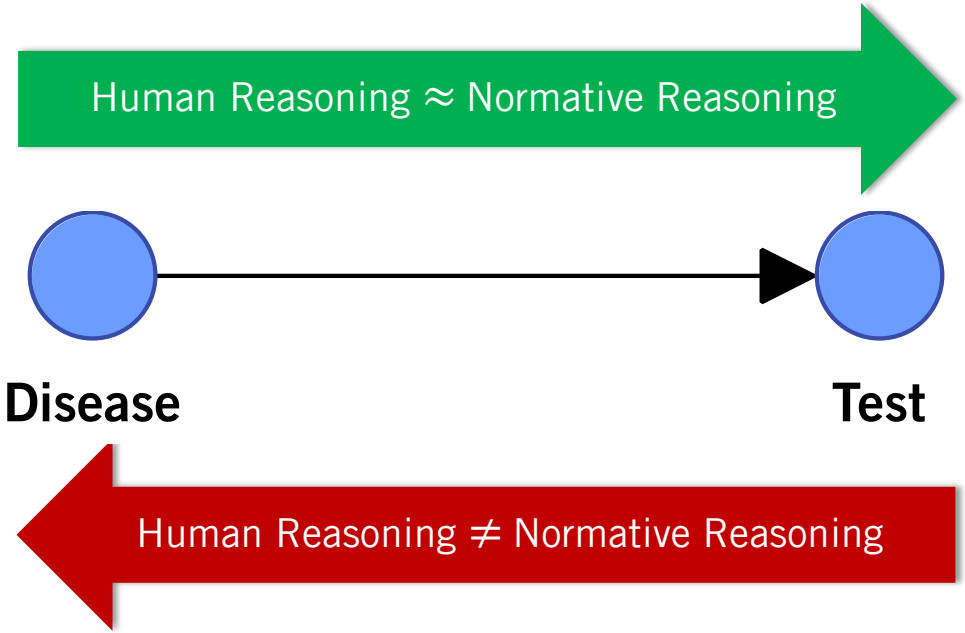
Human reasoning is flawed!



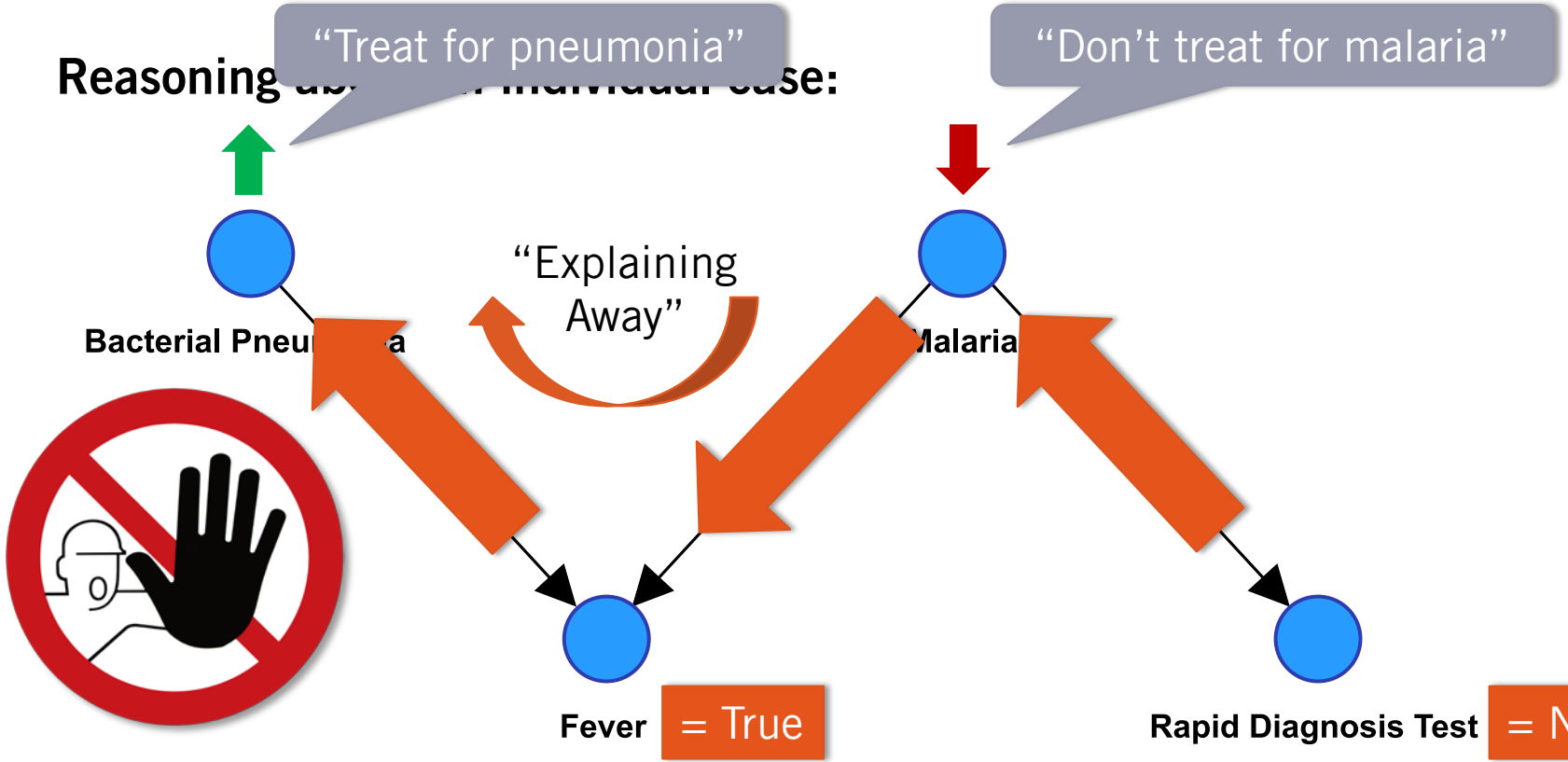
Probabilistic Reasoning

Human Cognitive Limitations and Biases Under Uncertainty





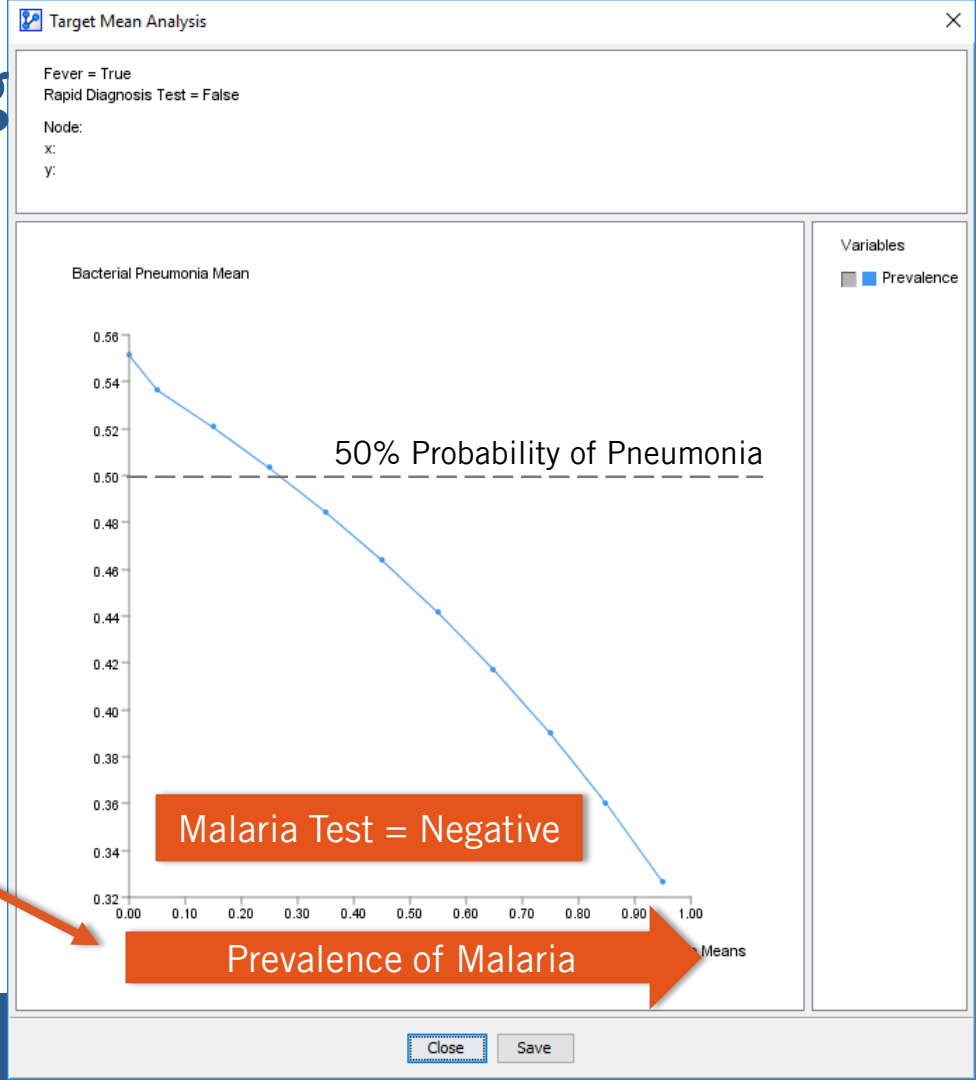
Probabilistic Reasoning



Probabilistic Reasoning

Why Not?

