



## Reasoning Under Uncertainty: Differential Diagnosis of Diseases

March 20, 2020

# Introduction



STEFAN CONRADY  
Managing Partner

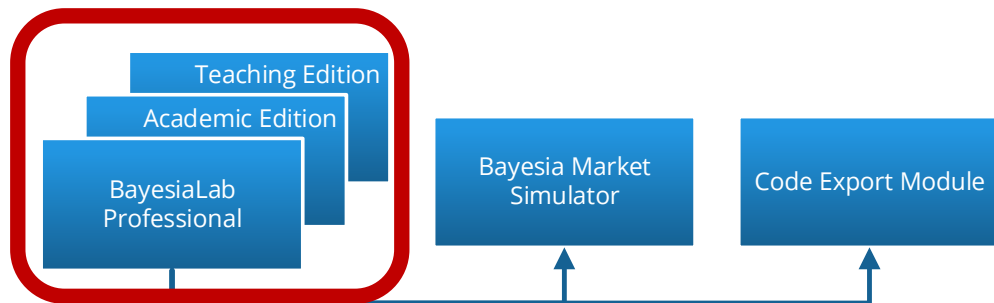
BAYESIA USA, LLC

stefan.conrady@bayesia.us  
+1 888.386.8383 main  
+1 615.870.4205 cell

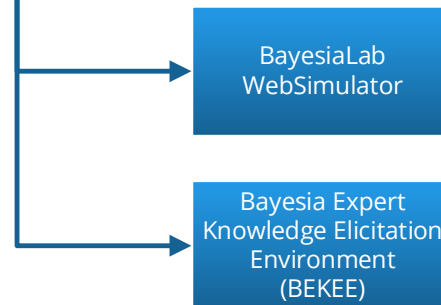
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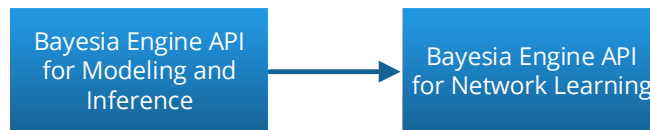
## Desktop Software



## Web Application



## API





# Today's Agenda

## Introduction

### Webinar Series: Reasoning Under Uncertainty

- Part 1: Differential Diagnosis of Diseases
- Part 2: Temporal Modeling of an Epidemic
- Part 3: “Test and Treat” vs. Presumptive Treatment

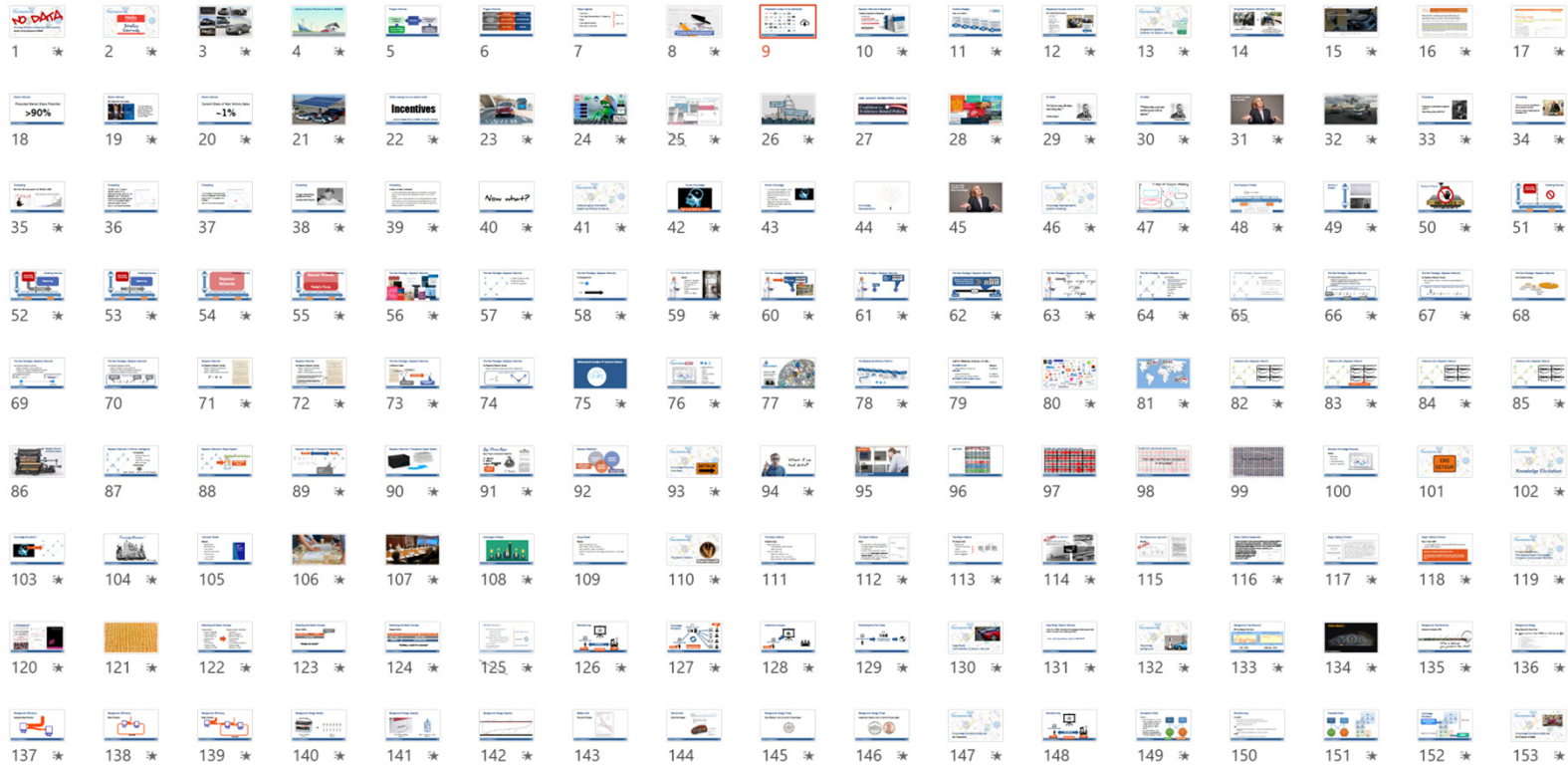
## Motivation


### Probabilistic Reasoning with Bayesian Networks

- Diagnostic Reasoning
- Differential Diagnosis of Lung Diseases

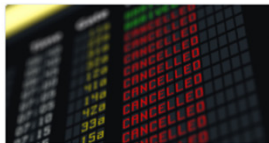


# Slides and Screen Recording: [forum.bayesia.us](http://forum.bayesia.us)



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**3-Day Introductory Course (Lives...**  
Wed May 6 - Fri May 8  
Online



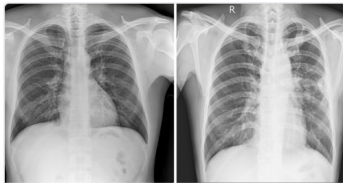
**3-Day Introductory Course in Sea...**  
Wed May 6 - Fri May 8

## Upcoming Events



# The BayesiaLab Community

## Videos



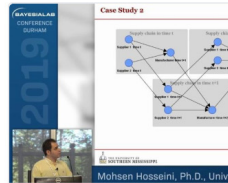
Webinar Series —  
Reasoning Under  
Uncertainty (Part 1):  
Differential Diagnosis of  
Diseases

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Target Dynamic Profile

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Integrated Markov  
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### Webinar Series — Reasoning Under Uncertainty Differential Diagnosis of Diseases

Updated now

Following 1

SHARE

f t in

Moderate topic

This is a placeholder post. The webinar recording plus all presentation materials will be posted here by the end of March 20, 2020.

#### Webinar Overview

With the outbreak of the COVID-19 pandemic, reasoning about diseases has gone mainstream. No longer is it just healthcare professionals that perform differential diagnoses. Newspapers and social media have been publicizing charts that compare symptoms of COVID-19, the "regular" flu, and the common cold so individuals can potentially self-diagnose and reduce the burden on healthcare providers.

While a chart can list symptoms, it is not an "inference engine." Deliberate reasoning still has to happen in the mind of the self-diagnosing individual to reach a conclusion. The difficult part, as humans are ill-equipped to handle probabilistic reasoning, is the cause, i.e., from symptom to disease.

In this webinar, we present Bayesian networks as a framework for reasoning about diseases and symptoms. Given this knowledge base, we then use Bayesian algorithms to update the probabilities of the potential conditions given the observed symptoms. A very similar model, the so-called "Visit Asia" network, was one of the first to illustrate the reasoning capabilities of Bayesian networks.

Please note that this webinar does not constitute medical advice. Although the reasoning is based on current events, we focus solely on the reasoning process. Thus, all numerical probabilities shown in the presentation should be considered fictional.

Please post all your questions and comments below.

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Reply to topic



# Warning

- The medical, healthcare, and health policy topics presented in this webinar are strictly for methodological illustration purposes.
- No medical advice is provided.
- No part of this seminar should be interpreted as a research finding or policy recommendation.
- All numerical values shown throughout the presentation should be considered fictional.



THE

FIRST OPINION

# A fiasco in the making? As the coronavirus pandemic takes hold, we are making decisions without reliable data

By JOHN P.A. IOANNIDIS / MARCH 17, 2020



A nurse holds swabs and a test tube to test people for Covid-19 at a drive-through station set up in the parking lot of the Beaumont Hospital in Royal Oak, Mich.

PAUL SANCYA/AP

Decision-Making



## CONTENTS

- The Big Question
- More Phones, Fewer Doctors
- IBM Aims to Make Medical Expertise a Commodity
- 23andMe Tries to Woo the FDA
- Mobile Health Monitoring Devices
- Mobile Health's Growing Pains
- Plus: CB's Crash, Data in Action at Mayo, Pharma's new transparency, and more

## Driven Care

a flood of molecular, oral patient information. medicine better?

## The Big Question

## Can Technology Fix Medicine?

Medical data is a hot spot for venture investing and product innovation. The goal: better care.

# DATA-DRIVEN HEALTHCARE

How Analytics and AI are Transforming the Industry



### Coronavirus (COVID-19)

Common symptoms include:

- Fever
- Cough
- Shortness of breath
- Fatigue
- Sore throat
- Runny nose
- Headache
- Nausea
- Diarrhea

Some people may experience symptoms for up to 14 days after exposure.

# COVID-19 Symptoms

## FEVER

## COUGH

## SHORTNESS OF BREATH

Symptoms may appear 2-14 days after exposure

### Going Viral: What to Watch For

Viruses can be contagious during the incubation period, before symptoms start.

Incubation period	CORONA	FLU	COMMON COLD	COVID-19*
Symptoms start	2-14 days	1-4 days	1-4 days	2-14 days
Typical time to death	10-15 days	1-2 days	1-2 days	10-15 days

\*Data for emerging information on COVID-19 coronavirus symptoms. NOTE: Some symptoms can occur in some cases with any of these viruses.

### Flu vs. Allergies vs. COVID-19

#### SYMPTOMS OF DIFFERENT RESPIRATORY ILLNESSES

Symptoms	Common Cold	Flu	COVID-19
Fever	No	Yes	Yes
Cough	Yes	Yes	Yes
Shortness of breath	No	No	Yes
Fatigue	No	Yes	Yes
Sore throat	Yes	Yes	Yes
Runny nose	Yes	Yes	Yes
Headache	No	Yes	Yes
Nausea	No	No	Yes
Diarrhea	No	No	Yes

### What are the symptoms of COVID-19?

Patients with COVID-19 report various symptoms. Symptoms can include:

- Fever
- Cough
- Shortness of breath

Some people may experience symptoms for up to 14 days after exposure.

## Symptoms of COVID-19

(2019 Novel Coronavirus)

### Fever

### Cough

### Shortness of Breath

### Do I have COVID-19, the flu or a cold?

Symptoms	COVID-19	Cold	Flu
Fever	Common	Rare	Common
Cough	Common	Common	Common
Shortness of breath	Common	Rare	Common
Fatigue	Common	Rare	Common
Sore throat	Common	Common	Common
Runny nose	Common	Common	Common
Headache	Common	Rare	Common
Nausea	Common	Rare	Common
Diarrhea	Common	Rare	Common

### Wuhan virus symptoms

Patients experience fever and possibly also fatigue, muscle pain and a dry cough.

A few may have had diarrhea or nausea 5-7 days before.

Severe cases develop signs of acute respiratory distress syndrome, where lungs can't supply vital organs with enough oxygen.

Patients with worsening breathing problems often require intensive care.

Fewer usually only need to be hospitalized for 10-12 days, while the average time to death is 18.8 days.

### Typical symptoms of COVID-19

Fever	87.9%
Dry cough	67.7%
Fatigue	38.1%
Sputum production	33.4%
Shortness of breath	18.6%
Myalgia or arthralgia	14.8%
Sore throat	13.9%
Headache	13.6%
Chills	11.4%
Nausea or vomiting	5.0%
Nasal congestion	4.8%
Diarrhea	3.7%
Hemoptysis	0.9%
Conjunctival congestion	0.8%

### COVID-19 vs Influenza vs Allergies

Symptoms	COVID-19	Influenza	Allergies
Fever	Common	Common	Rare
Cough	Common	Common	Common
Shortness of breath	Common	Rare	Rare
Fatigue	Common	Common	Rare
Sore throat	Common	Common	Common
Runny nose	Common	Common	Common
Headache	Common	Rare	Rare
Nausea	Common	Rare	Rare
Diarrhea	Common	Rare	Rare

## COVID-19 vs Influenza vs Allergies

- COVID-19:**
  - Fever
  - Cough
  - Shortness of breath
  - Symptoms 2-14 days after exposure
- Influenza:**
  - Fever
  - Cough
  - Sore throat
  - Head/body aches
  - Runny/stuffy nose
  - Fatigue
- Allergies:**
  - Sneezing
  - Coughing
  - Runny nose
  - Scratchy throat
  - Itchy, red, or watery eyes

UNSURE? CONTACT YOUR HEALTH PROVIDER BY PHONE OR ONLINE

### COVID-19 compared to other common conditions

Symptom	COVID-19	Common Cold	Flu	Allergies
Fever	Common	Rare	Common	Sometimes
Dry cough	Common	Mild	Common	Sometimes
Shortness of breath	Common	No	No	Common
Headaches	Sometimes	Rare	Common	Sometimes
Aches and pains	Sometimes	Common	Common	No
Sore throat	Sometimes	Common	Common	No
Fatigue	Sometimes	Sometimes	Common	Sometimes
Diarrhea	Rare	No	Sometimes*	No
Runny nose	Rare	Common	Sometimes	Common
Sneezing	No	Common	No	Common

\*Sometimes for children

### COVID-19 Symptoms & Warning Signs

- Fever
- Cough
- Shortness of breath
- Persistent pain or chest pressure
- Bluish lips or face

IF YOU DEVELOP SYMPTOMS AND HAVE BEEN IN CONTACT WITH SOMEONE WITH COVID-19, OR TRAVELED TO AN AREA WITH ONGOING SPREAD, CALL YOUR DOCTOR.

### COVID-19 vs Influenza vs Allergies

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Runny nose	Common	Common	Common
Headache	Common	Rare	Rare
Nausea	Common	Rare	Rare
Diarrhea	Common	Rare	Rare



Testing to the Rescue





# Diagnostic Reasoning



Fictional Example

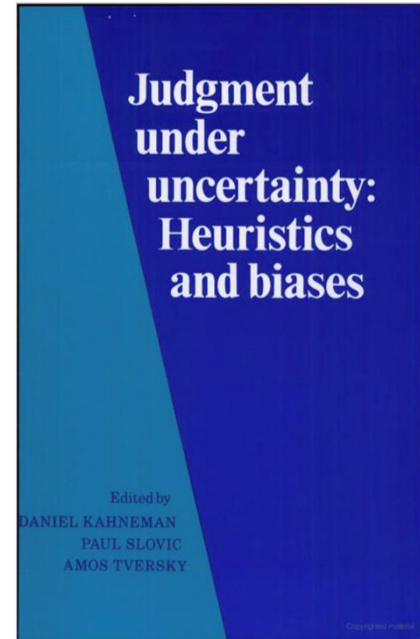
# Diagnostic Reasoning



Fictional Scenario

## Human Reasoning Experiment\*

- A new and serious infectious disease appears in a population.
- At this time, the prevalence of infection is believed to be 0.1%.
- A test is available to detect the infection long before any symptoms appear. This test has a
  - sensitivity of 99.9% and a
  - specificity of 99.9%.
- As a disease control measure, you are tested for the disease.



