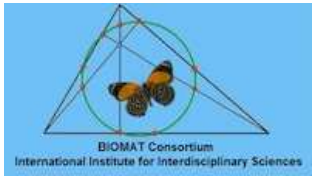

Toronto, November 4 , 2013
04:00 pm – 05:30 pm - 4th Oral Session

MACC
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INSTITUTO NACIONAL DE CIÊNCIA E TECNOLOGIA

A Support System for Diagnosis of Dementia, Alzheimer or Mild Cognitive Impairment

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LABORATÓRIO MÍDIACOM

Introduction

- Population aging has occurred as a **global phenomenon**.
- In 2020, Brazilian population aged 60 years old and over will be **beyond 32 million**.
- In Canada, the number of seniors aged 65 and over **increased 14.1%** between. This rate of growth was **higher than all others** segments (The Canadian Population: Age and Sex – Statistic Canada) .
- **High prevalence of diseases related to aging.**

What Is Dementia?

- **Dementia is a general term** for a decline in **mental ability** severe enough **to interfere with daily life (**Memory loss is an example).

- Dementia symptoms **gradually worsen**.

- **Early** dementia **detection** and **treatment** allows better clinical results.

Alzheimer's and dementia basics

- **Alzheimer's is the most common** type of **dementia (** 60 to 80 % of cases) .

- Others are vascular dementia , front temporal dementia, etc.

- By 2025, the number of elderly people with Alzheimer’s disease is estimated to reach **6.7 millions** .

- Up to 5% of people with the disease have **early onset** of Alzheimer's (it often appears when someone is in 40s or 50s).

Alzheimer's is progressive disease

It is the **sixth** leading cause of **death** in the **United States**.

Those with Alzheimer's live an average of **8 years after symptoms become noticeable**, but survival can range from 4 to 20 years.

Although current Alzheimer's treatments cannot stop progressing, they can temporarily **slow the worsening** of dementia symptoms and **improve quality of life**.

7 Stages of Alzheimer's

Stage 1: No impairment (normal function)

Stage 2: Very mild decline (only the **person** may feel symptoms).

Stage 3: Mild decline (Friends, family or co-workers begin to notice difficulties)

Stage 4: Moderate decline (**medical** interview should be able to detect)

Stage 5: Moderately severe decline (begin to **need help** with day-to-day activities)

Stage 6: Severe decline (**personality changes** may take place and individuals need extensive **help with daily** activities)

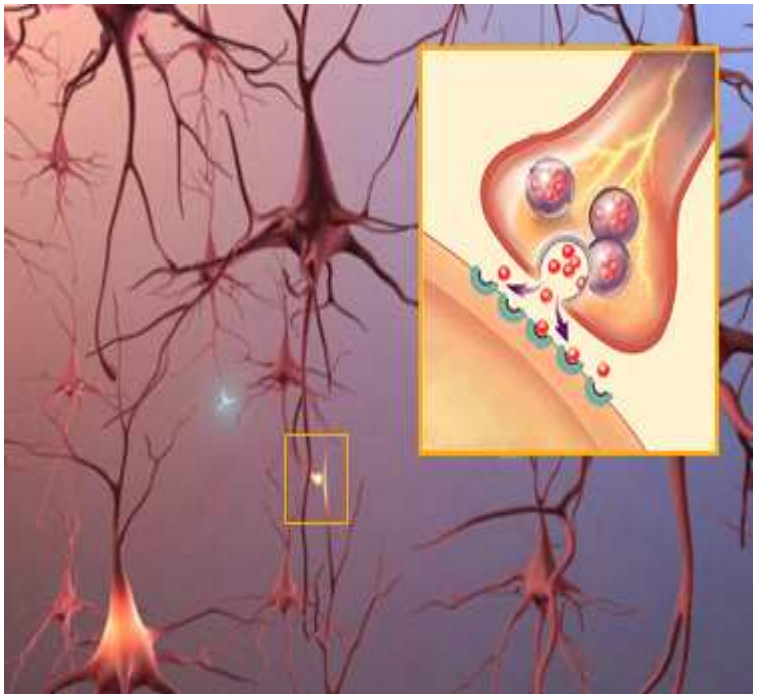
Stage 7: Very severe decline (individuals lose the ability to respond to their environment, to carry on a conversation and, eventually, to control movement, need help with daily personal care, lose the ability to smile, to sit without support and to hold their heads up. Reflexes become abnormal. Muscles grow rigid. Swallowing impaired.)

Neurons are the chief type of cell destroyed by Alzheimer's disease

Signals that form memories and thoughts move **through nerve cell as electric charge**.