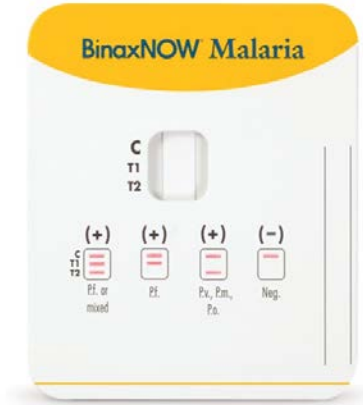
- The probability of pneumonia given a negative malaria test result depends on:
  - Prevalence of pneumonia
  - Sensitivity & Specificity of RDT
  - Prevalence of malaria



New Health Policy?

Hypothetical Example

Testing for Malaria and Pneumonia?



&

Rapid Diagnosis Test for Malaria

C-reactive protein (CRP) Test for Pneumonia

New Health Policy?

Policy Questions

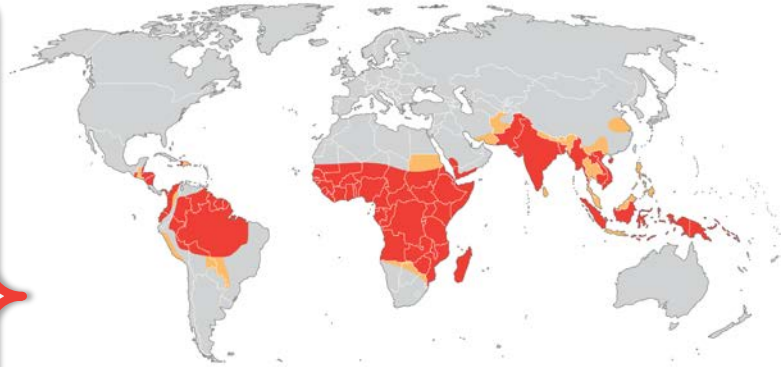
- For Malaria
    - Test & Treat **or** Presumptive Treatment
- For Bacterial Pneumonia
    - Test & Treat **or** Presumptive Treatment

New Health Policy?

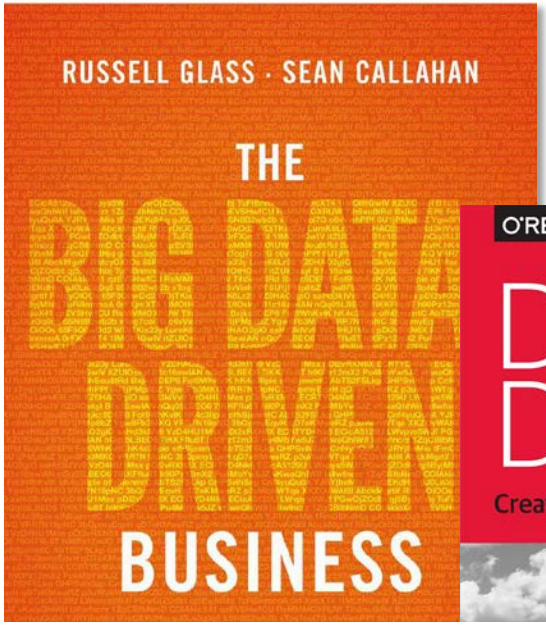
Hypothetical Example

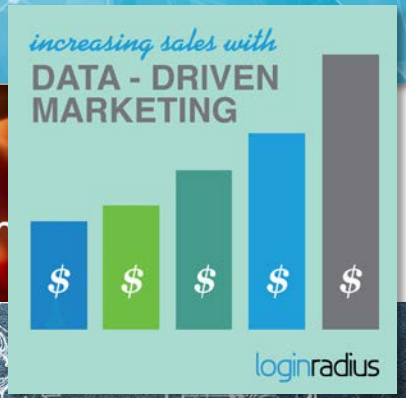
Additional Considerations for New Guidelines

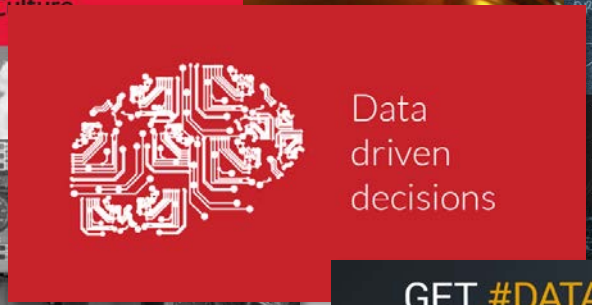
- Cost of tests
- Cost of treatments
- Limited resources
- Efficacy of treatments
- Unintended consequences of overtreatment, e.g., antibiotics resistance
- Adherence to protocols
- Prevalence of diseases
- Comorbidities
- Regional factors, e.g., climate, seasonality

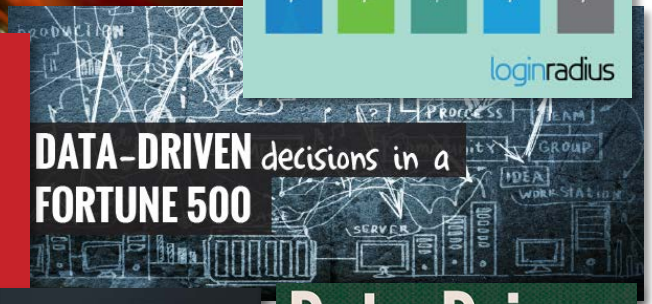


If it is difficult to reason about a single case, how can we establish a policy for the world?