\*adapted from Kahneman  
& Tversky, 1980



# Diagnostic Reasoning



Fictional Values

## Are you infected?

- Prevalence of infection in population: 0.1%
- Test Performance:
  - Sensitivity: 99.9%
  - Specificity: 99.9%
- The test results come back, and you are positive.





# Diagnostic Reasoning

## Are you infected?

- More specifically, what is your probability of being infected?
  - $P(\text{Infection}=\text{true} \mid \text{Test}=\text{positive})=99.9\%$
  - $P(\text{Infection}=\text{false} \mid \text{Test}=\text{negative})=99.9\%$
  - $P(\text{Infection}=\text{true} \mid \text{Test}=\text{negative})=0.1\%$
  - $P(\text{Infection}=\text{false} \mid \text{Test}=\text{positive})=0.1\%$

**SO, WHY DO YOU EVEN ASK?**



# Diagnostic Reasoning

Your probability of being infected is...

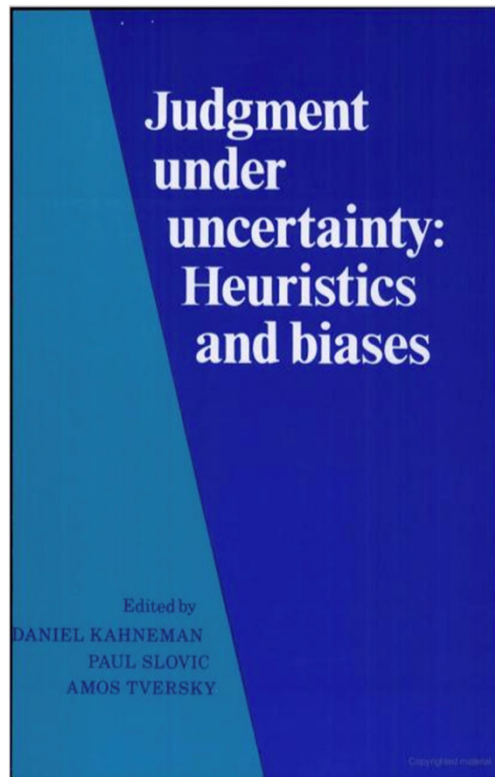
**50/50**



# The Prosecutor's Fallacy



# Diagnostic Reasoning

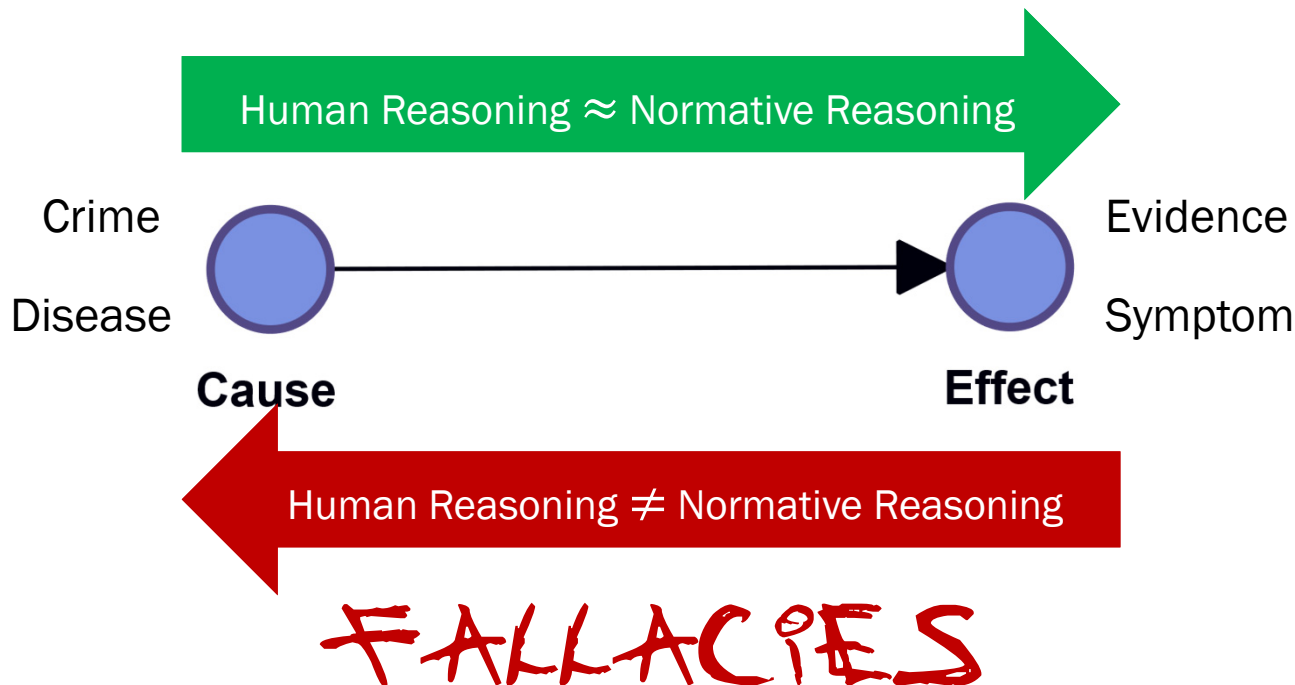


HUMAN REASONING  
IS FLAWED



# Diagnostic Reasoning

## Human Cognitive Limitations and Biases Under Uncertainty



# Rev. Thomas Bayes

## Bayes' Theorem for Conditional Probabilities

H: Hypothesis

E: Evidence

$$P(H | E) = \frac{P(E | H)P(H)}{P(E)}$$

“Probability of the Hypothesis given the Evidence”



T. Bayes.

1763

## PHILOSOPHICAL TRANSACTIONS

[ 370 ]

quodque solum, certa nitri signa præbere, sed plura  
concurrere debere, ut de vero nitro producto dubium  
non relinquatur.

LII. *An Essay towards solving a Problem in  
the Doctrine of Chances. By the late Rev.  
Mr. Bayes, F. R. S. communicated by Mr.  
Price, in a Letter to John Canton, A. M.  
F. R. S.*

Dear Sir,

Read Dec. 23, 1763. I Now send you an essay which I have  
found among the papers of our de-  
ceased friend Mr. Bayes, and which, in my opinion,  
has great merit, and well deserves to be preserved.  
Experimental philosophy, you will find, is nearly in-  
terested in the subject of it; and on this account there  
seems to be particular reason for thinking that a com-  
munication of it to the Royal Society cannot be im-  
proper.

He had, you know, the honour of being a mem-  
ber of that illustrious Society, and was much esteem-  
ed by many in it as a very able mathematician. In an  
introduction which he has writ to this Essay, he says,  
that his design at first in thinking on the subject of it  
was, to find out a method by which we might judge  
concerning the probability that an event has to hap-  
pen, in given circumstances, upon supposition that we  
know nothing concerning it but that, under the same circum-

# Diagnostic Reasoning

- Bayes' Rule allows us to compute the probability  $P(\text{Infection}=\text{true} \mid \text{Test}=\text{positive})$

$$P(H \mid E) = \frac{P(E \mid H)P(H)}{P(E)}$$



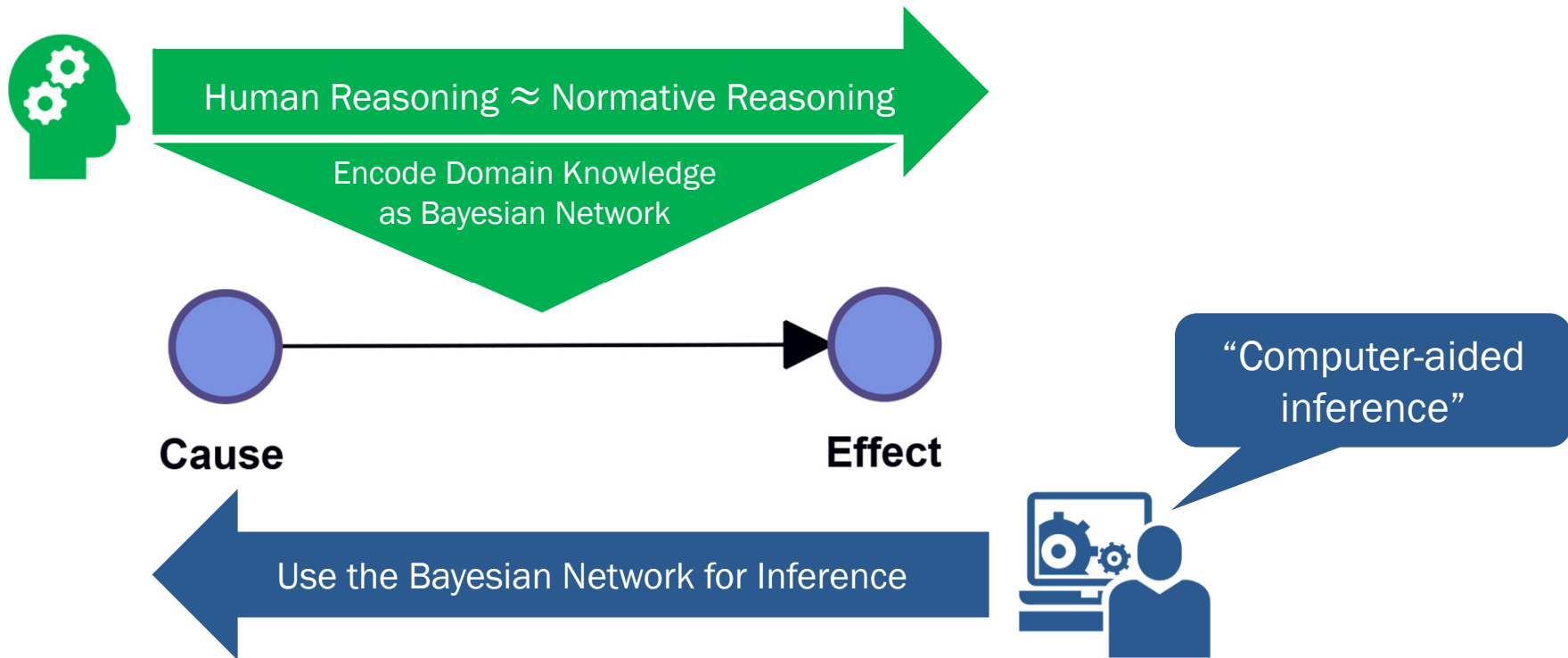
*T. Bayes.*

$$P(\text{Infection} = \text{true} \mid \text{Test} = \text{positive}) = \frac{P(\text{Test} = \text{positive} \mid \text{Infection} = \text{true})P(\text{Infection} = \text{true})}{P(\text{Test} = \text{positive})} =$$
$$\frac{P(\text{Test} = \text{positive} \mid \text{Infection} = \text{true})P(\text{Infection} = \text{true})}{P(\text{Test} = \text{positive} \mid \text{Infection} = \text{true})P(\text{Infection} = \text{true}) + P(\text{Test} = \text{positive} \mid \text{Infection} = \text{false})P(\text{Infection} = \text{false})}$$

**correct, but cumbersome, even in trivial cases.**

# Bayesian Networks to the Rescue!

## Overcoming our Limitations

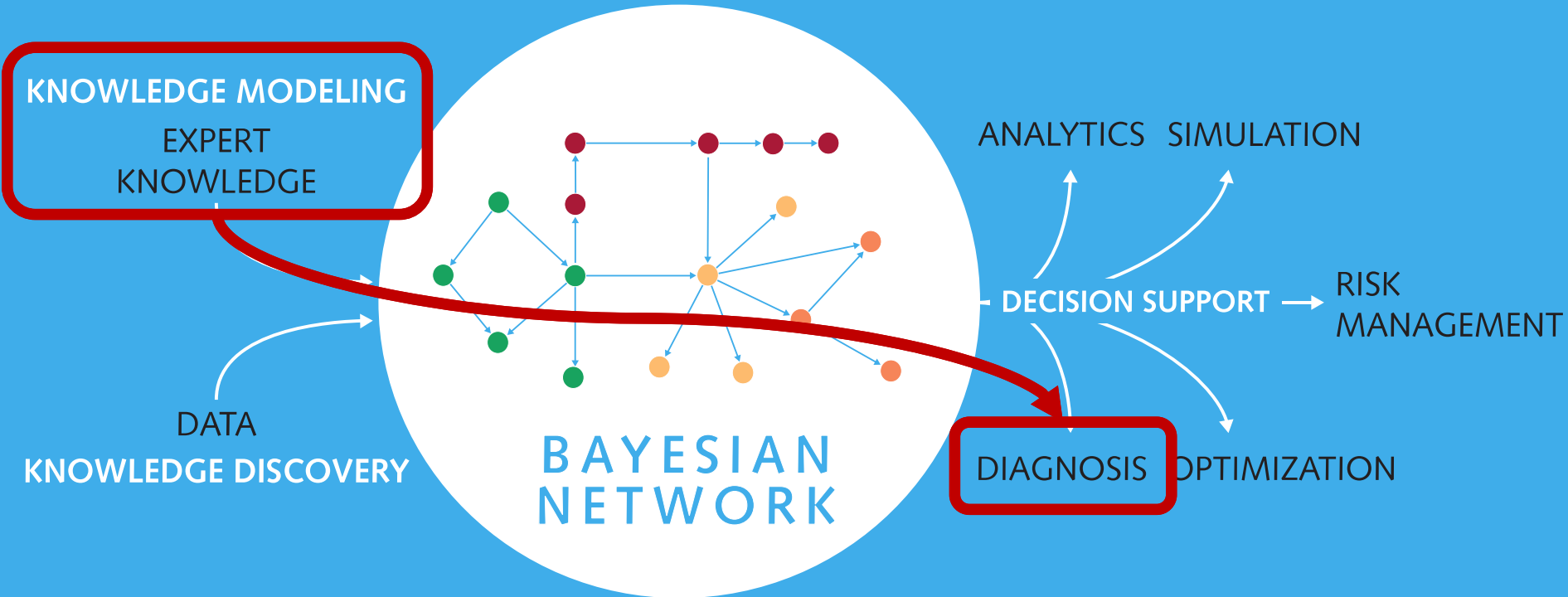






We need an  
inference engine!