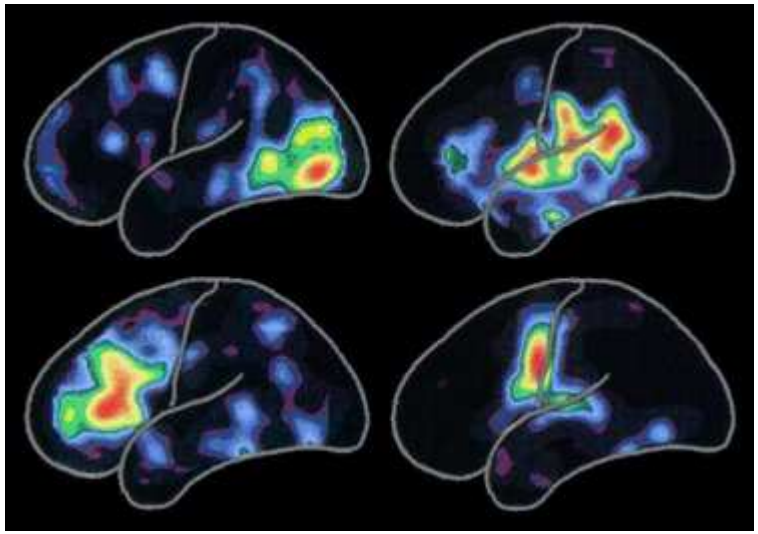
Nerve cells connect to one another at **synapses**. When a charge reaches a synapse, it bursts destroying neurotransmitters.

Alzheimer's disease disrupts both the way electrical charges **travel within cells** and the activity of **neurotransmitters**.



The **positron emission tomography** (PET) scan shows typical patterns of brain activity associated with oxygen and fuel carry by blood.

Reading words



Hearing words

Thinking about words

Saying words

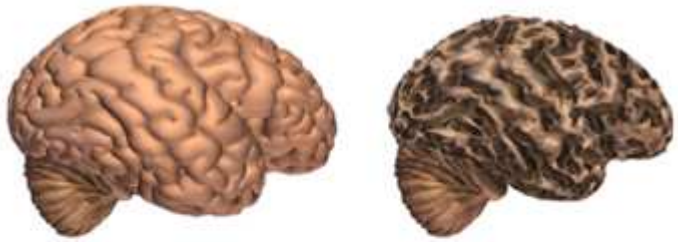
The **normal patterns change** when **Alzheimer's** disease or a related disorder **disrupts nerve cells and their connections .**

Alzheimer's disease leads to nerve cell death and tissue loss throughout the brain.

- Over time, the brain **shrinks** dramatically, affecting nearly **all its functions**

A brain with advanced Alzheimer's

A normal brain

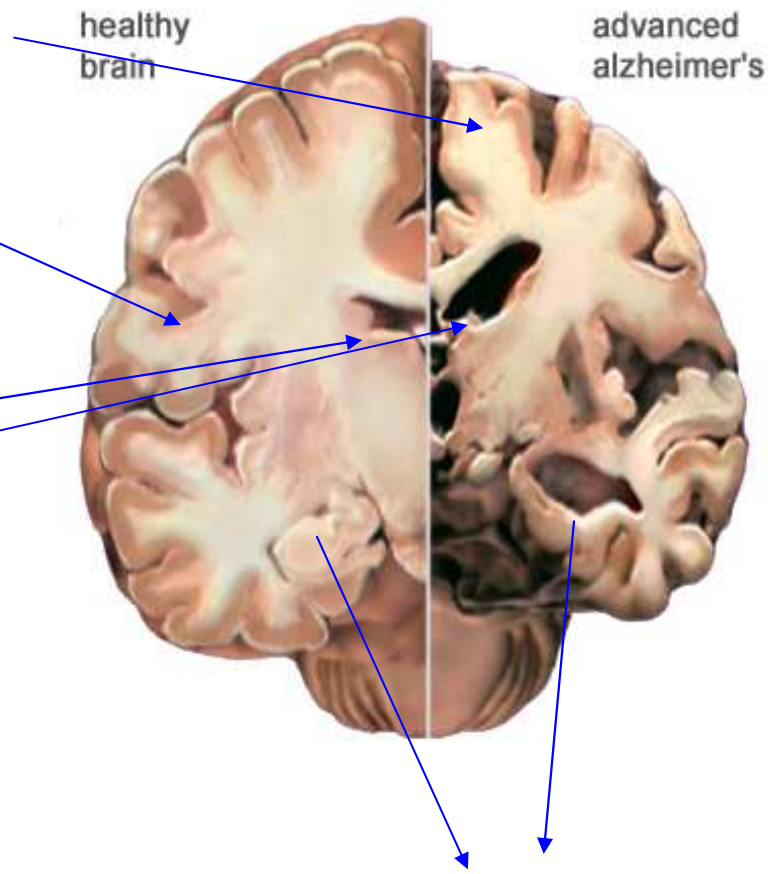


two brains merged

Alzheimer's brain:

The **cortex shrivels up**, damaging areas involved in **thinking, planning and remembering**.