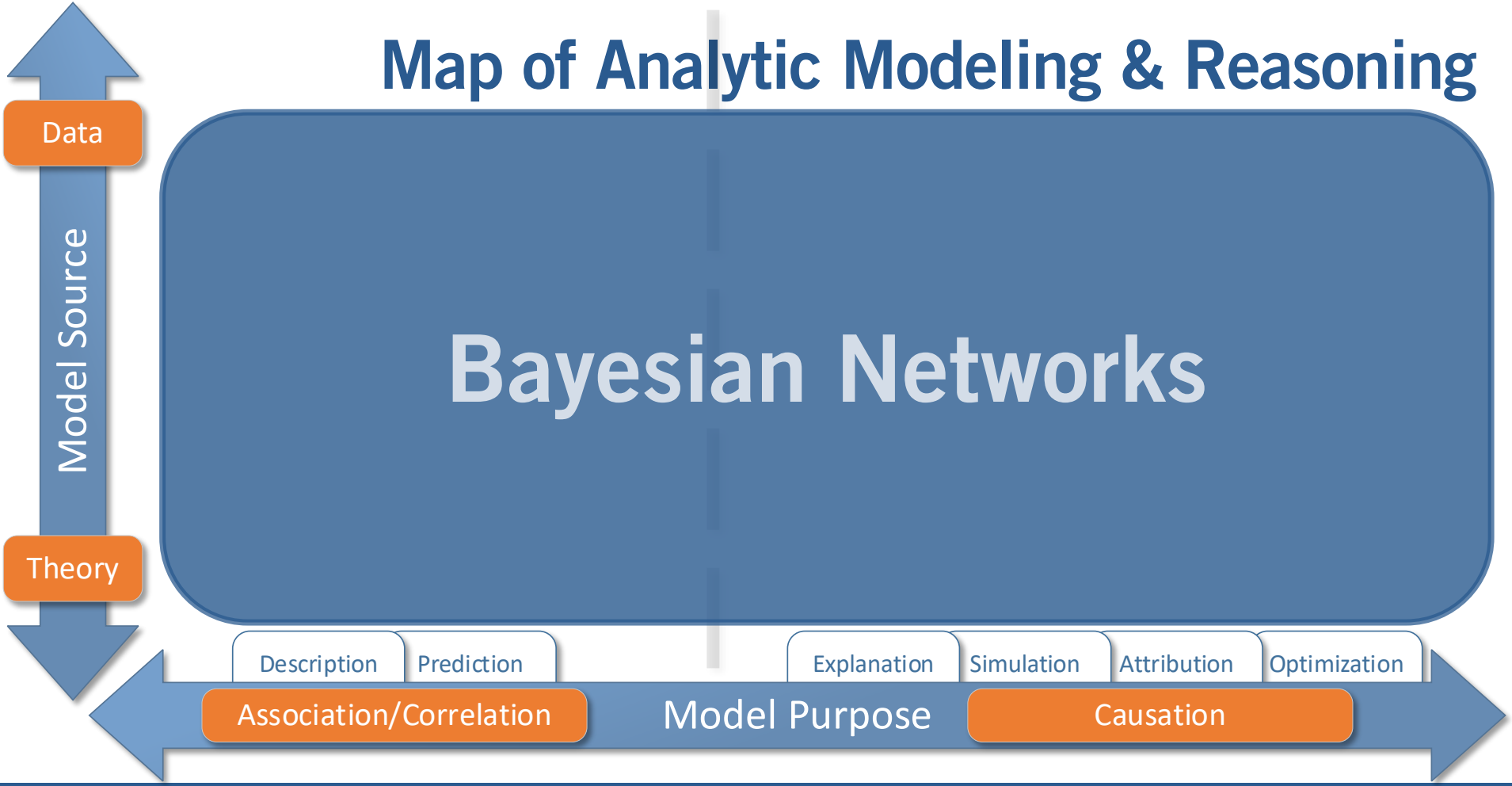
MAKING
DATA-DRIVEN
DECISIONS

with
+ tableau +

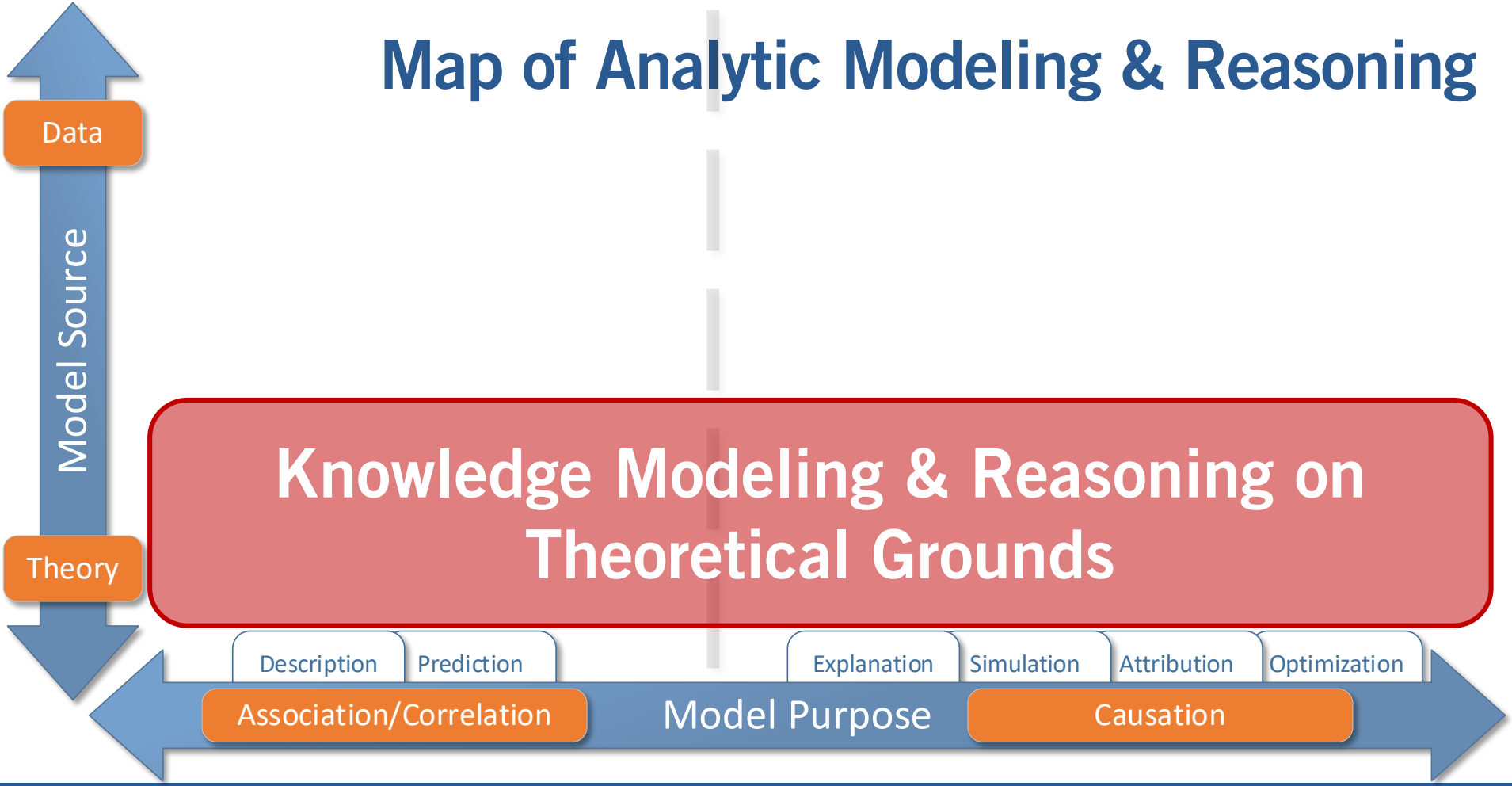
stefan.conrady@bay


Big Data?
No Data!

Map of Analytic Modeling & Reasoning



Map of Analytic Modeling & Reasoning



Reasoning

Knowledge Modeling & Reasoning on tical Grounds

Webinar on March 2, 2018

Theory

Model Purpose

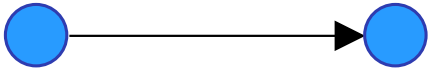
Description | Prediction | Explanation | Simulation | Attribution | Optimization

Association/Correlation | Causation

New Health Policy?