# Bayesian Networks



# Diagnostic Reasoning

We encode our knowledge regarding the problem domain

False	True
99.900	0.100

Prevalence=Marginal  
Probability of Disease



**Disease**

# Diagnostic Reasoning

We encode our knowledge regarding the problem domain

Conditional  
Probability Table

False	True
99.900	0.100

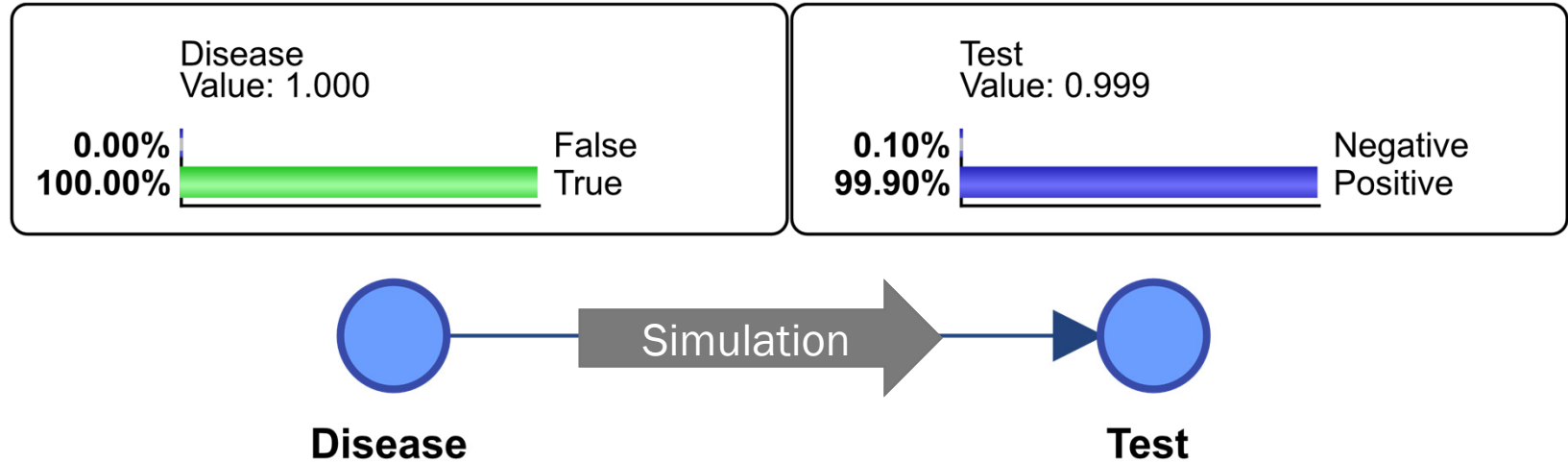
Disease	Negative	Positive
False	99.900	0.100
True	0.100	99.900





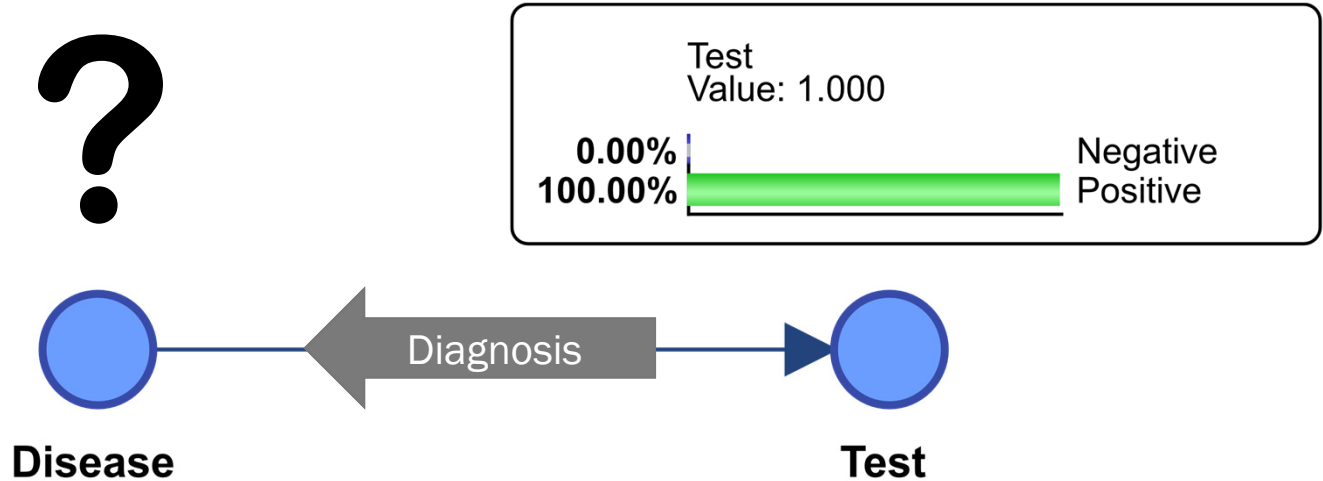
# Diagnostic Reasoning

We use this Bayesian network to perform inference



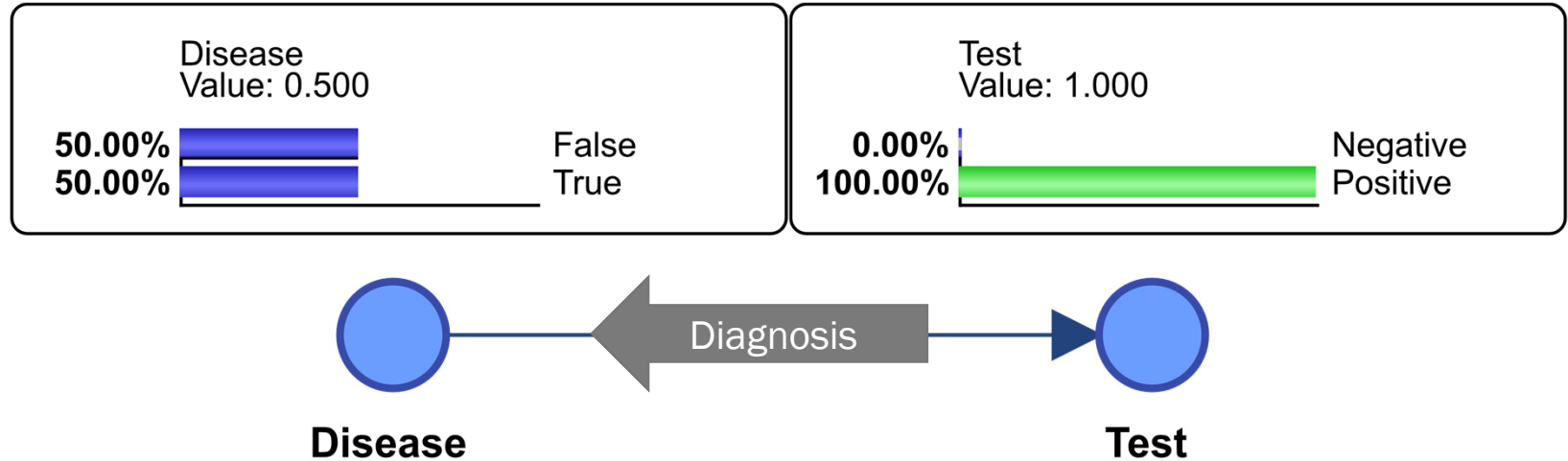
# Diagnostic Reasoning

We use this Bayesian network to perform inference



# Diagnostic Reasoning

We use this Bayesian network to perform inference

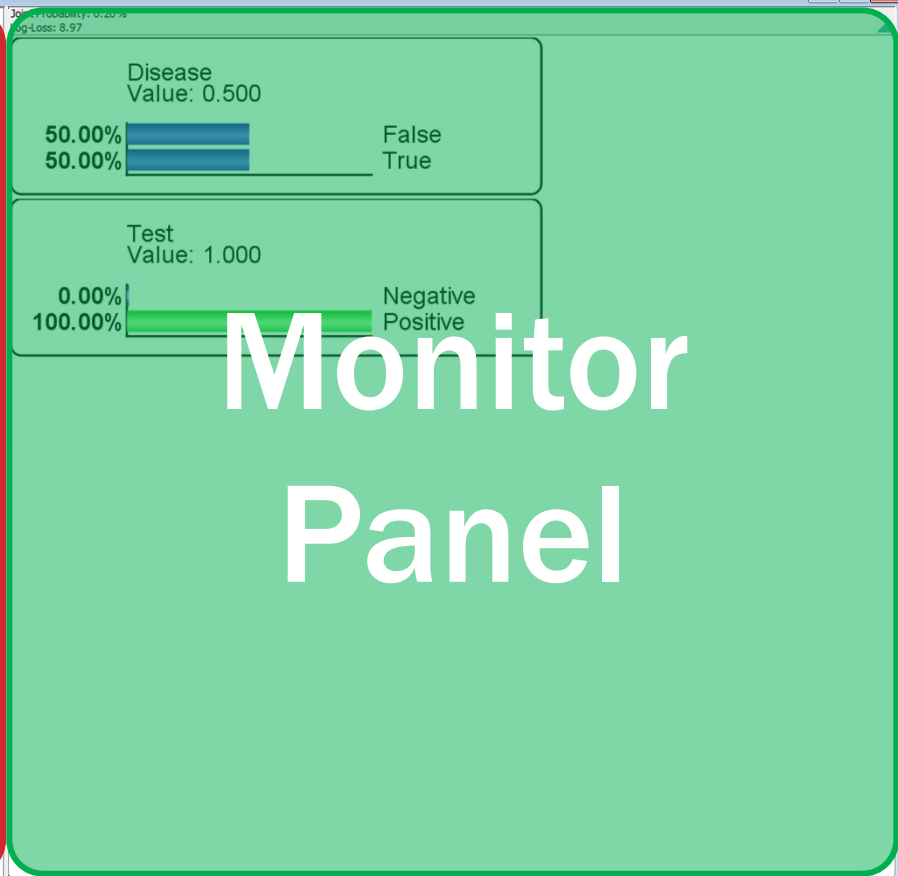




New graph 3.xbl \*



# Graph Panel



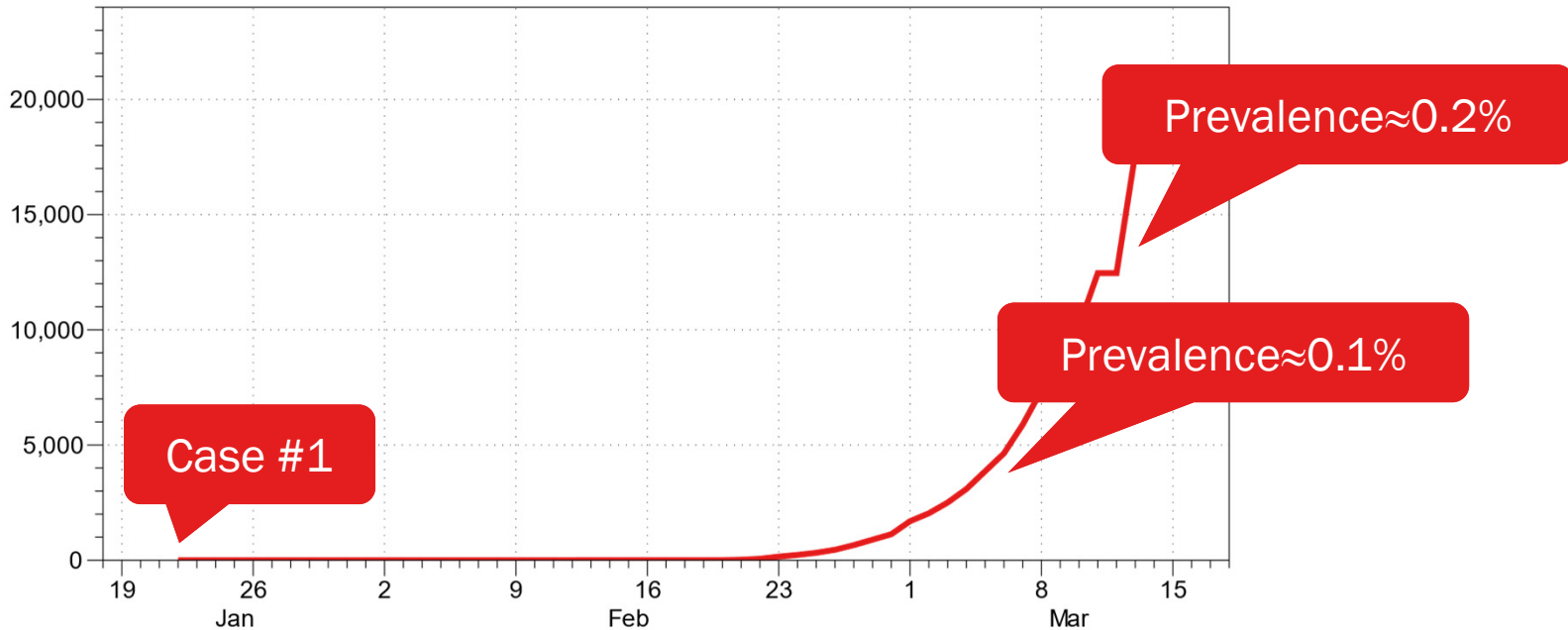


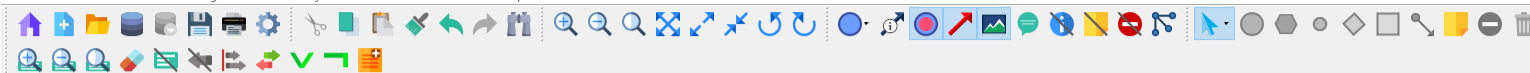
# Diagnostic Reasoning



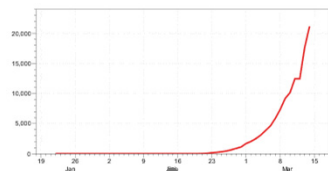
Fictional Values

## Infections Over Time





Test.xbl



Time

Prevalence

Disease

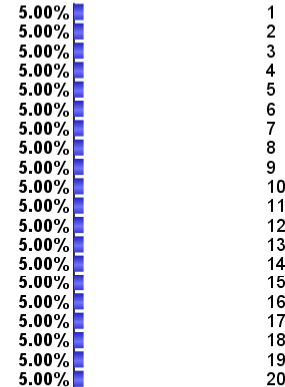
Test

Time dependence

Our model so far

Joint Probability: 100.00%  
Log-Loss: 0  
Total Value: 10.552  
Mean Value: 3.517

Time  
Mean: 10.500 Dev: 5.766  
Value: 10.500



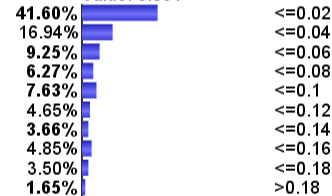
Disease  
Mean: 0.001 Dev: 0.023  
Value: 0.001

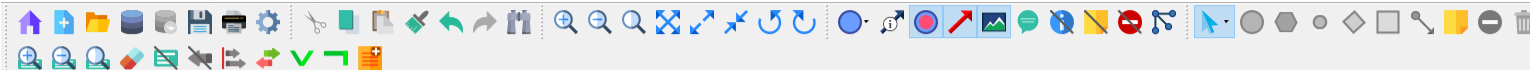


Test  
Value: 0.002



Prevalence  
Mean: 0.051 Dev: 0.051  
Value: 0.051



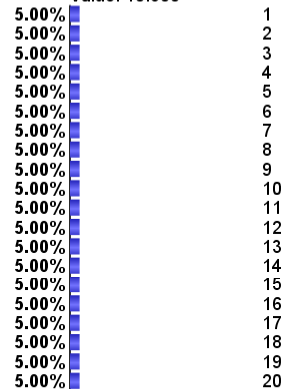


Test.xbl

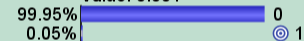


Joint Probability: 100.00%  
Log-Loss: 0  
Total Value: 10.552  
Mean Value: 3.517

**Time**  
Mean: 10.500 Dev: 5.766  
Value: 10.500



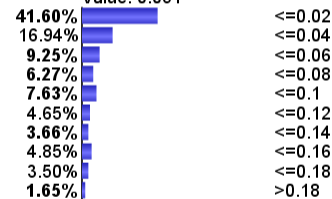
**Disease**  
Mean: 0.001 Dev: 0.023  
Value: 0.001