Ventricles (fluid-filled spaces within the brain) grow larger.



Shrinkage is especially severe in the **hippocampus** (an area of the cortex that plays a key role in formation of **new memories**)

What **causes** cell death and tissue loss in the Alzheimer's brain are **yet not well known**, but plaques and tangles are prime suspects.

Alzheimer's tissue has fewer nerve cells and synapses than a healthy brain.

Plaques, abnormal clusters of protein fragments, build up between nerve cells.

Dead and dying nerve cells contain *tangles,* which are made up of twisted strands of proteins.

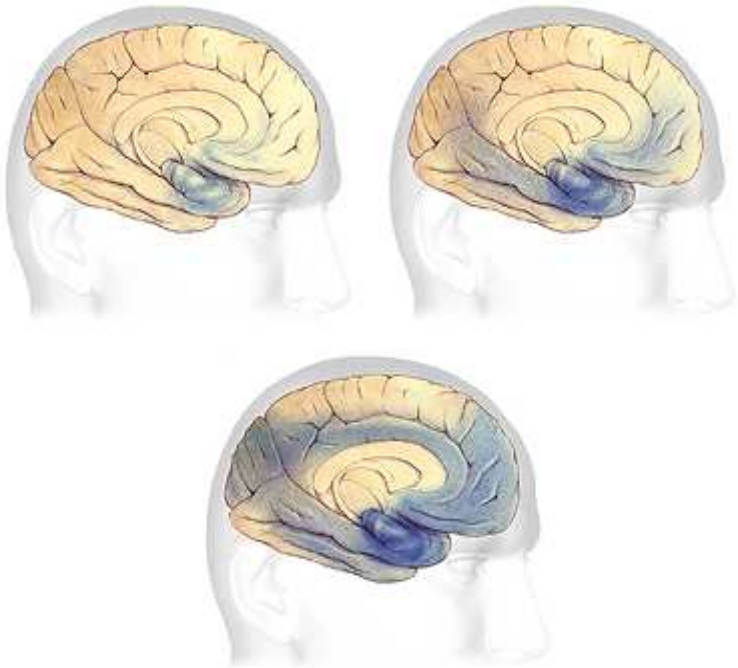
Plaques and tangles tend to spread through the cortex as Alzheimer's disease progresses.

The rate of progression varies greatly.

The course of the disease depends in part on age at diagnosis (+ treatments) and whether a person has other health conditions.

Earliest Alzheimer's - 20 years or more before diagnosis.

Mild to moderate Alzheimer's stages



Severe Alzheimer's

Definition

- Clinical Decision Support Systems (CDSS) are interactive Computer software designed to assist health professionals in determining diagnosis from all of patient data at the point of care.

- In CDSS, characteristics of individual patients are matched to a knowledge base and an algorithm generates patient-specific assessments and recommendations.

Objective

- This work describes a CDSS for diagnosis of dementia and related disorder (as Alzheimer's Disease - AD and Mild Cognitive Impairment – MCI).

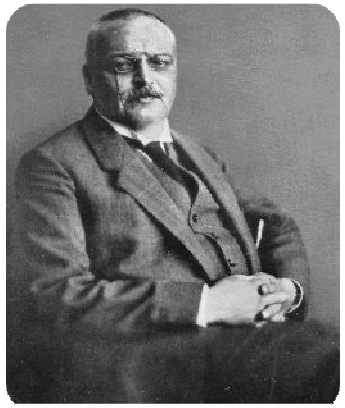
- Proper disease identification;
- Prevention of diagnostic error and diagnostic error rate;
- Delay in detection; and
- Improvement of clinical decision.

Importance

- The most commonly used criteria for diagnoses were established by DSM-IV (Diagnostic and Statistical Manual for Mental Disorders 4th edition) published by American Psychiatric Association

- For such diseases **there is no single test to prove a person has Alzheimer's or other types of dementia.** Diagnosing these requires careful medical evaluation, including:
  - Medical history (physician)
  - Mental status tests (psychology)
  - A physical and neurological exam (medical doctors)
  - Clinics and Laboratorial tests (such as blood tests and brain imaging) to rule out other causes of dementia-like symptoms.

Alois Alzheimer (1864–1915)



Former works:

- 1984: MCKHANN, G. *et al. Clinical diagnosis of Alzheimer's disease: Report of the* NINCDS-ADRDA (*National Institute of Neurological and Communicative Disorders and Stroke - Alzheimer's Disease and Related Disorders Association*).