Proposed Policy Development Approach

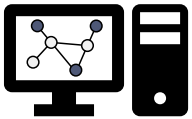
- Domain Knowledge Encoding

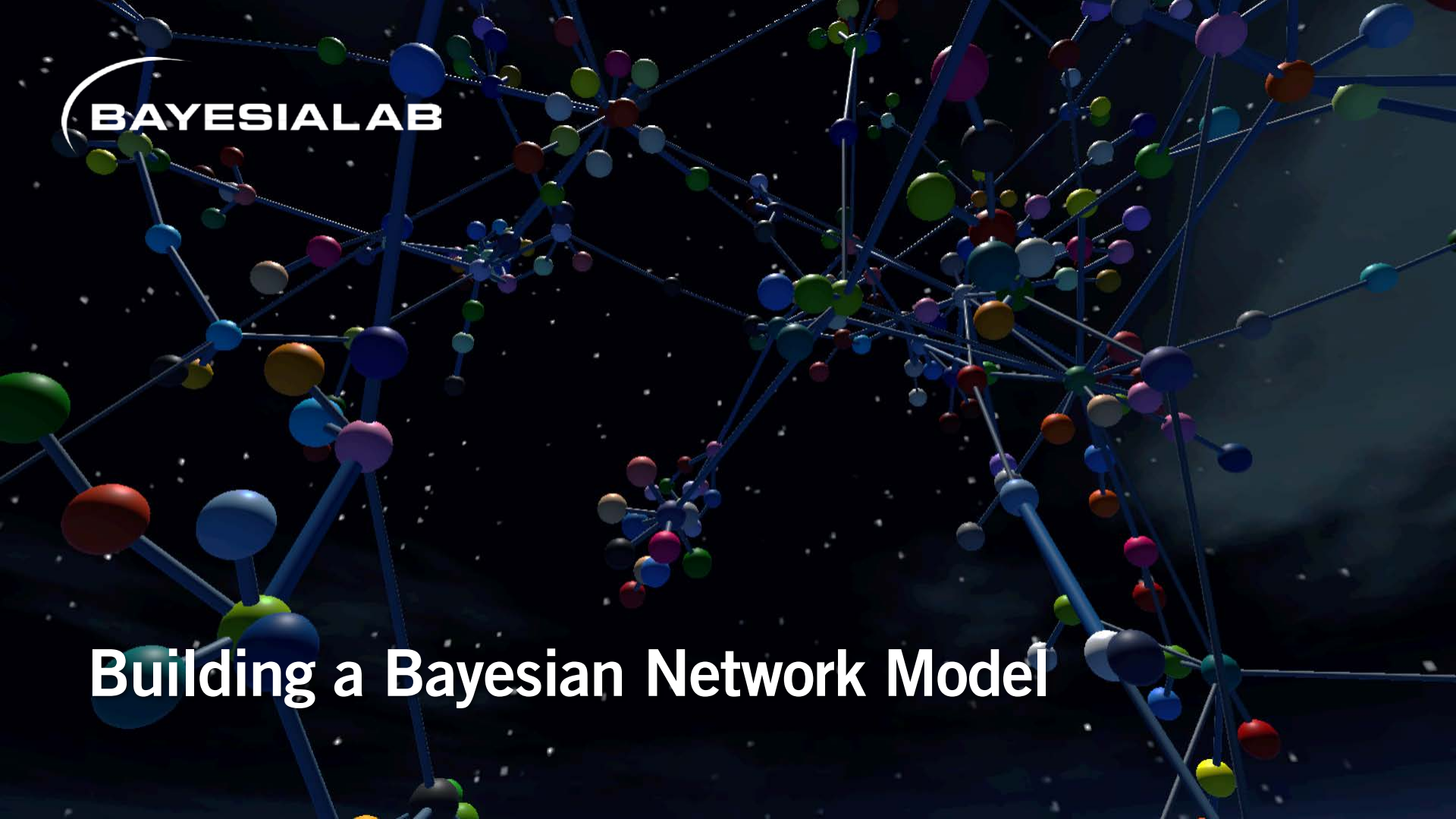


- Probability Elicitation

- Cost/Utility Assessment

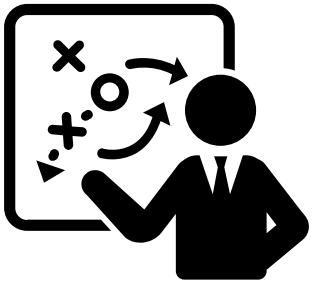
- Optimization





Building a Bayesian Network Model

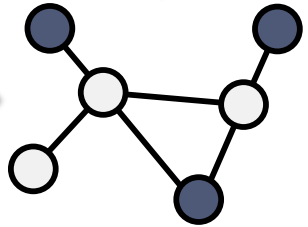
1. Brainstorming & Model Construction



Facilitator

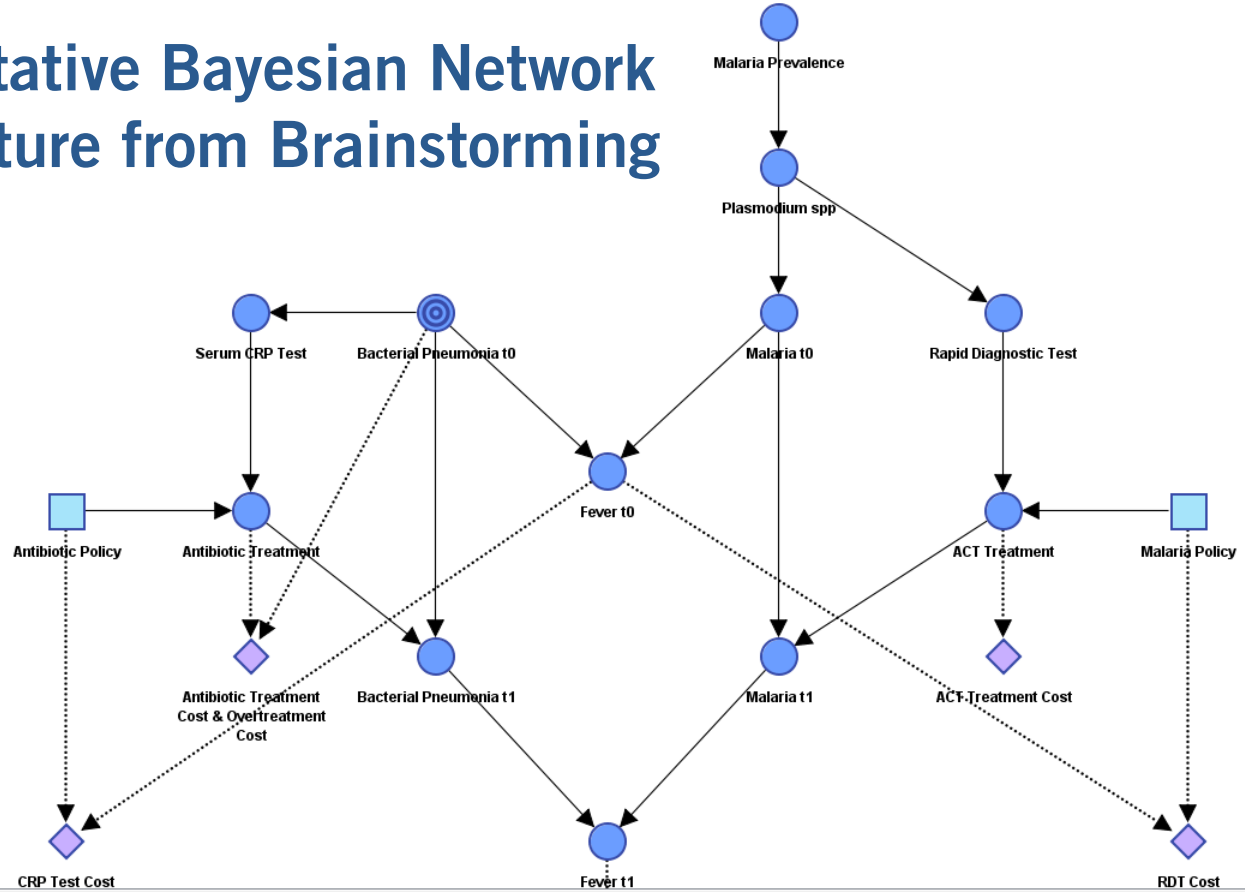
Experts

- Variables of interest
- Causal relationships

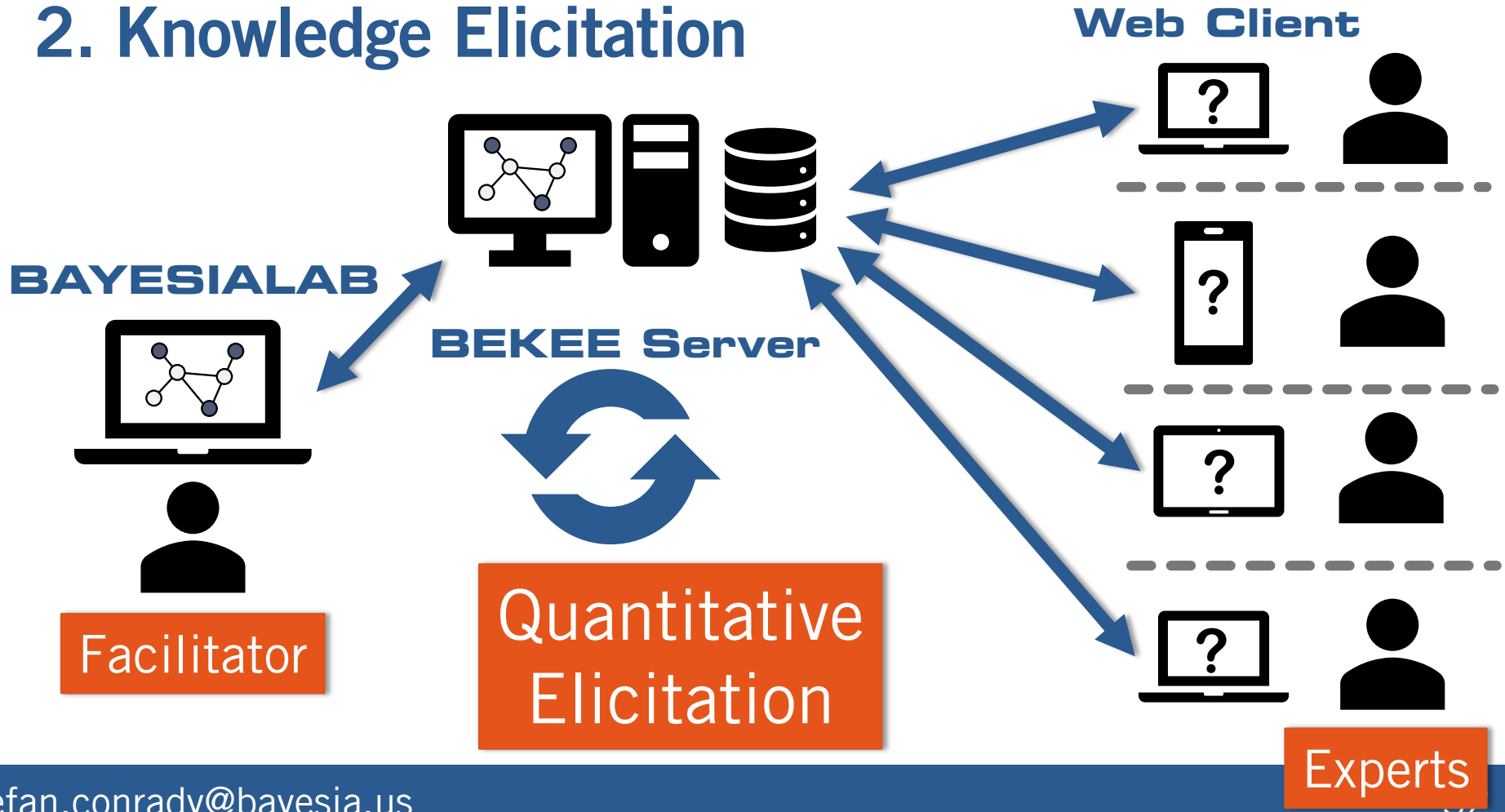


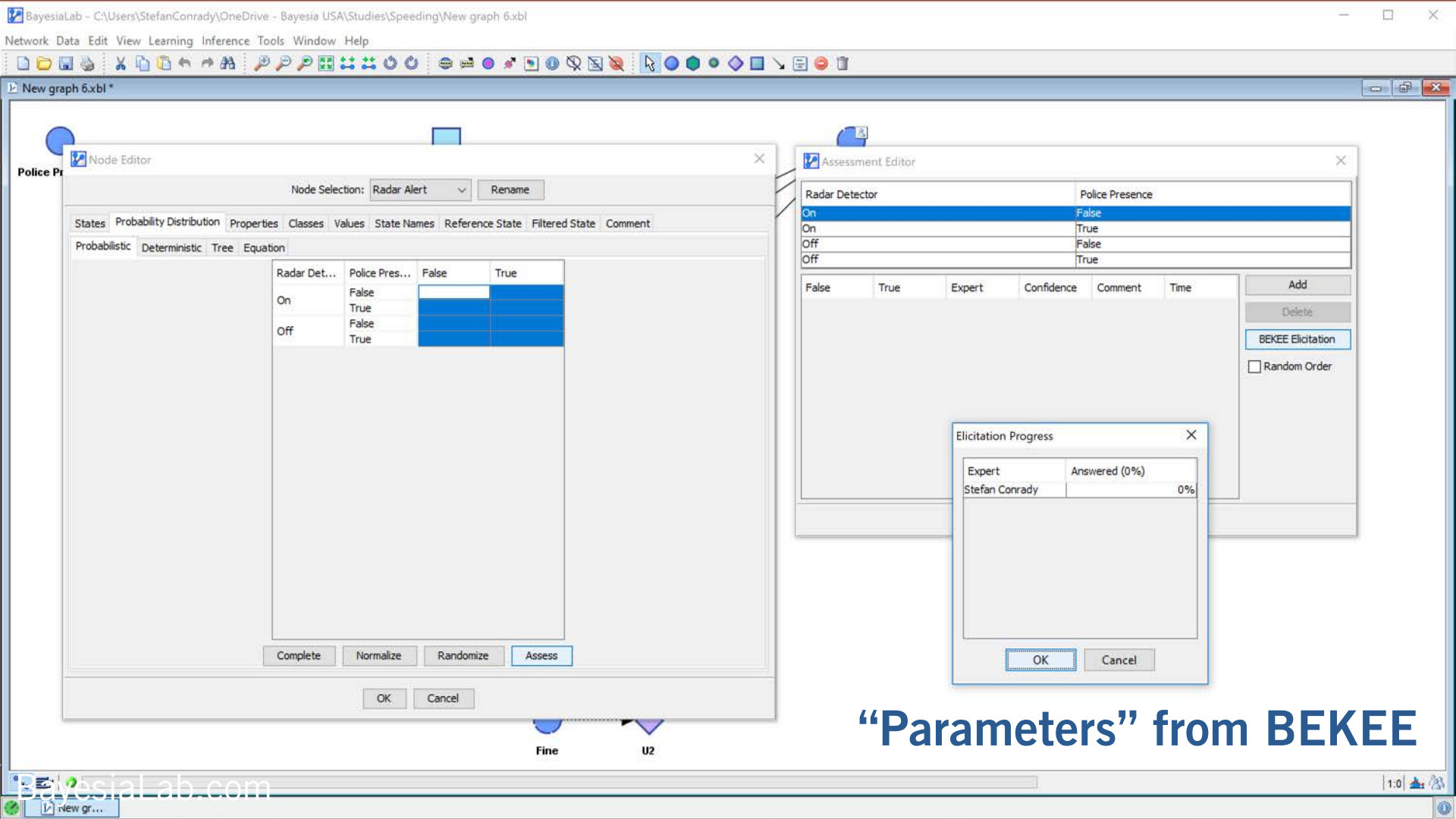
Qualitative Network

Qualitative Bayesian Network Structure from Brainstorming

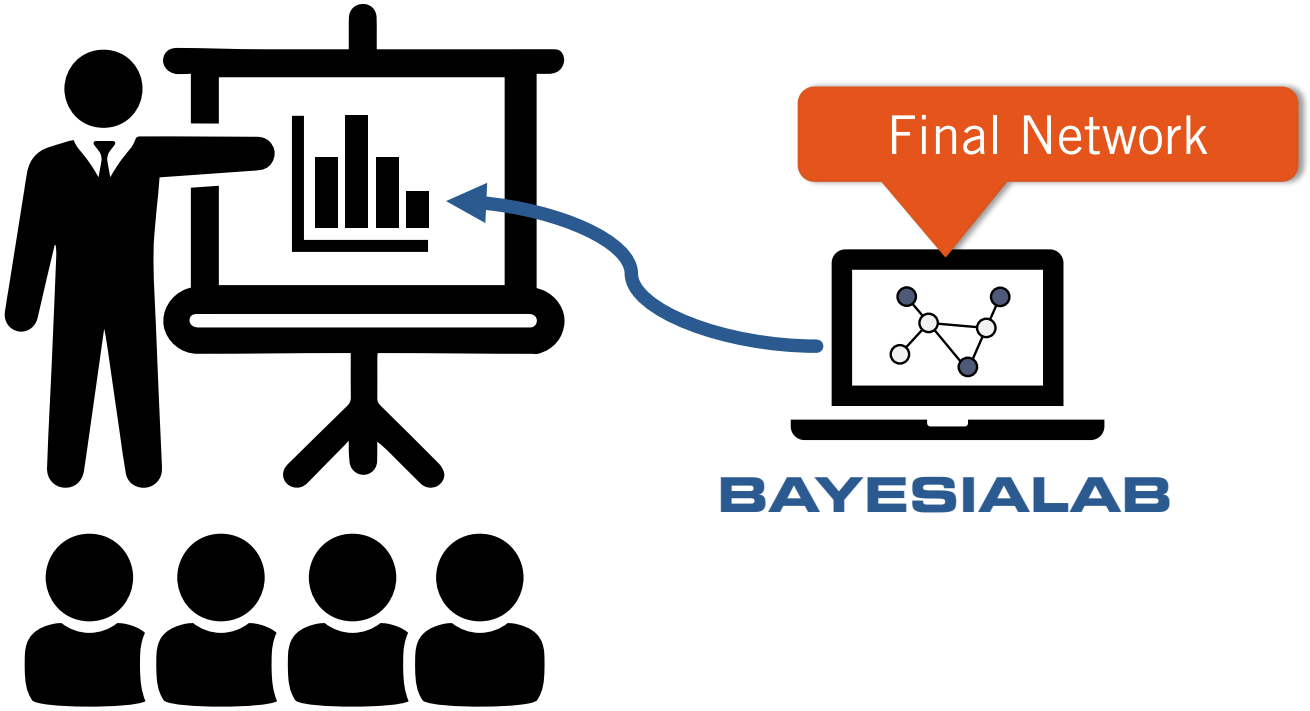


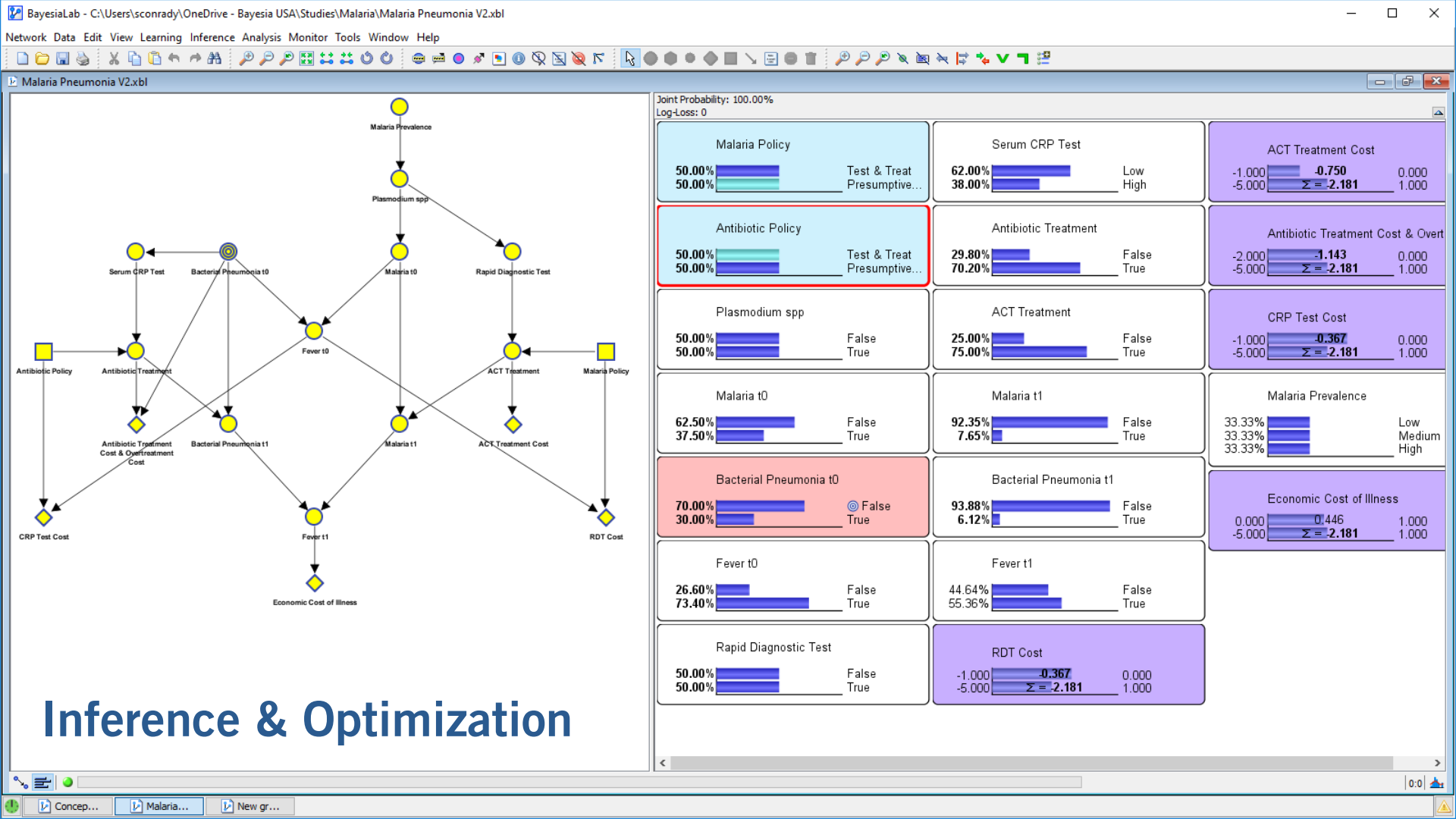
2. Knowledge Elicitation

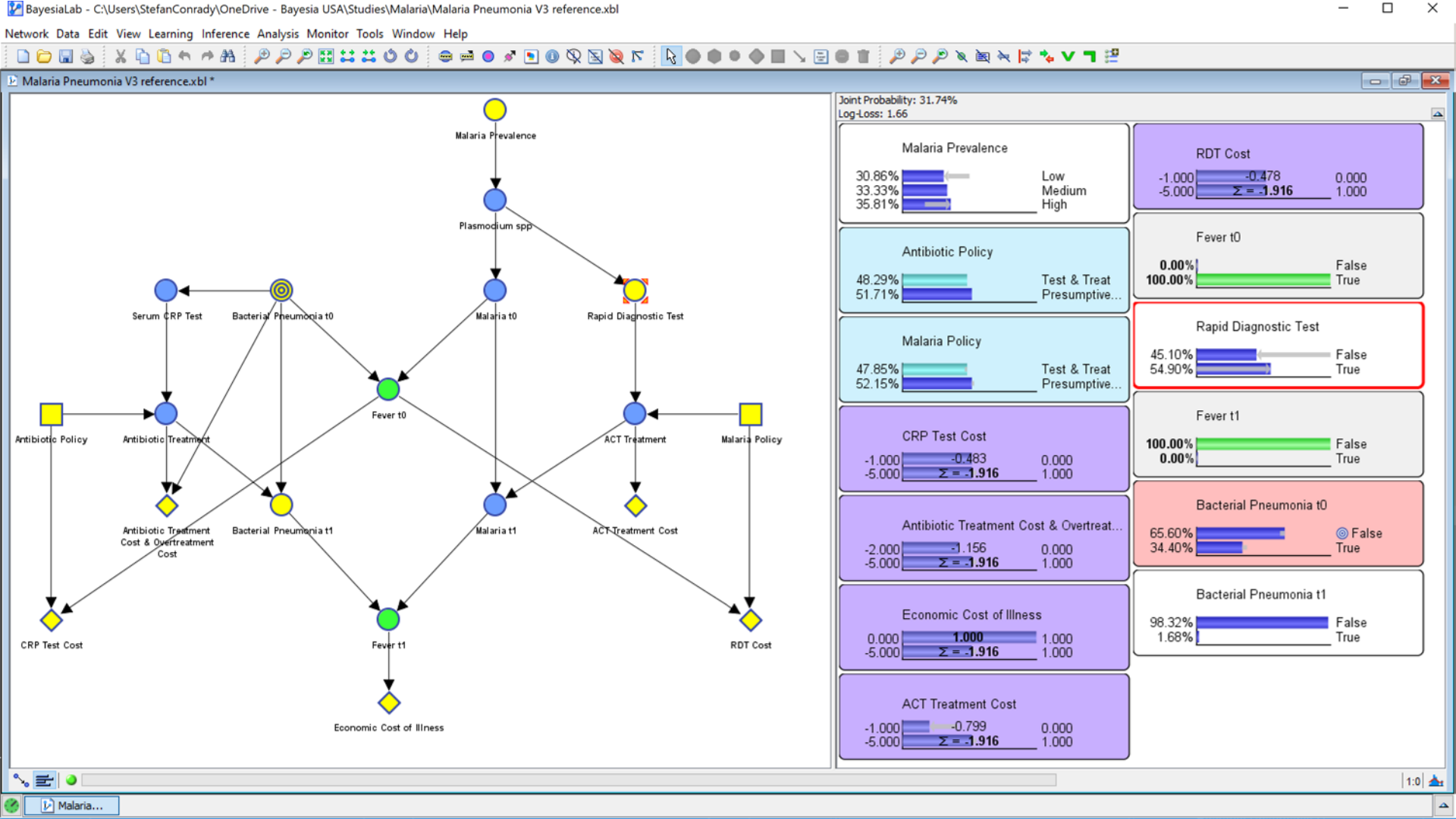



BayesiaLab - C:\Users\StefanConrady\OneDrive - Bayesia USA\Studies\Speeding\New graph 6.xbl
Network Data Edit View Learning Inference Tools Window Help
New graph 6.xbl *
Node Editor
Node Selection: Radar Alert
Rename
States Probability Distribution Properties Classes Values State Names Reference State Filtered State Comment