**Test**  
Value: 0.002

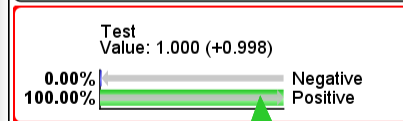
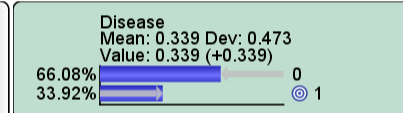
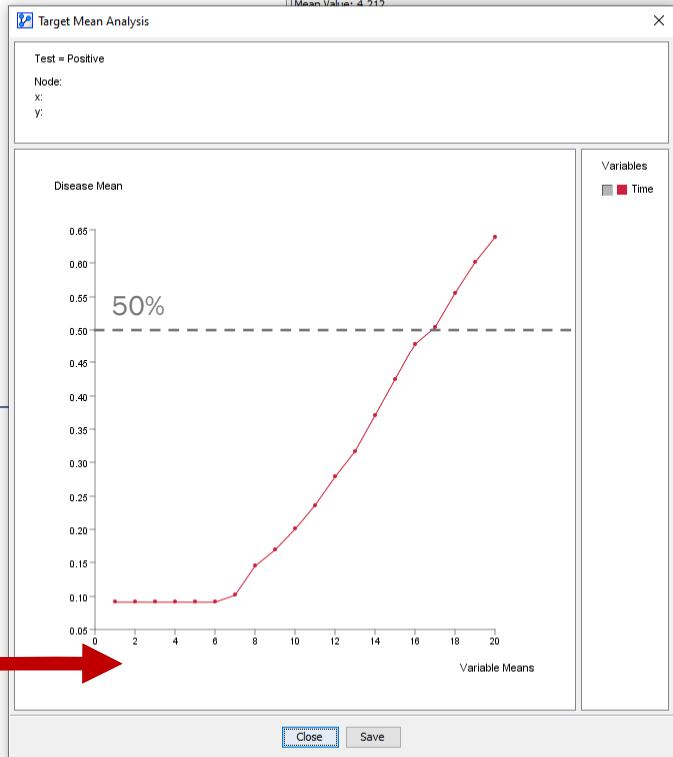


**Prevalence**  
Mean: 0.051 Dev: 0.051  
Value: 0.051





Joint Probability: 0.15%  
Log-Loss: 9.37  
Total Value: 12.636  
Mean Value: 4.312



Test=Positive

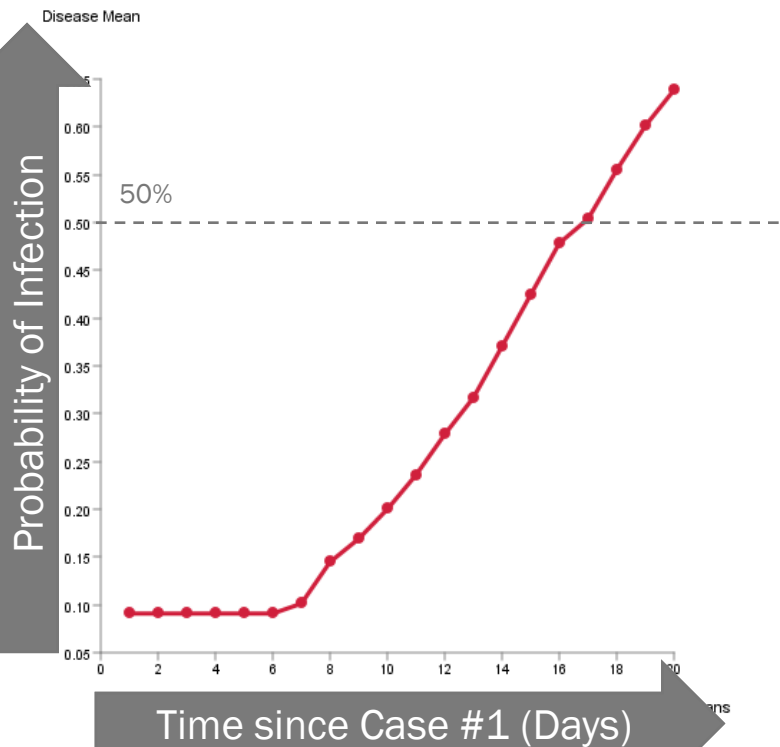


Test = Positive

Node: Time

x: 16

y: 0.47839



Variables

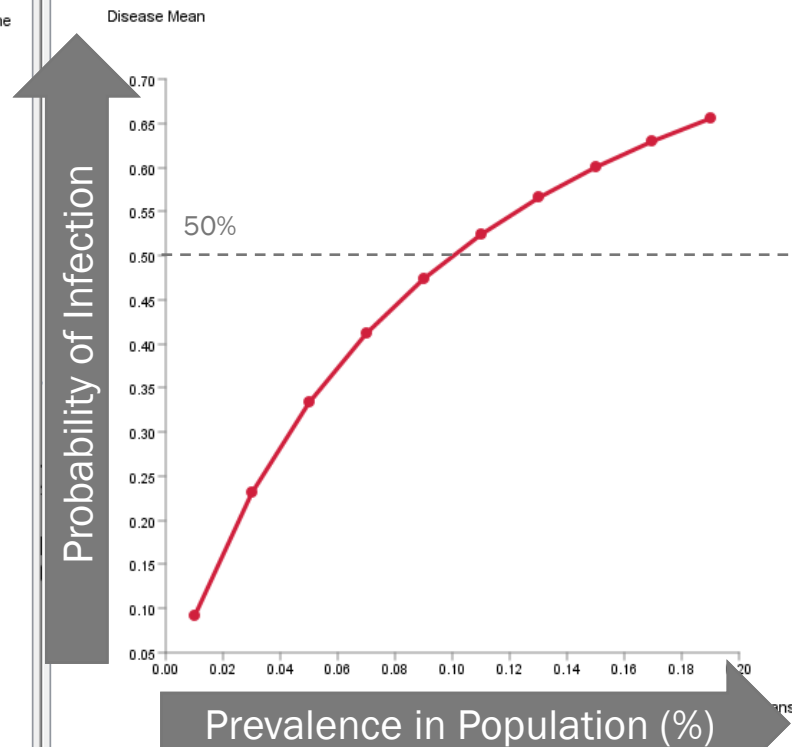
☒ Time

Test = Positive

Node: Prevalence

x: 0.11

y: 0.52383



Variables

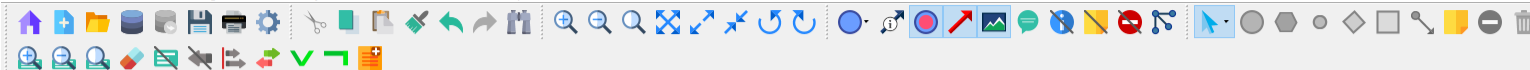
☒ Prevalence

Close

Save

Close

Save



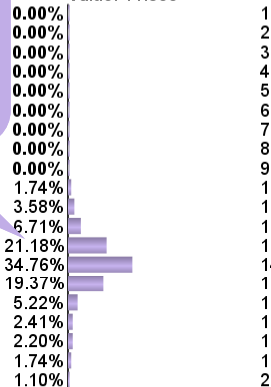
Test.xbl \*



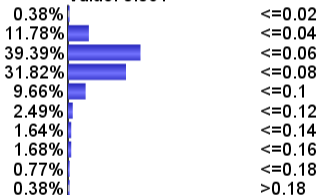
Encoding uncertain assumptions as a distribution.

Joint Probability: 0.022%  
Log-Loss: 12.1  
Total Value: 14.527  
Mean Value: 4.842

**Time**  
Mean: 14.088 Dev: 1.695  
Value: 14.088



**Prevalence**  
Mean: 0.064 Dev: 0.026  
Value: 0.064



**Disease**  
Mean: 0.375 Dev: 0.484  
Value: 0.375



**Test**  
Value: 1.000





## Differential Diagnosis of Lung Diseases

# Differential Diagnosis



**Fictional Scenario**

## Example

- Decision support for the differential diagnosis of lung diseases that have common symptoms:
  - Bronchitis
  - Pneumonia
  - Tuberculosis
  - Lung Cancer



Case courtesy of Radswiki, Radiopaedia.org, rID: 12040

# Differential Diagnosis



**This is an inference task!**

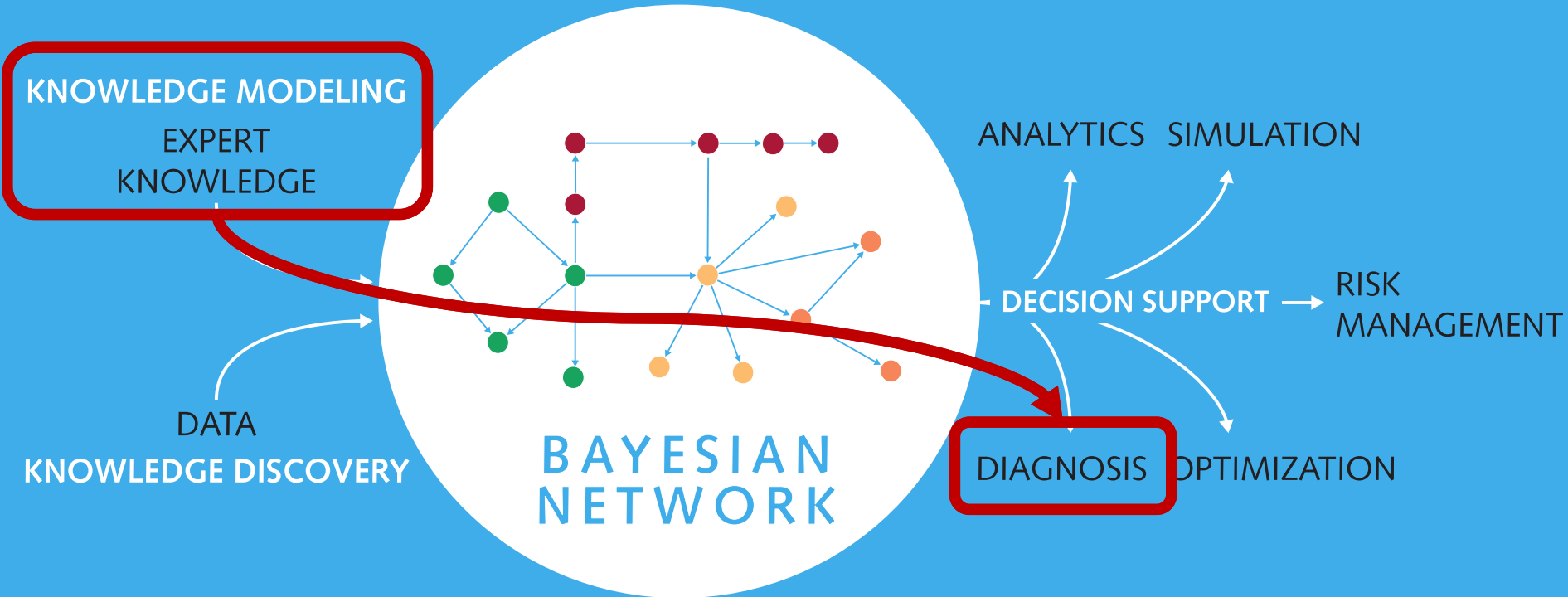
- $P(\text{Bronchitis} \mid \text{Symptom}_1, \dots, \text{Symptom}_n, \text{Risk Factor}_1, \dots, \text{Risk Factor}_n) = ?$
- $P(\text{Pneumonia} \mid \text{Symptom}_1, \dots, \text{Symptom}_n, \text{Risk Factor}_1, \dots, \text{Risk Factor}_n) = ?$
- $P(\text{Lung Cancer} \mid \text{Symptom}_1, \dots, \text{Symptom}_n, \text{Risk Factor}_1, \dots, \text{Risk Factor}_n) = ?$

Probability of  $s \mid \text{Symptom}_1, \dots, \text{Symptom}_n, \text{Risk Factor}_1, \dots, \text{Risk Factor}_n) = ?$

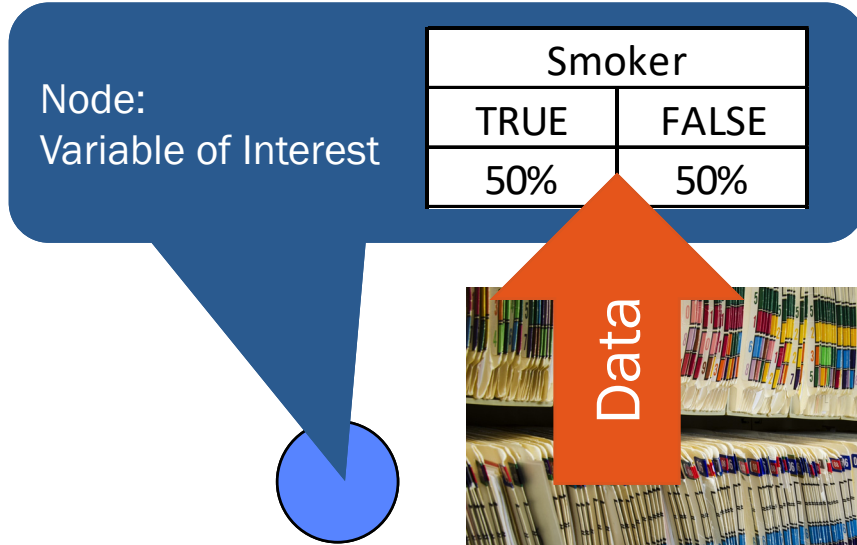
given



# Bayesian Networks



# Differential Diagnosis



# Differential Diagnosis



Smoker



Node:  
Variable of  
Interest

Lung Cancer	
TRUE	FALSE
5.5%	94.5%



# Differential Diagnosis



Fictional Values

Conditional  
Probability Table

Discrete & Nonparametric  
Probabilistic Relationship  
 $P(\text{Lung Cancer}|\text{Smoker})$



Smoker	Lung Cancer	
	FALSE	TRUE
FALSE	99%	1%
TRUE	90%	10%

Arc

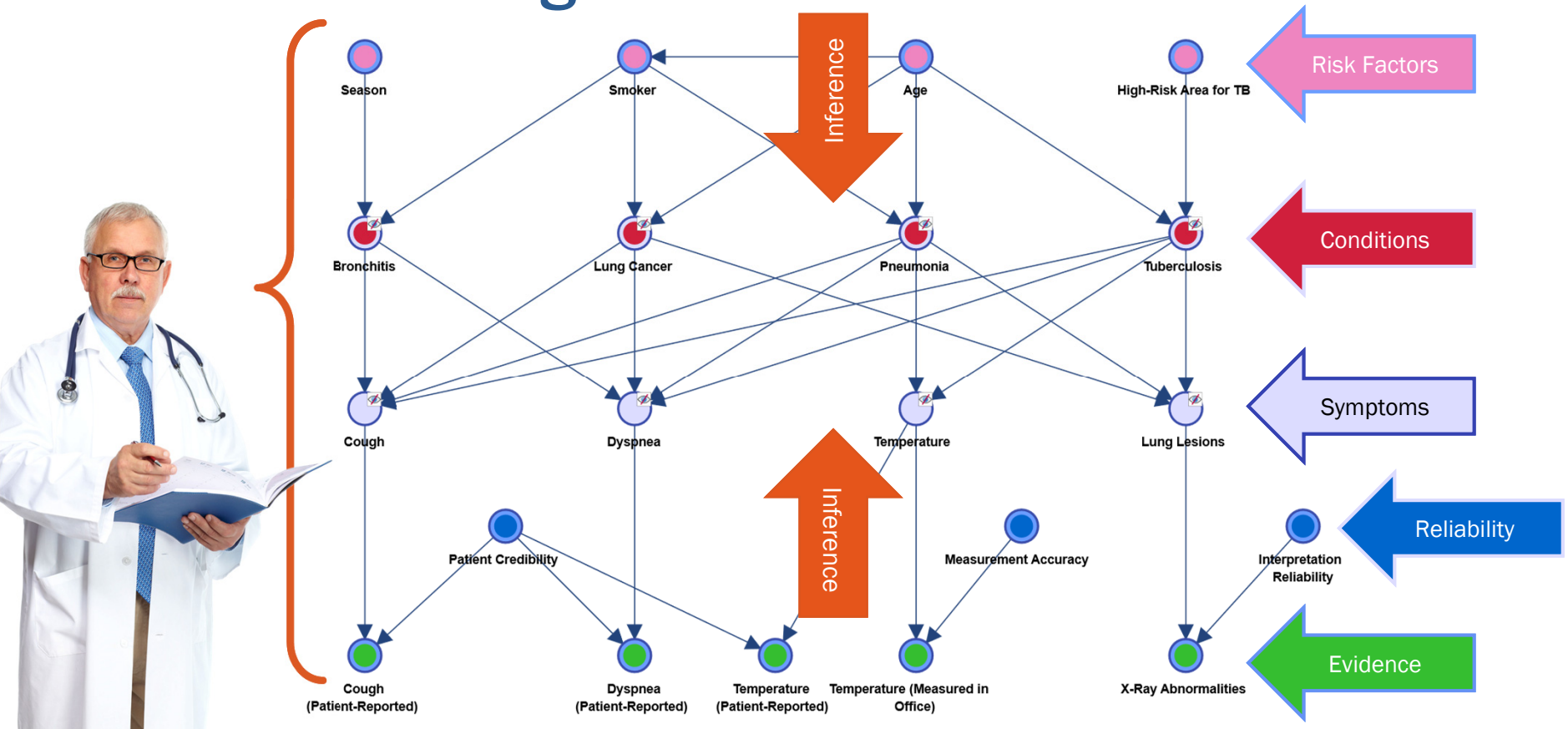


Smoker



Lung Cancer

# Differential Diagnosis





# Differential Diagnosis



Fictional Scenario

## Example of a Patient

- 19-year-old smoker
- No known comorbidities
- 1. Visit to general practitioner:
  - Reports cough
  - Diagnosis: bronchitis
- 2. Visit to general practitioner, one week later:
  - Reports cough, fever, chest pain, and shortness of breath
  - X-Ray is positive for lung lesions
  - Diagnosis: pneumonia
  - Treatment: antibiotics



# Differential Diagnosis



Fictional Scenario

- Patient dies one week later
- Autopsy reveals cause of death: tuberculosis



# Differential Diagnosis



Fictional Scenario

- Parents of deceased file lawsuit against treating physician claiming wrongful death as a result of negligence.
- The plaintiff states that all common symptoms of tuberculosis were present in the patient, which the physician should have recognized.



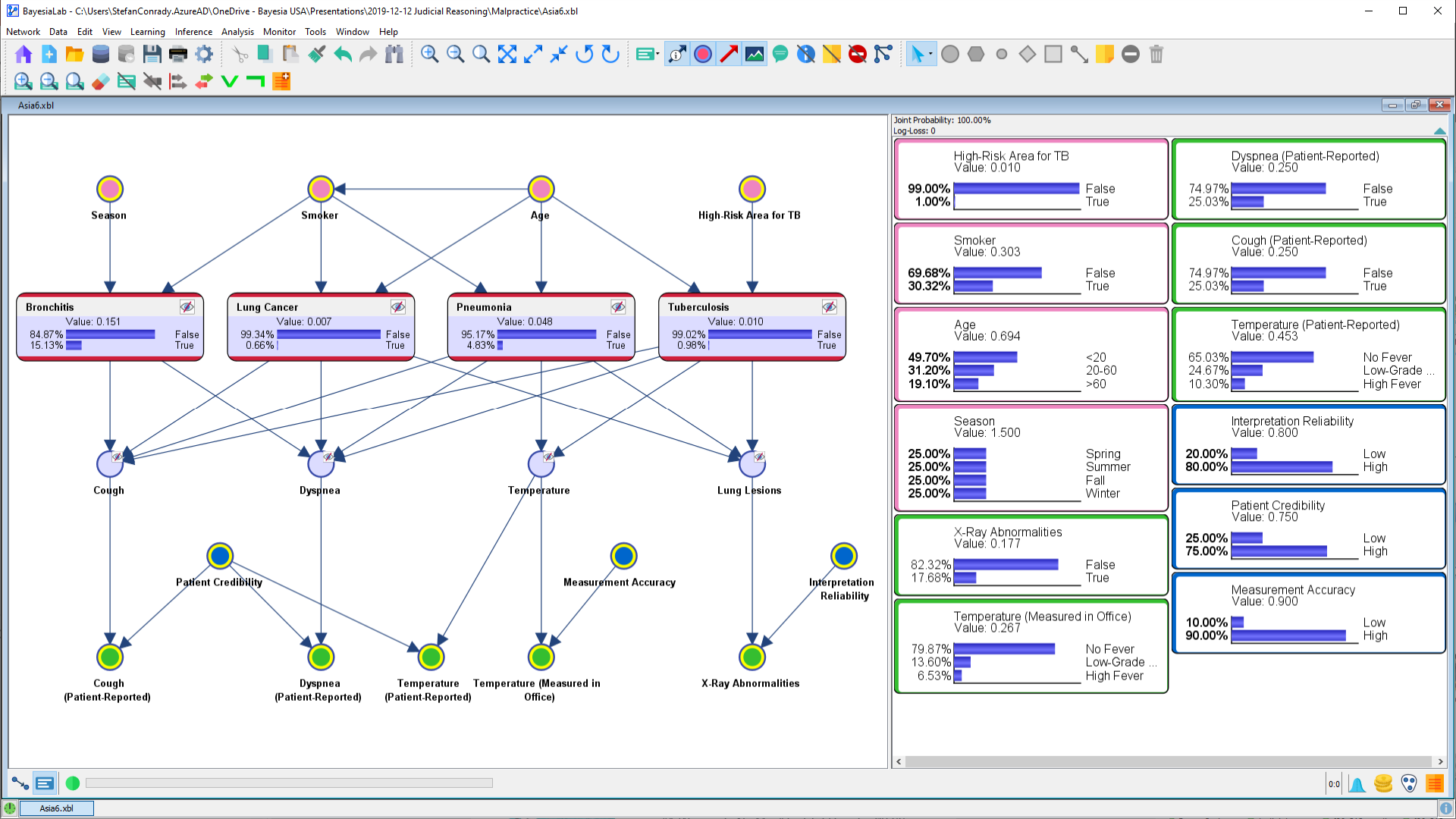
# Differential Diagnosis



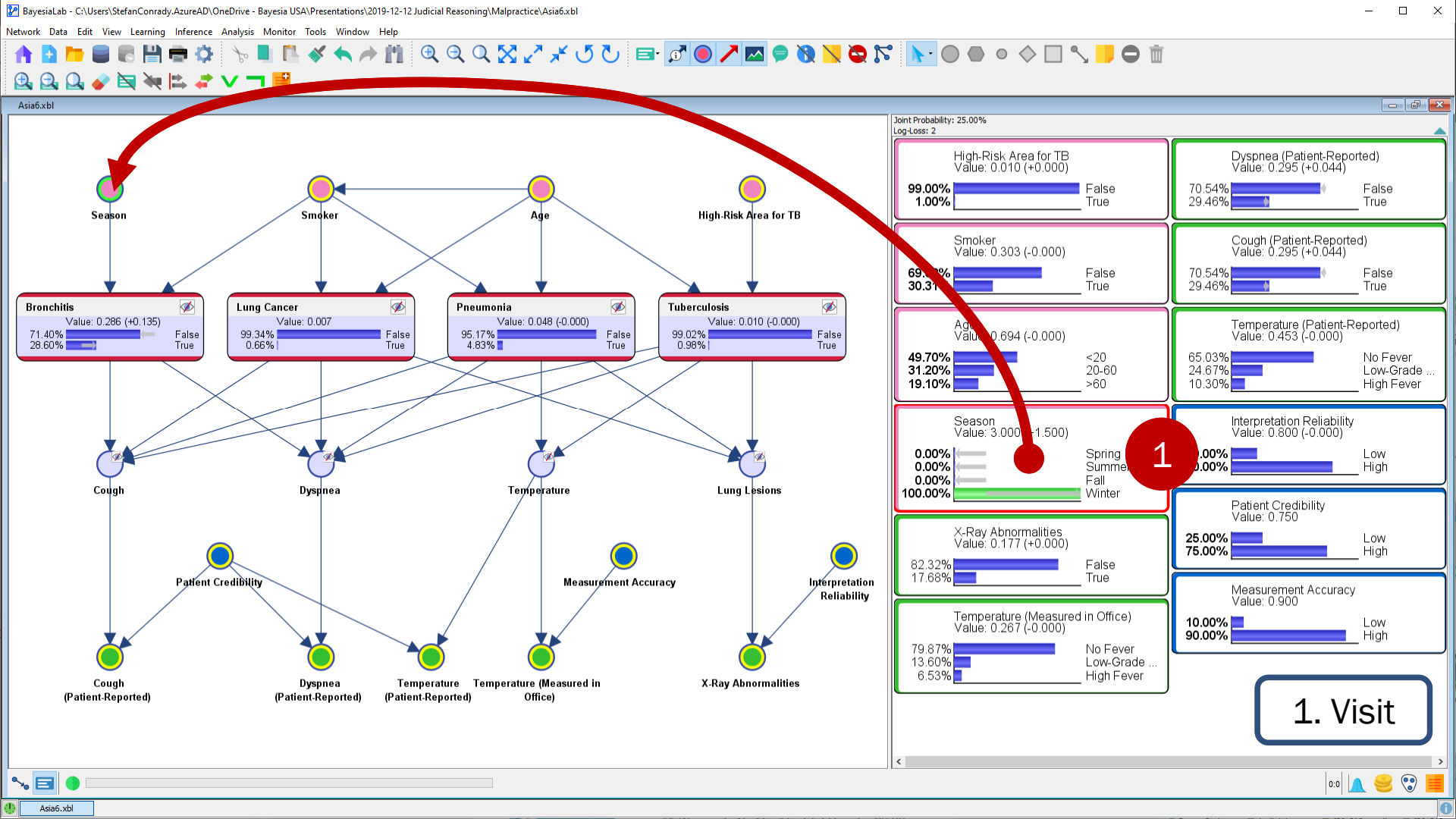
Fictional Scenario

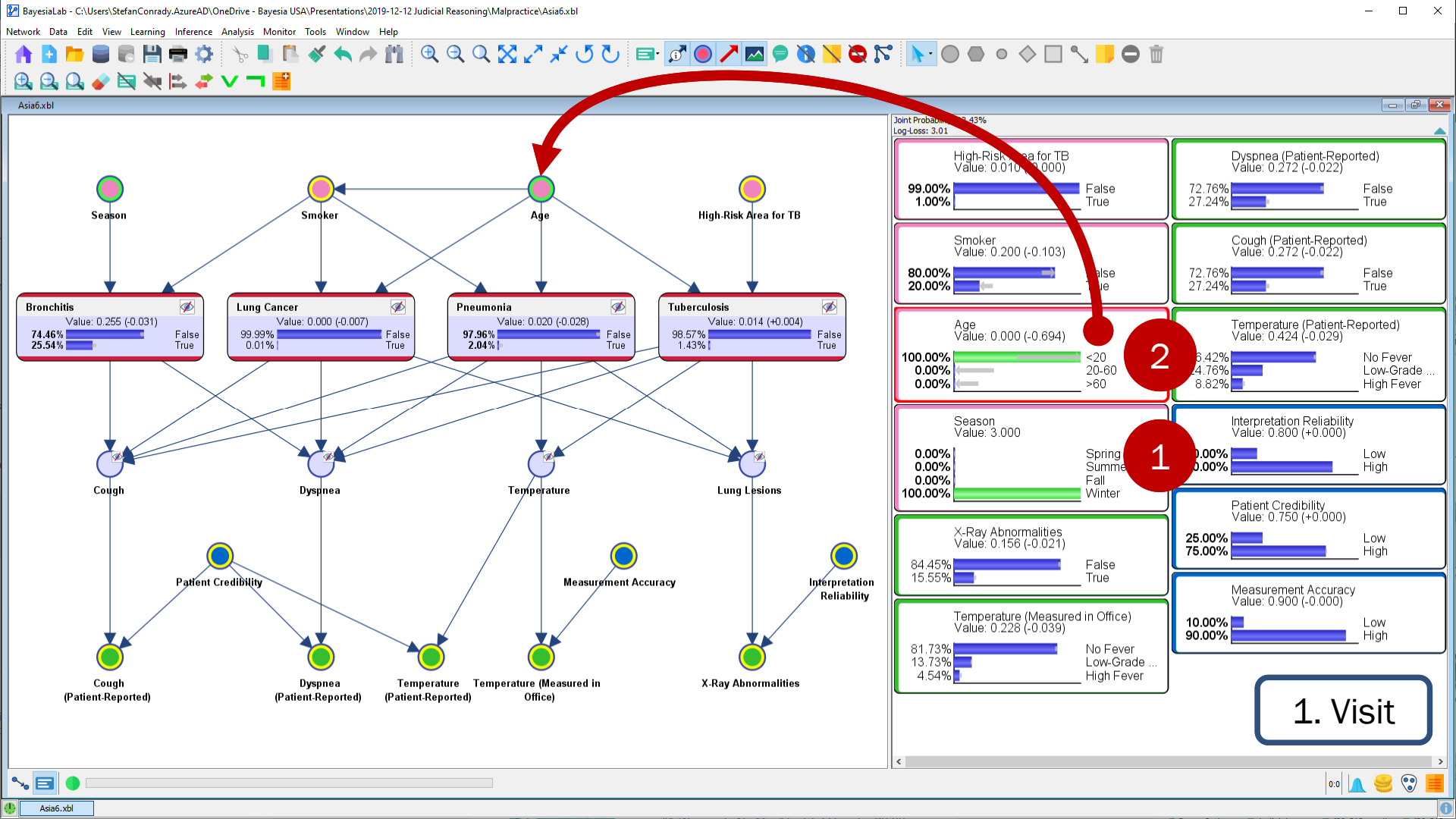
## Replicating the Diagnosis Steps of First Visit

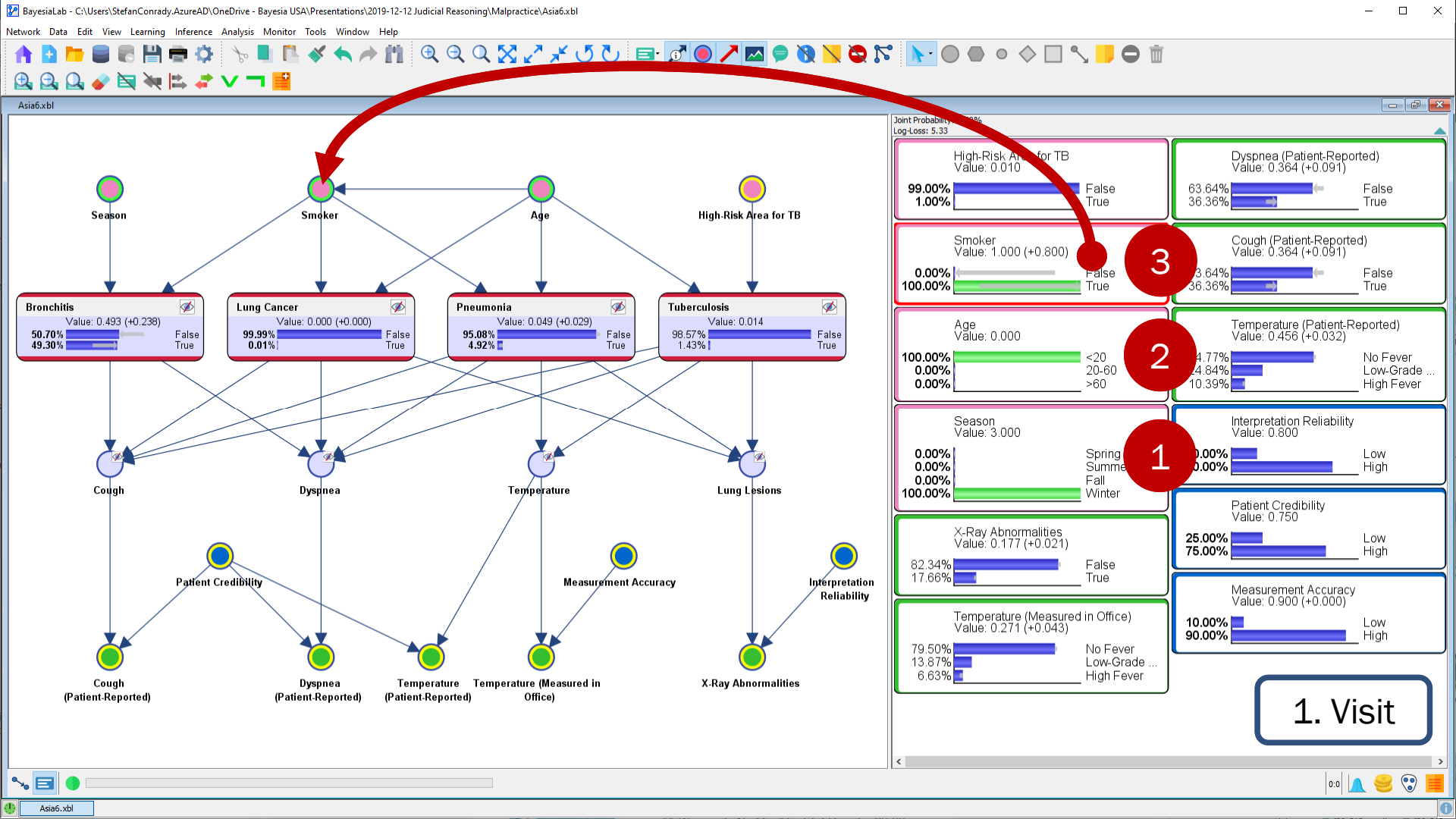
- Season=Winter
- Age<20
- Smoker=True
- Cough (Patient Report)=True
- Temperature (Patient Report)=Low-Grade Fever
- Temperature (Measured in Office)=No Fever
- Patient Credibility=Low