Probabilistic Deterministic Tree Equation
Radar Det... Police Pres... False True
On False
True
Off False
True
Complete Normalize Randomize Assess
OK Cancel
Assessment Editor
Radar Detector Police Presence
On False
On True
Off False
Off True
False True Expert Confidence Comment Time
Add
Delete
BEKEE Elicitation
Random Order
Elicitation Progress
Expert Answered (0%)
Stefan Conrady 0%
OK Cancel
Police Pr
Fine
U2
"Parameters" from BEKEE
BayesiaLab.com

3. Inference, Analysis, and Optimization



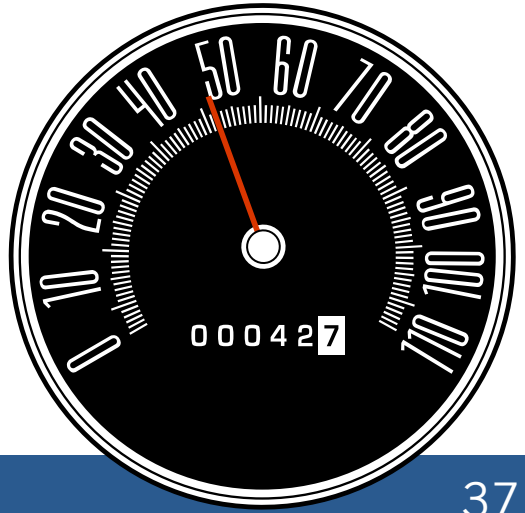

BayesiaLab - C:\Users\sconrady\OneDrive - Bayesia USA\Studies\Malaria\Malaria Pneumonia V2.xbl
Network Data Edit View Learning Inference Analysis Monitor Tools Window Help
Malaria Pneumonia V2.xbl
Malaria Prevalence
Plasmodium spp
Serum CRP Test
Bacterial Pneumonia t0
Malaria t0
Rapid Diagnostic Test
Antibiotic Policy
Antibiotic Treatment
Fever t0
ACT Treatment
Malaria Policy
Antibiotic Treatment Cost & Overtreatment Cost
Bacterial Pneumonia t1
Malaria t1
ACT Treatment Cost
CRP Test Cost
Fever t1
RDT Cost
Economic Cost of Illness
Joint Probability: 100.00%
Log-Loss: 0
Malaria Policy
50.00% Test & Treat
50.00% Presumptive...
Serum CRP Test
62.00% Low
38.00% High
ACT Treatment Cost
-1.000 -0.750 0.000
-5.000 Σ = -2.181 1.000
Antibiotic Policy
50.00% Test & Treat
50.00% Presumptive...
Antibiotic Treatment
29.80% False
70.20% True
Antibiotic Treatment Cost & Overt
-2.000 -1.143 0.000
-5.000 Σ = -2.181 1.000
Plasmodium spp
50.00% False
50.00% True
ACT Treatment
25.00% False
75.00% True
CRP Test Cost
-1.000 -0.367 0.000
-5.000 Σ = -2.181 1.000
Malaria t0
62.50% False
37.50% True
Malaria t1
92.35% False
7.65% True
Malaria Prevalence
33.33% Low
33.33% Medium
33.33% High
Bacterial Pneumonia t0
70.00% False
30.00% True
Bacterial Pneumonia t1
93.88% False
6.12% True
Economic Cost of Illness
0.000 0.446 1.000
-5.000 Σ = -2.181 1.000
Fever t0
26.60% False
73.40% True
Fever t1
44.64% False
55.36% True
Rapid Diagnostic Test
50.00% False
50.00% True
RDT Cost
-1.000 -0.367 0.000
-5.000 Σ = -2.181 1.000
Inference & Optimization


BayesiaLab - C:\Users\StefanConrady\OneDrive - Bayesia USA\Studies\Malaria\Malaria Pneumonia V3 reference.xbl
Network Data Edit View Learning Inference Analysis Monitor Tools Window Help