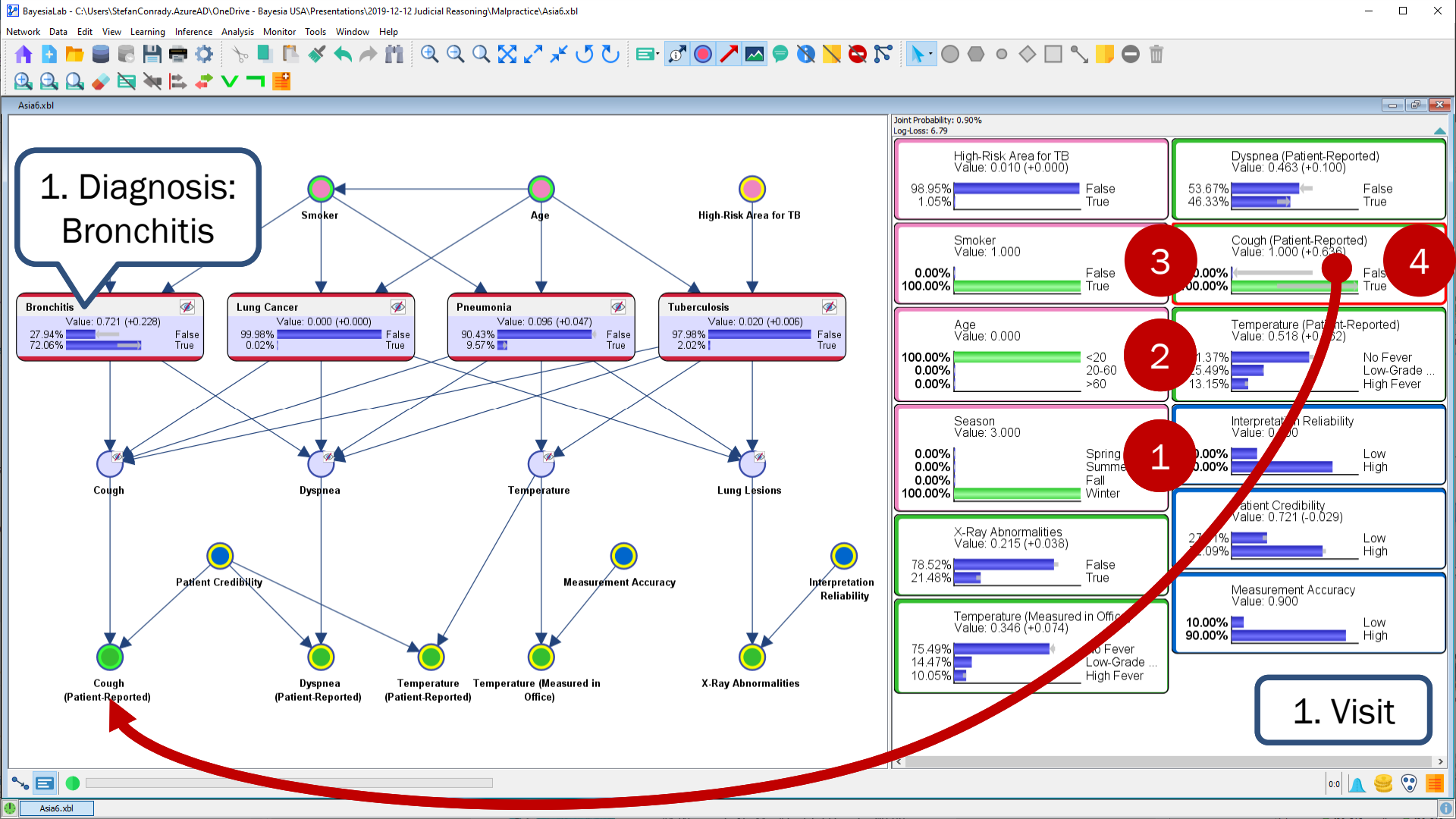






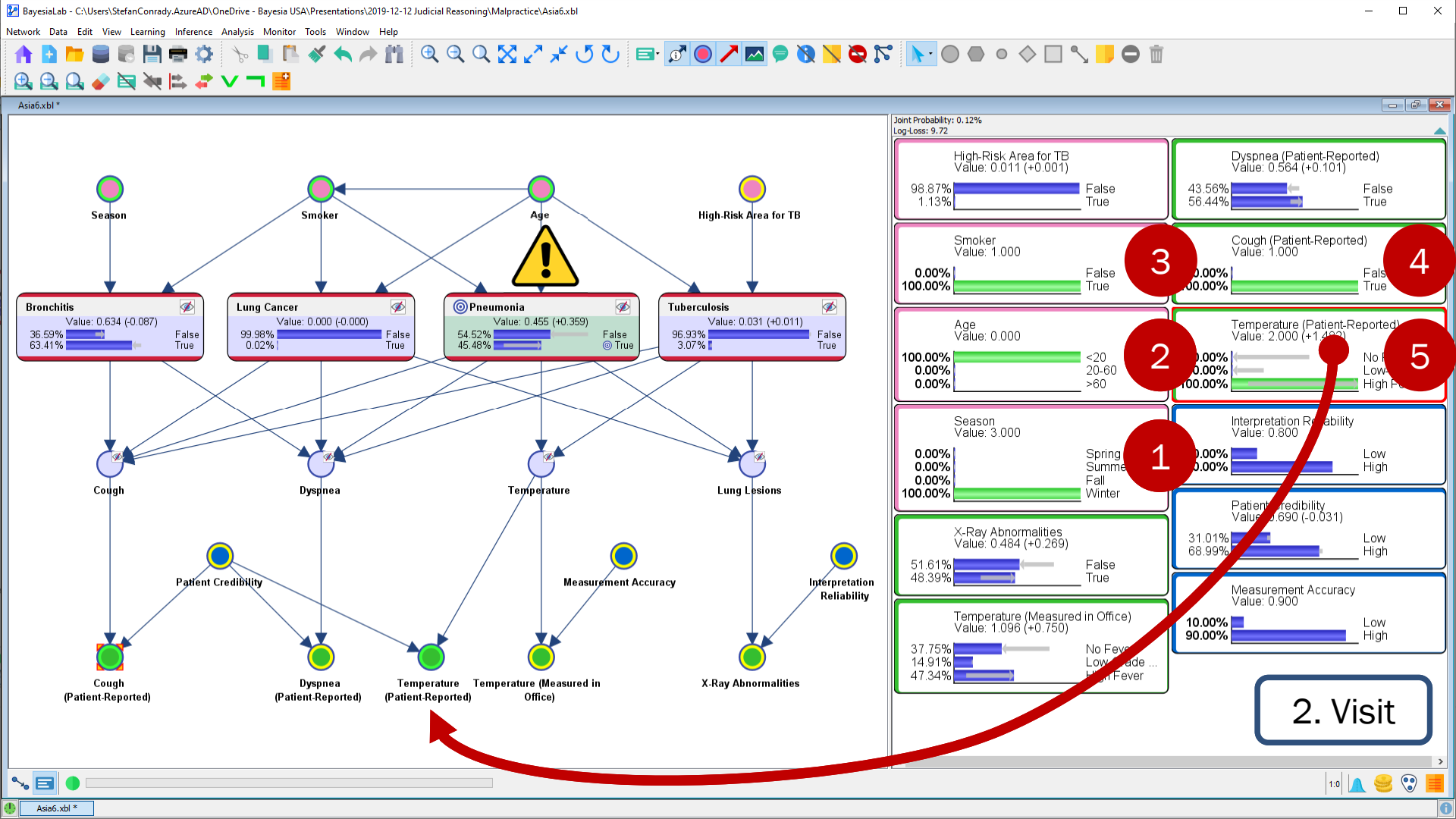


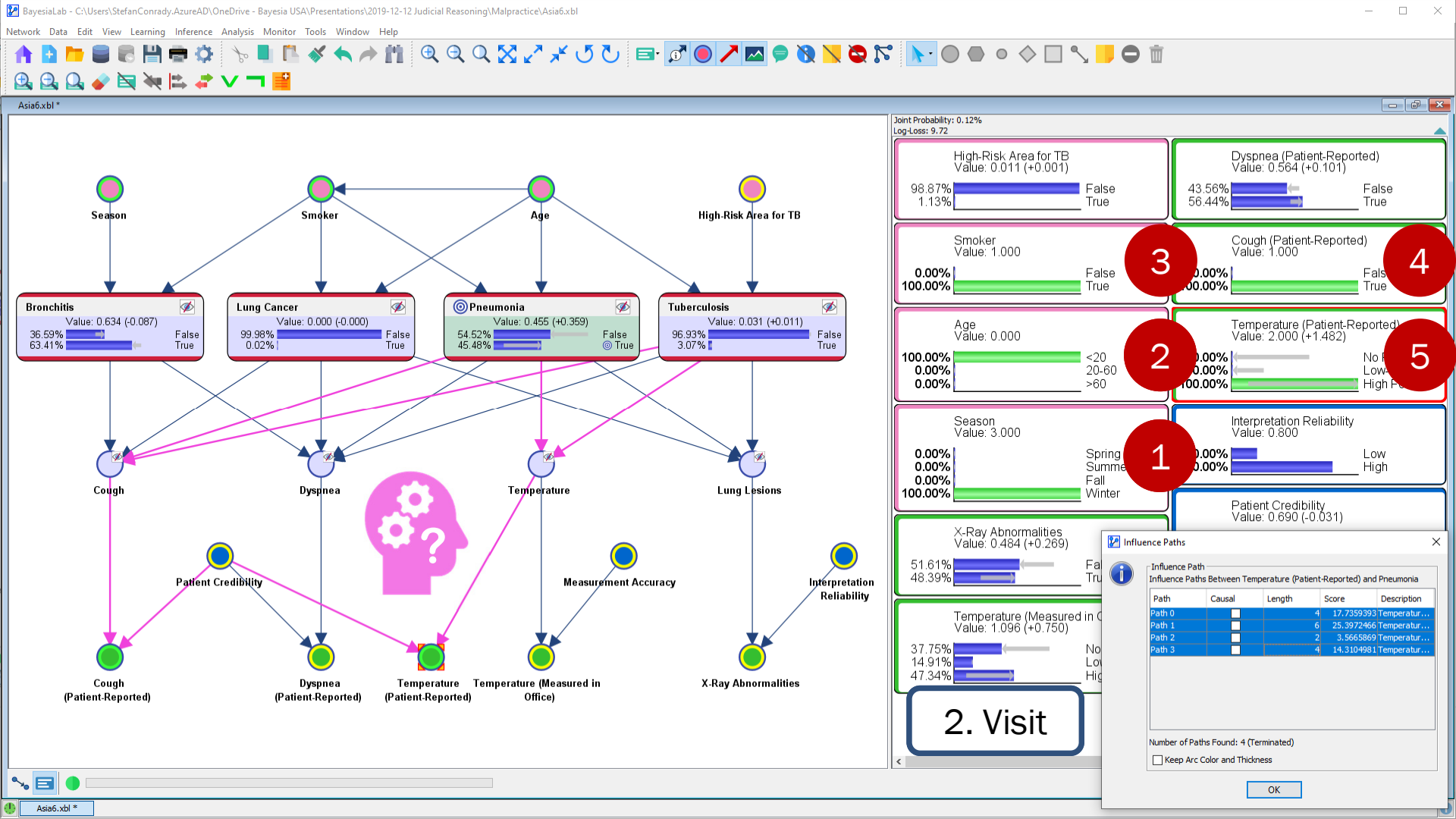


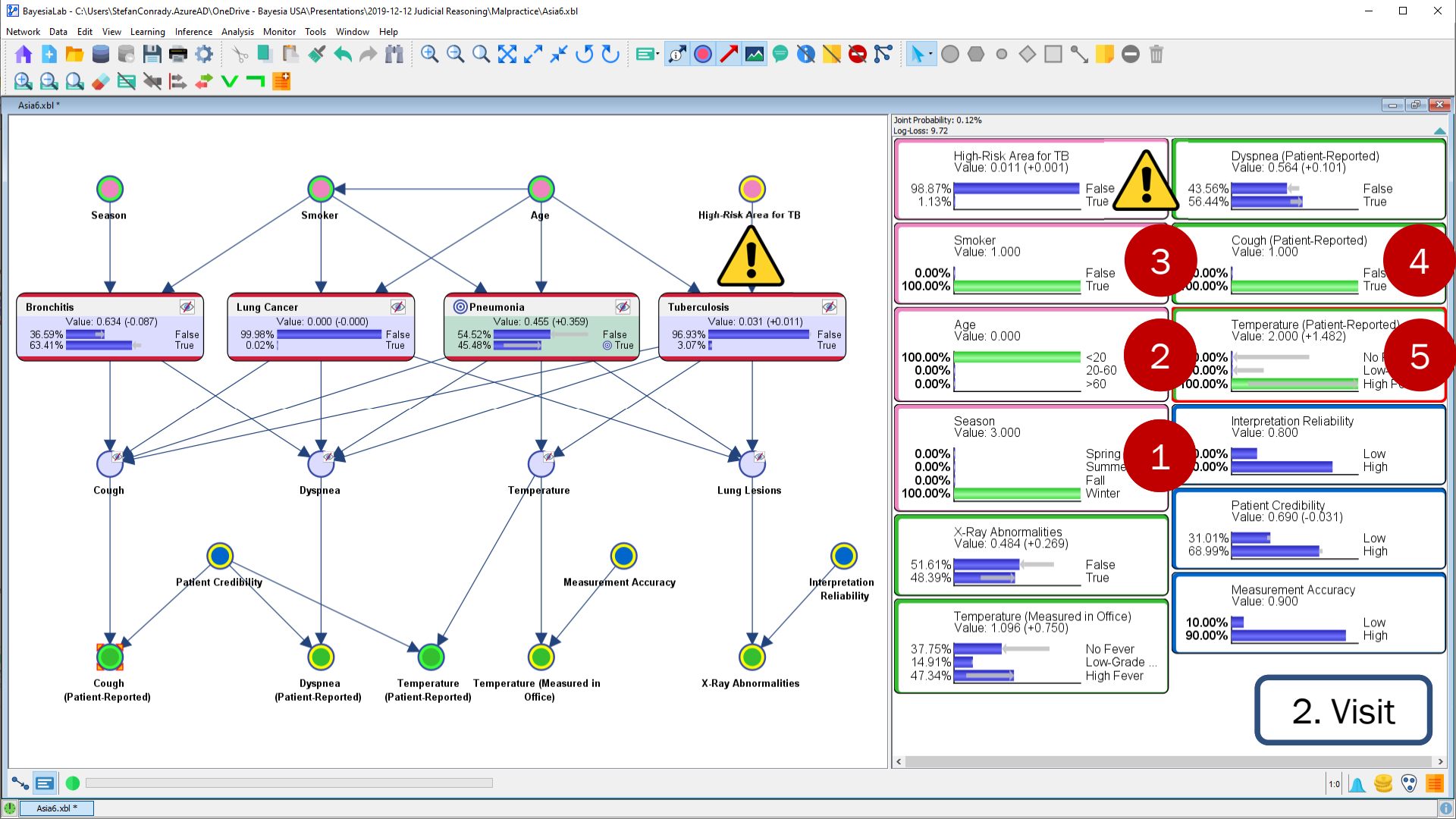






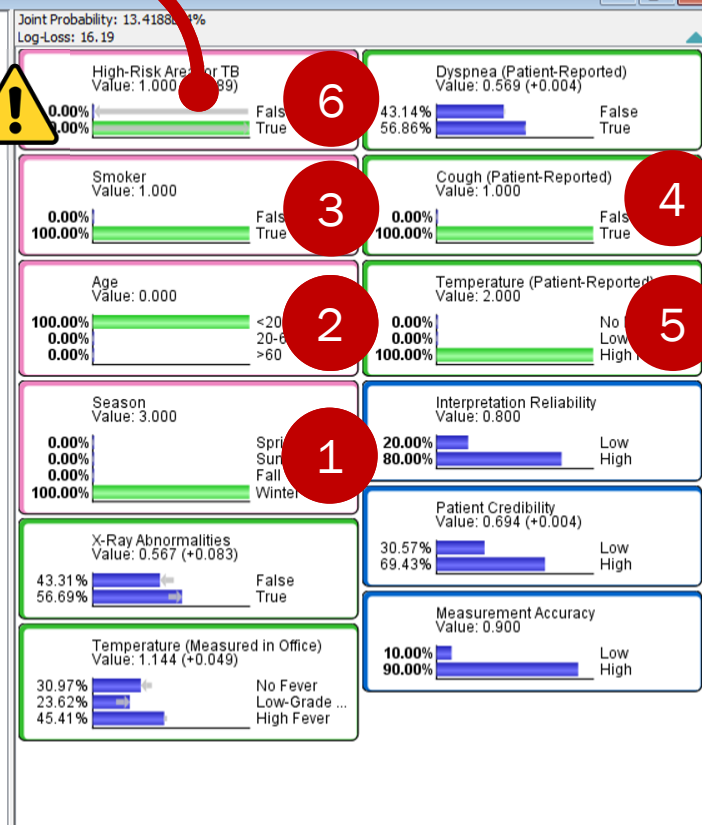
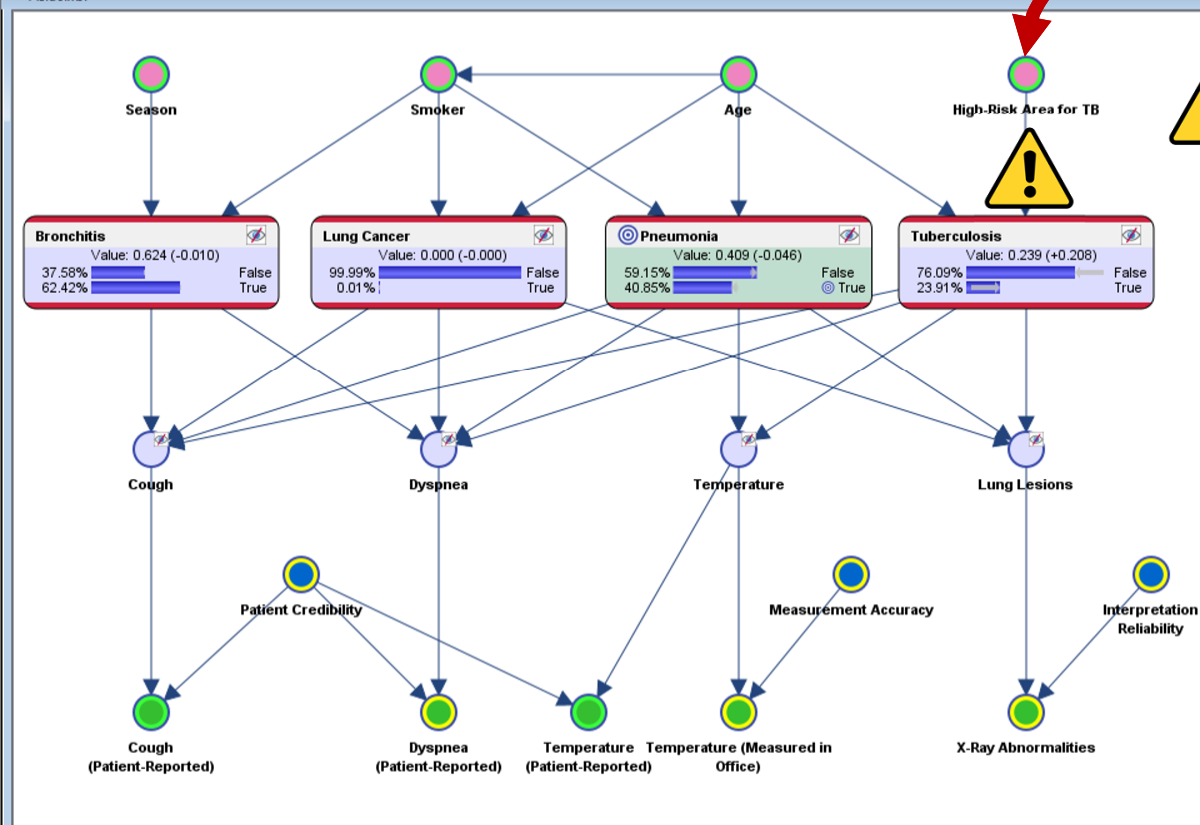






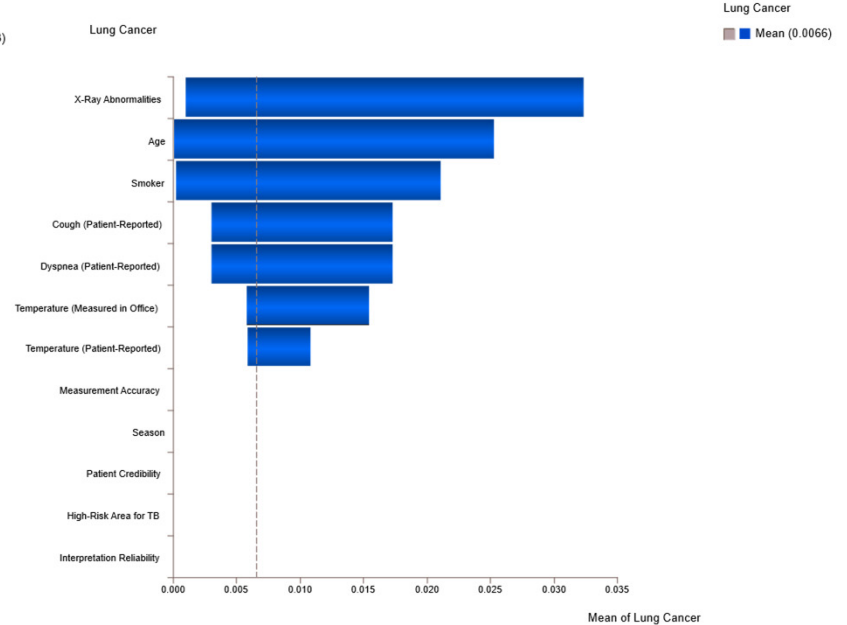
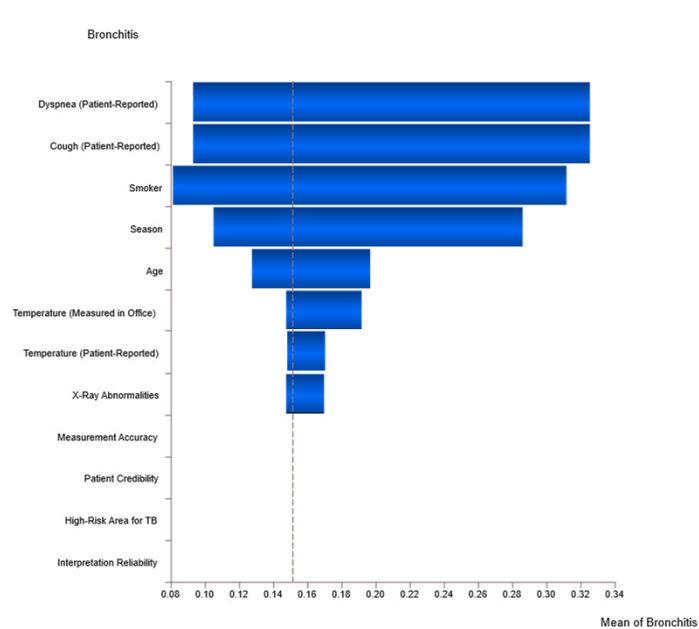


Asia6.xbl \*



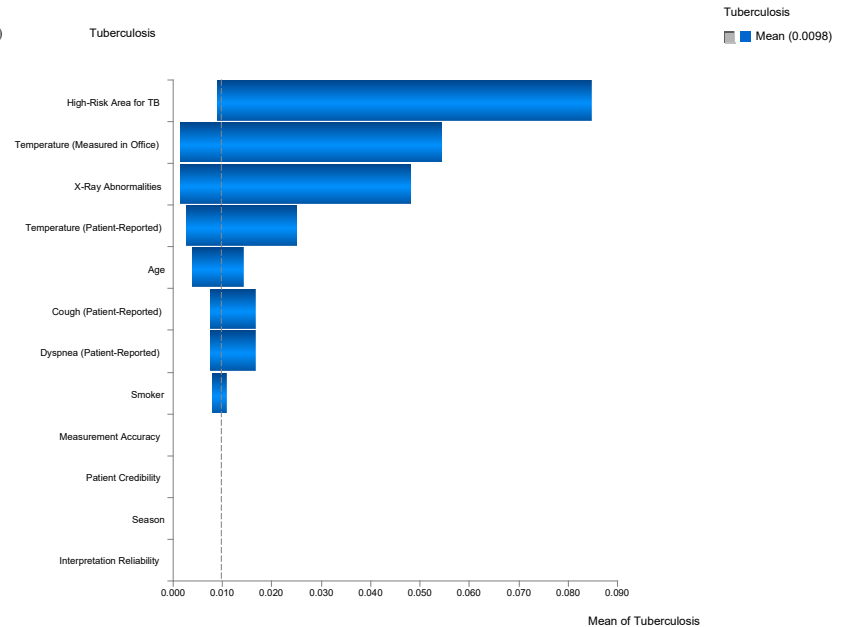
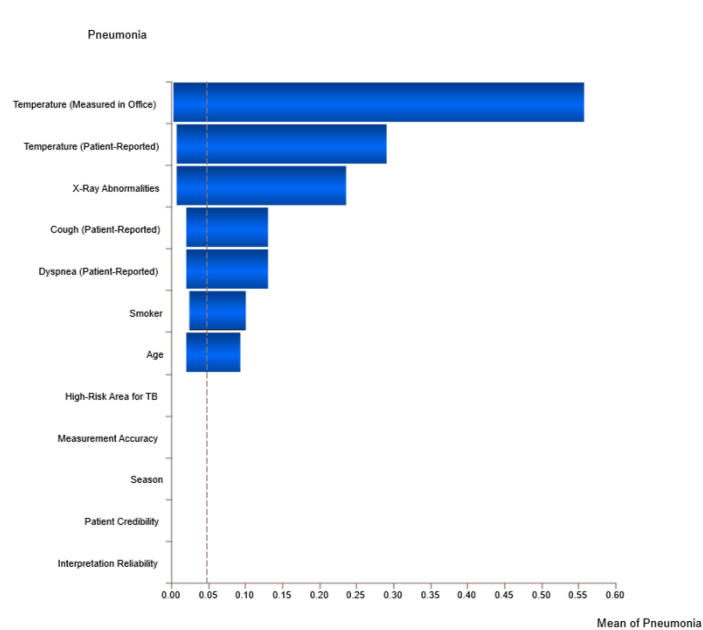
# Differential Diagnosis

## Tornado Diagrams



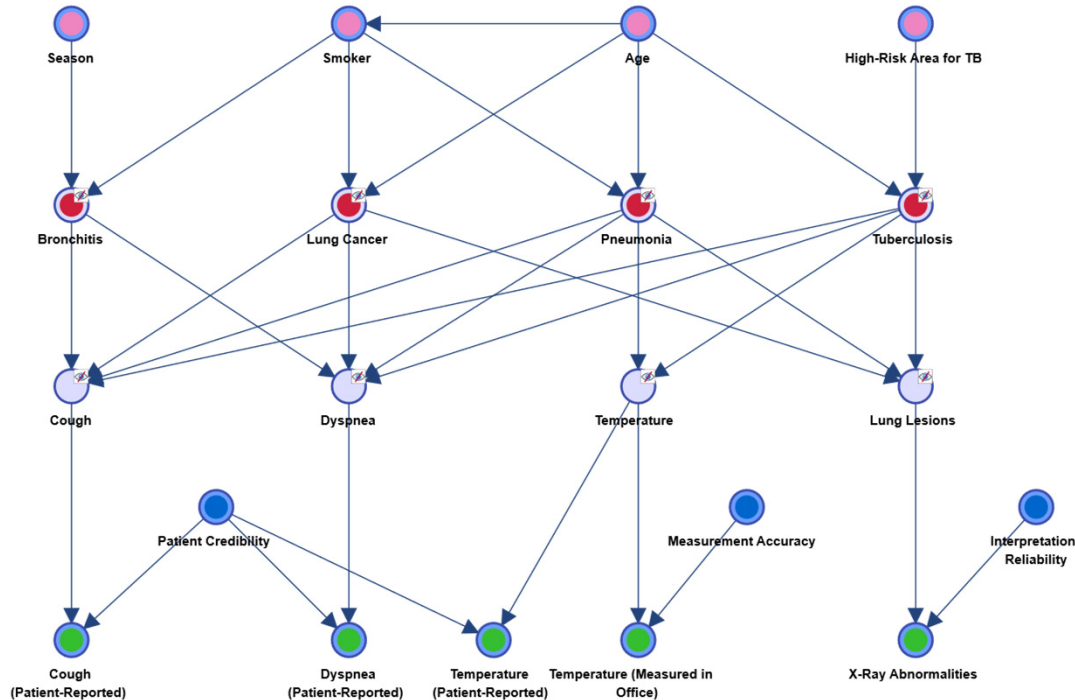
# Differential Diagnosis

## Tornado Diagrams





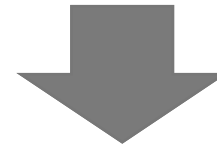
# Bayesian Networks = Artificial Intelligence



## Knowledge Base

- Declarative/Propositional Knowledge
- Associational Knowledge
- Causal Knowledge