Malaria Pneumonia V3 reference.xbl *
Malaria Prevalence
Plasmodium spp
Serum CRP Test
Bacterial Pneumonia t0
Malaria t0
Rapid Diagnostic Test
Antibiotic Policy
Antibiotic Treatment
Fever t0
ACT Treatment
Malaria Policy
Antibiotic Treatment Cost & Overtreatment Cost
Bacterial Pneumonia t1
Malaria t1
ACT Treatment Cost
CRP Test Cost
Fever t1
RDT Cost
Economic Cost of Illness
Joint Probability: 31.74%
Log-Loss: 1.66
Malaria Prevalence
30.86% Low
33.33% Medium
35.81% High
Antibiotic Policy
48.29% Test & Treat
51.71% Presumptive...
Malaria Policy
47.85% Test & Treat
52.15% Presumptive...
CRP Test Cost
-1.000 -0.483 0.000
-5.000 Σ = -1.916 1.000
Antibiotic Treatment Cost & Overtreat...
-2.000 -1.156 0.000
-5.000 Σ = -1.916 1.000
Economic Cost of Illness
0.000 1.000 1.000
-5.000 Σ = -1.916 1.000
ACT Treatment Cost
-1.000 -0.799 0.000
-5.000 Σ = -1.916 1.000
RDT Cost
-1.000 -0.478 0.000
-5.000 Σ = -1.916 1.000
Fever t0
0.00% False
100.00% True
Rapid Diagnostic Test
45.10% False
54.90% True
Fever t1
100.00% False
0.00% True
Bacterial Pneumonia t0
65.60% False
34.40% True
Bacterial Pneumonia t1
98.32% False
1.68% True
Malaria...