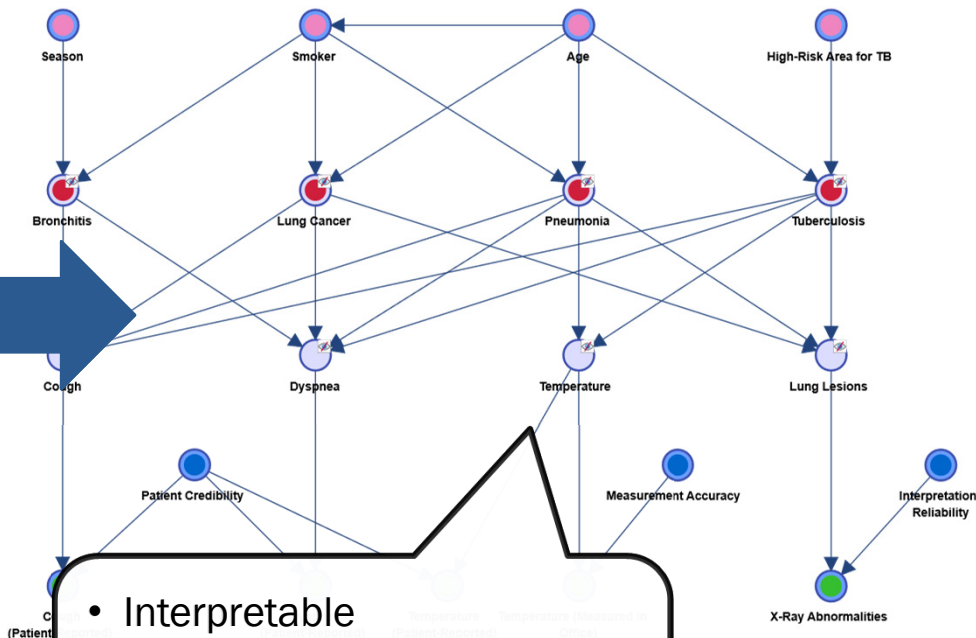
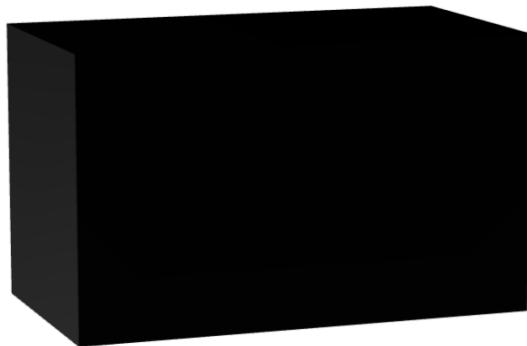
## Inference Engine



Expert System  
→ Artificial Intelligence

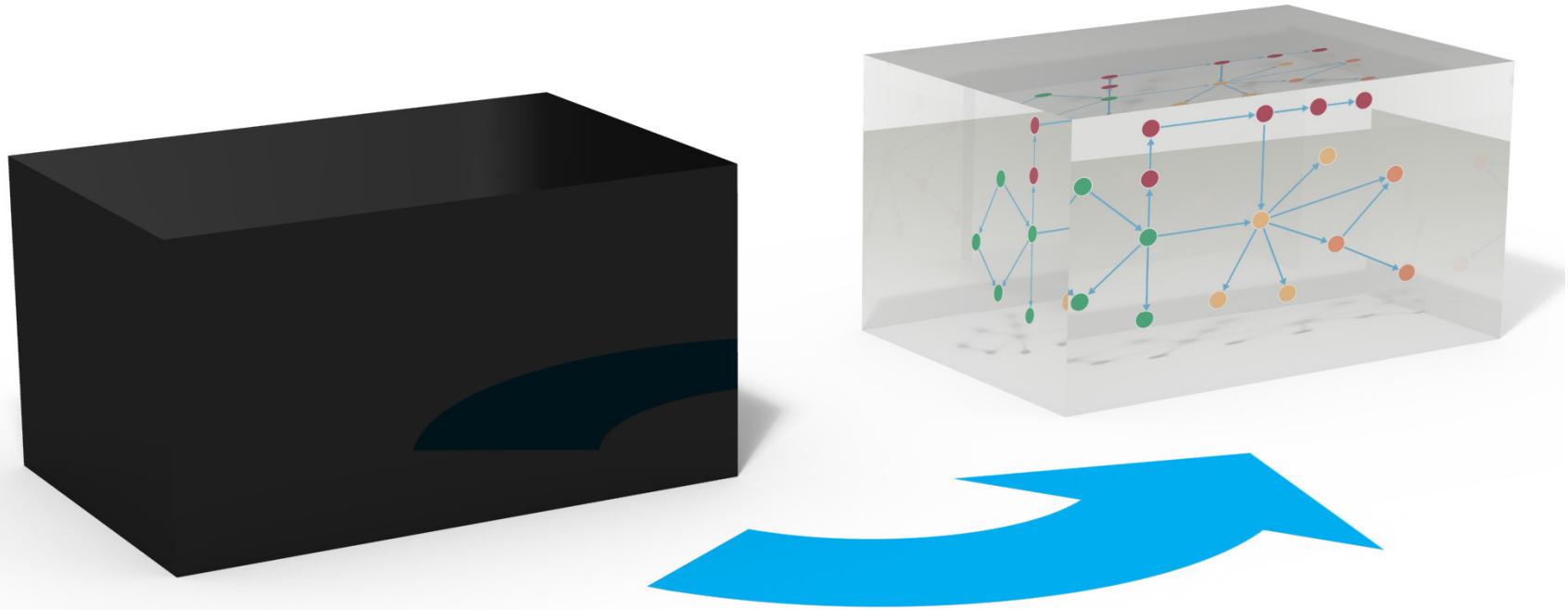
# Bayesian Networks = Transparent Expert System

$$\frac{dI_{F3}^{MT}}{dt} = \underbrace{\tau_{F2}^{MT} I_{F2}^{MT}}_{\text{Progress from F2 during treatment}} + \underbrace{\eta_{F3}^M I_{F3}^M}_{\text{Commenced treatment (F3)}} - \left( \underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\xi}_{\text{Exit rate}} \right) + \underbrace{\lambda_{HIV}}_{\text{Force of HIV infection}} + \underbrace{(1 - \gamma_{F3}^M) \nu_F^M}_{\text{Cease treatment (F3)}} + \underbrace{\gamma_{F3}^M \nu_F^M}_{\text{Viral clearance on treatment (F3)}} + \underbrace{\tau_{F3}^{MT}}_{\text{Progress to F4 during treatment}}$$



- Interpretable
- Transparent
- Intuitive
- Less “cognitive overhead”

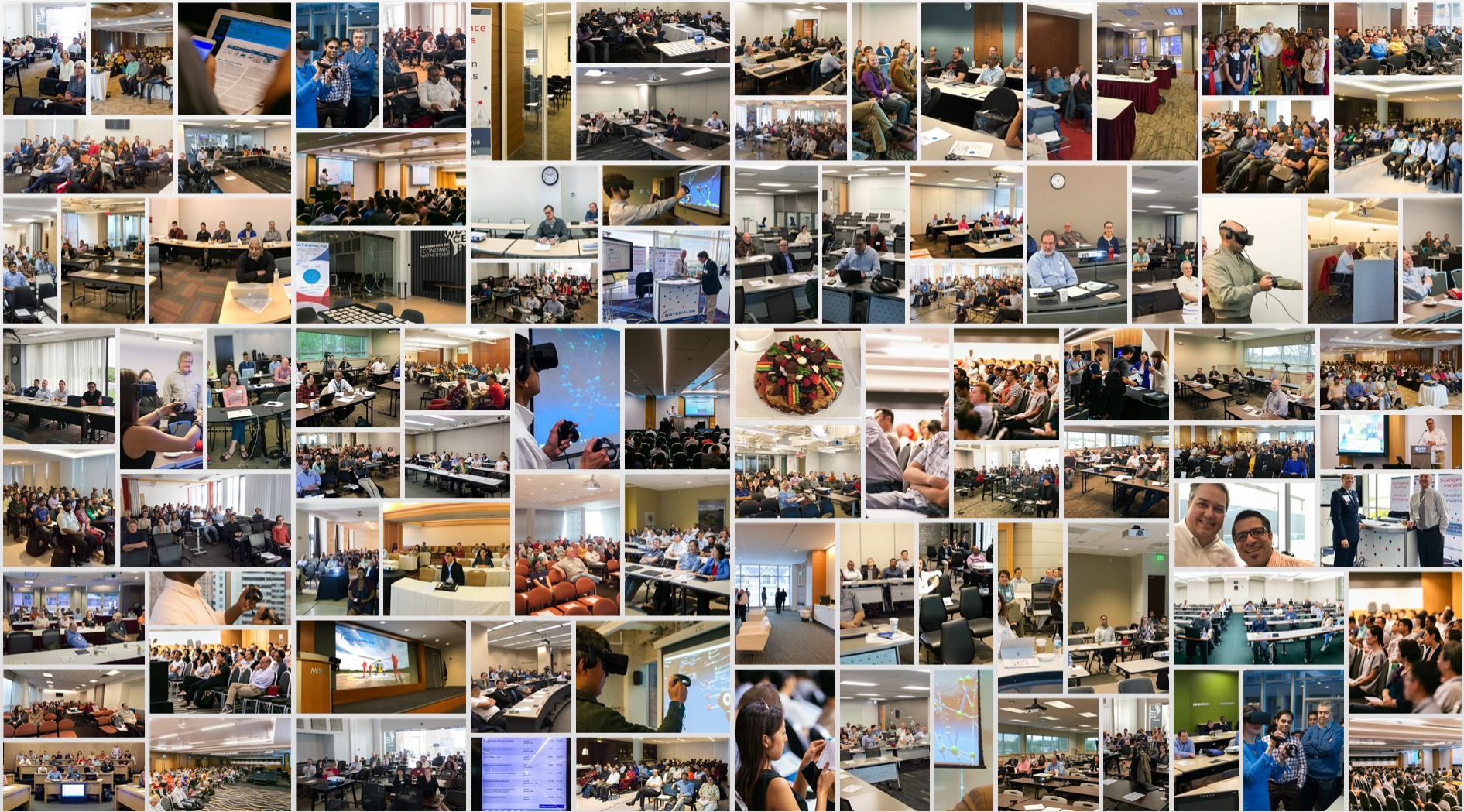
# Bayesian Networks = Transparent Expert System



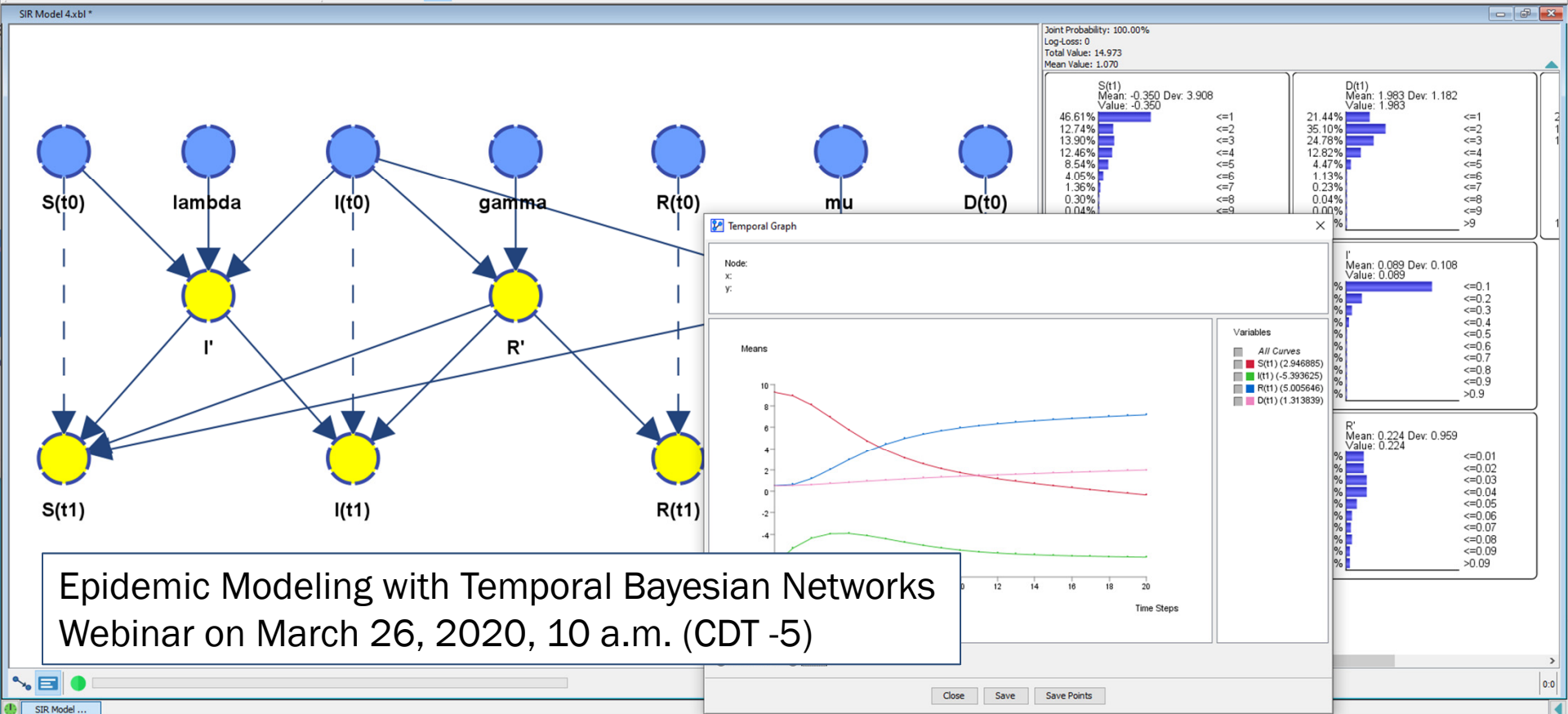
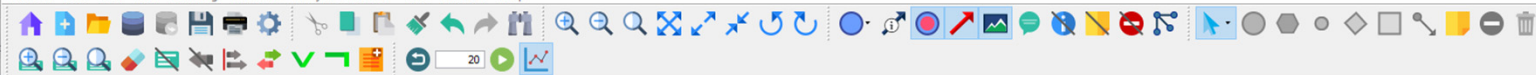


**In Conclusion...**









Epidemic Modeling with Temporal Bayesian Networks  
Webinar on March 26, 2020, 10 a.m. (CDT -5)



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60-Day License to BayesiaLab Education Edition

20+ Hours of Screen/Lecture Recordings

300-Page Training Manual



# Bayesian Networks & BayesiaLab

## A Practical Introduction for Researchers

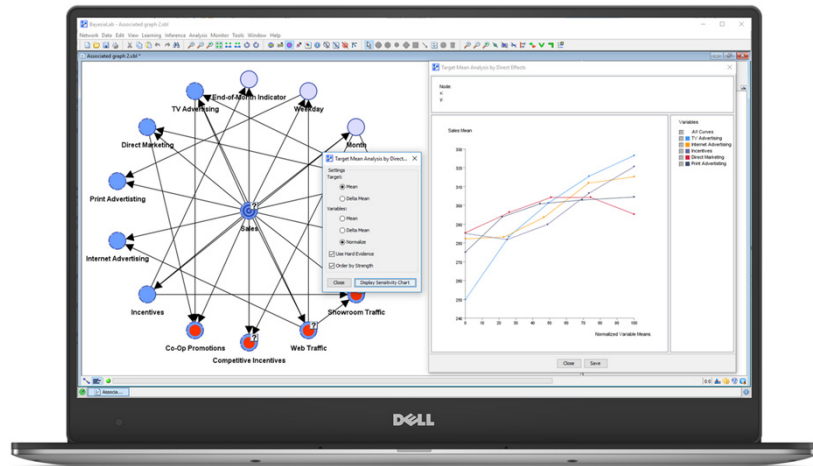
- Free download:  
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# 8th Annual BayesiaLab Conference

ON SCHEDULE



# 8<sup>th</sup> Annual BayesiaLab Conference

**October 8–9, 2020**

The Exchange Tower  
Ivey Donald K. Johnson Centre  
130 King Street West  
Toronto, ON M5X 1K6, Canada

Registration is now open:

[bayesia.com/bayesialab-conference-2020](https://bayesia.com/bayesialab-conference-2020)



# Thank you and be safe!



[stefan.conrady@bayesia.us](mailto:stefan.conrady@bayesia.us)



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