Previous Examples

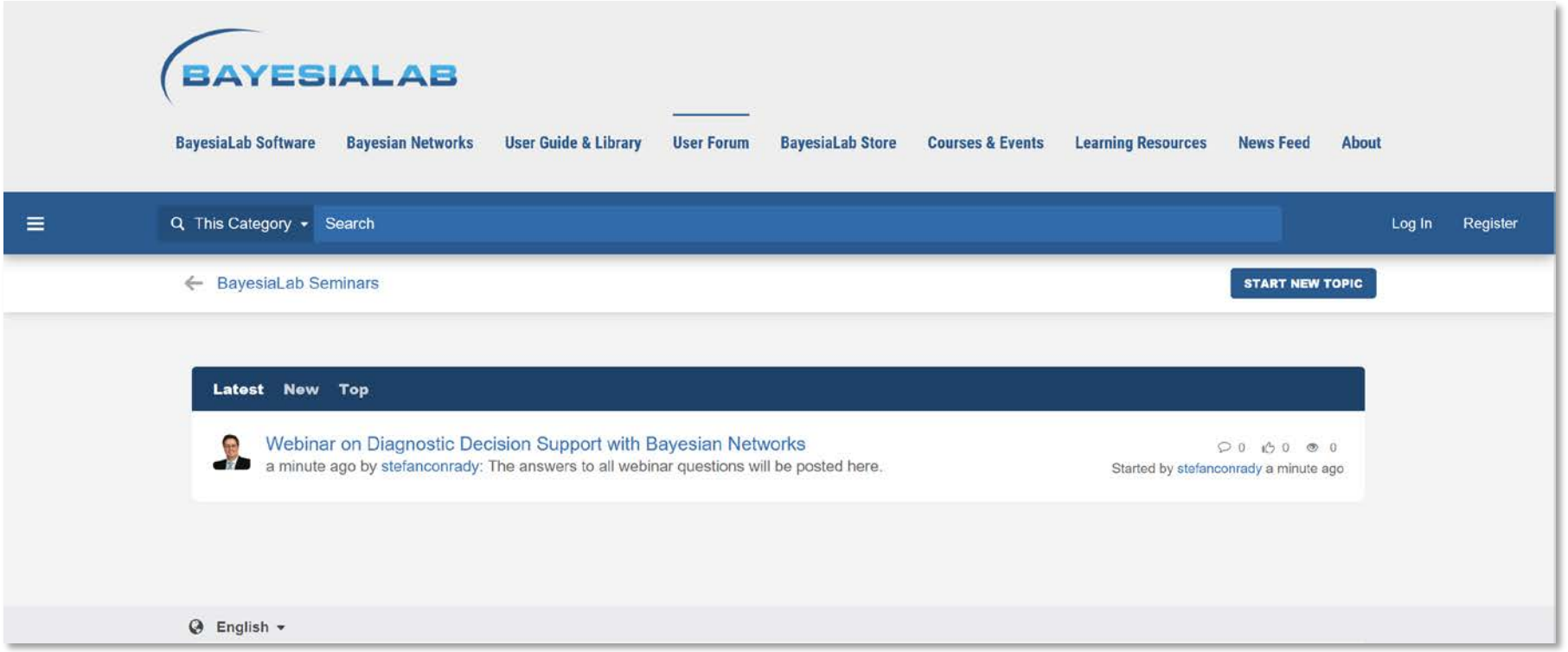
Sounds Familiar?

- It's all about encoding a qualitative structure and eliciting probabilities.

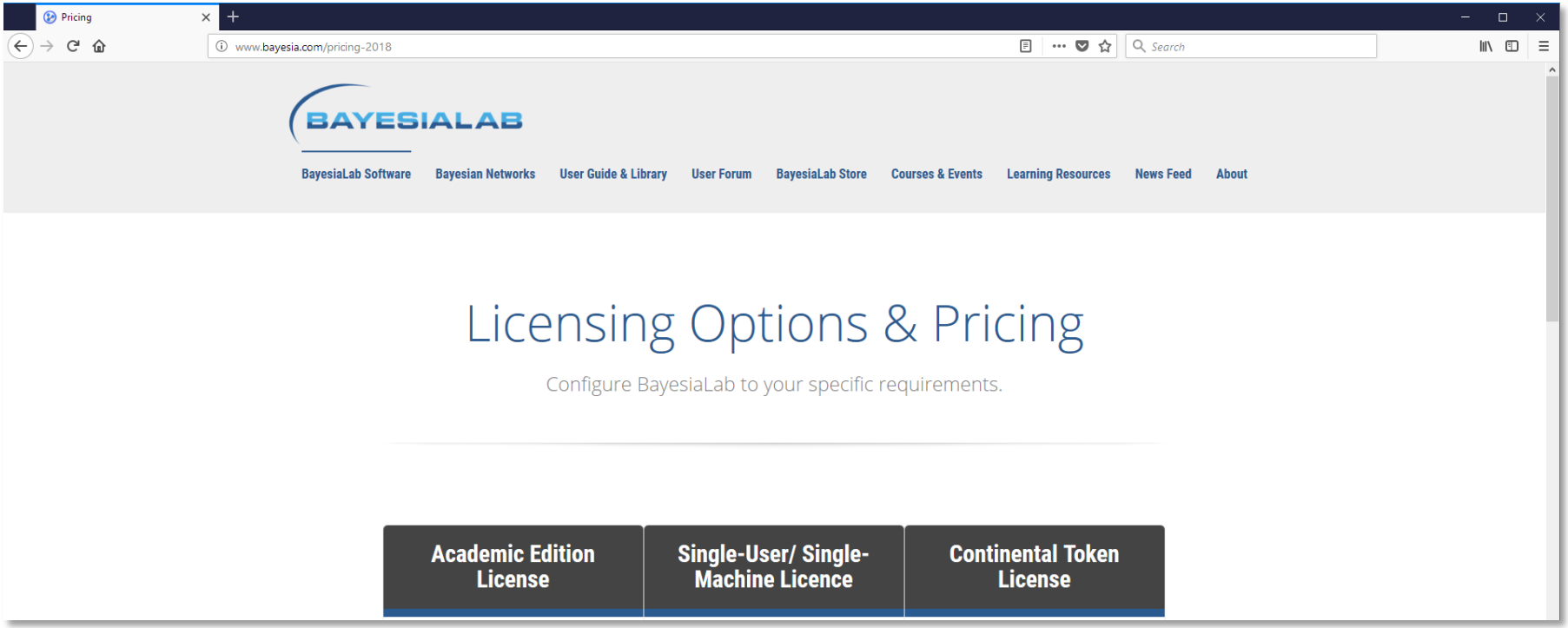



BAYESIALAB
In Conclusion…

User Forum: bayesia.com/community



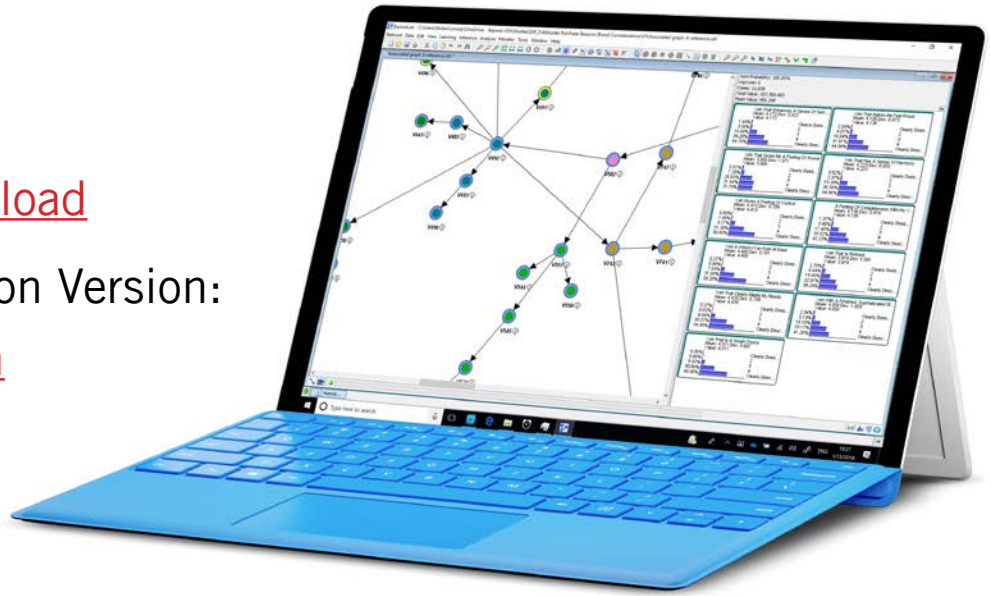
bayesia.com/pricing-2018



BayesiaLab Trial

Try BayesiaLab Today!

- Download Demo Version:
  www.bayesialab.com/trial-download
- Apply for Unrestricted Evaluation Version:
  www.bayesialab.com/evaluation



Webinar Series: Friday at 1 p.m. (Central)

Upcoming Webinars:

- March 23 Quantifying Product Cannibalization — A Case Study in Marketing Science
- March 30 t.b.d.

Register here: bayesia.com/events

BayesiaLab Courses Around the World in 2018

- April 11–13
  Sydney, Australia
- May 16–18
  Seattle, WA
- June 26–28
  Boston, MA
- July 23–25
  San Francisco, CA
- August 29–31
  London, UK
- September 26–28
  New Delhi, India
- October 29–31
  Chicago, IL
- December 4–6
  New York, NY

Learn More & Register: bayesia.com/events

Introductory BayesiaLab Course in San Francisco, California July 23–25, 2018

6th Annual BayesiaLab Conference in Chicago
November 1–2, 2018

Thank You!

stefan.conrady@bayesia.us

BayesianNetwork

linkedin.com/in/stefanconrady

facebook.com/bayesia