- 2007: DUBOIS, B. *et al. Research criteria for the diagnosis of Alzheimer's Disease: revising the* NINCDS-ADRDA *criteria*.

- 2011: MCKHANN, G. M. *et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup.*

Some criteria used for diagnosis

Dementia AD MCI

- Decrease cognitive activities
- Smelling deficiency
- Difficulties with new information
- Difficulties with complex work
- Difficulties with space and visual recognitions
- Difficulties with remembering names
- Behavior changes
- Neuropsychological tests
- Alteration of the biomarkers
- **Hippocampus atrophy**
- History of AD in relatives

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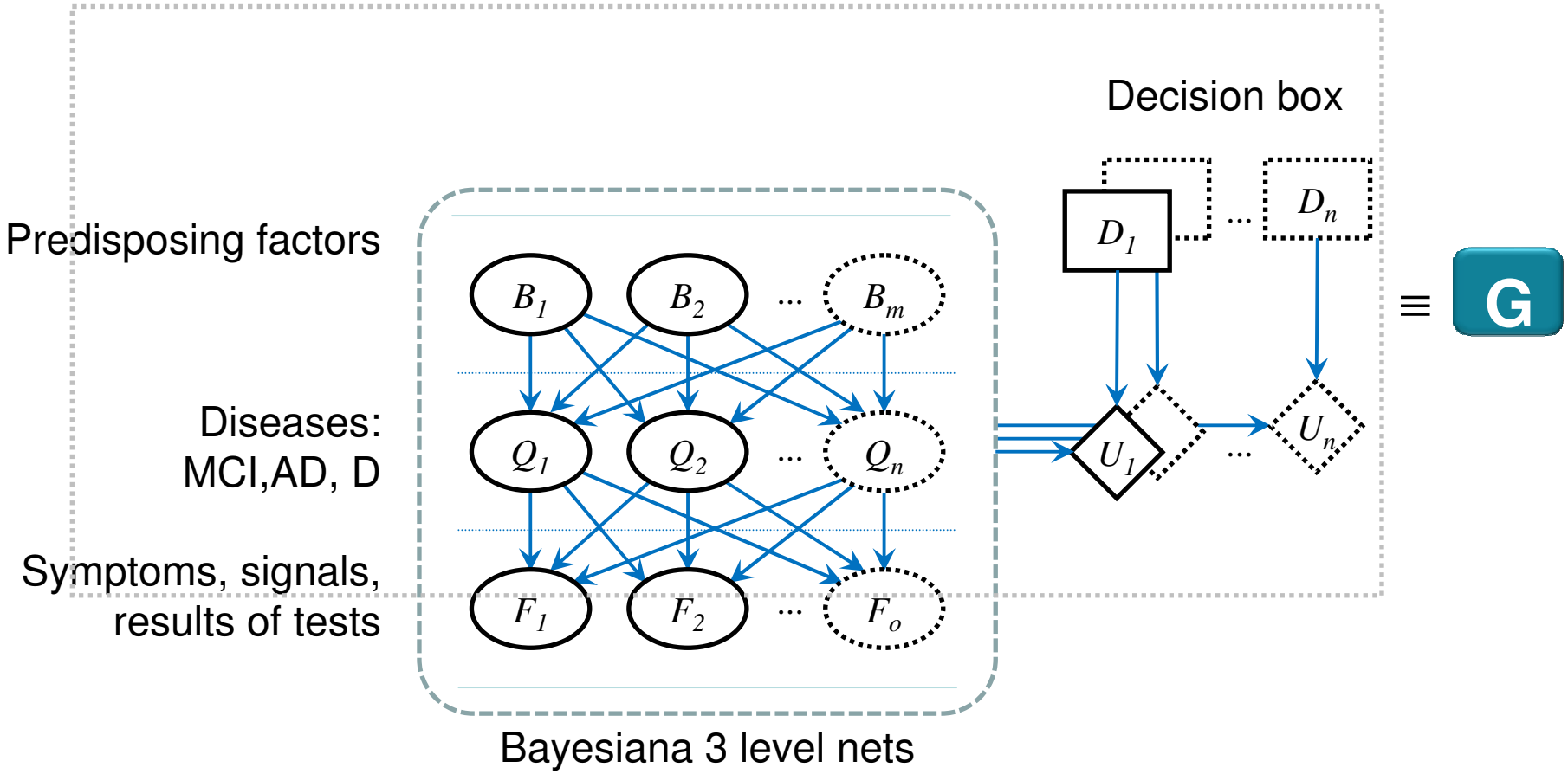
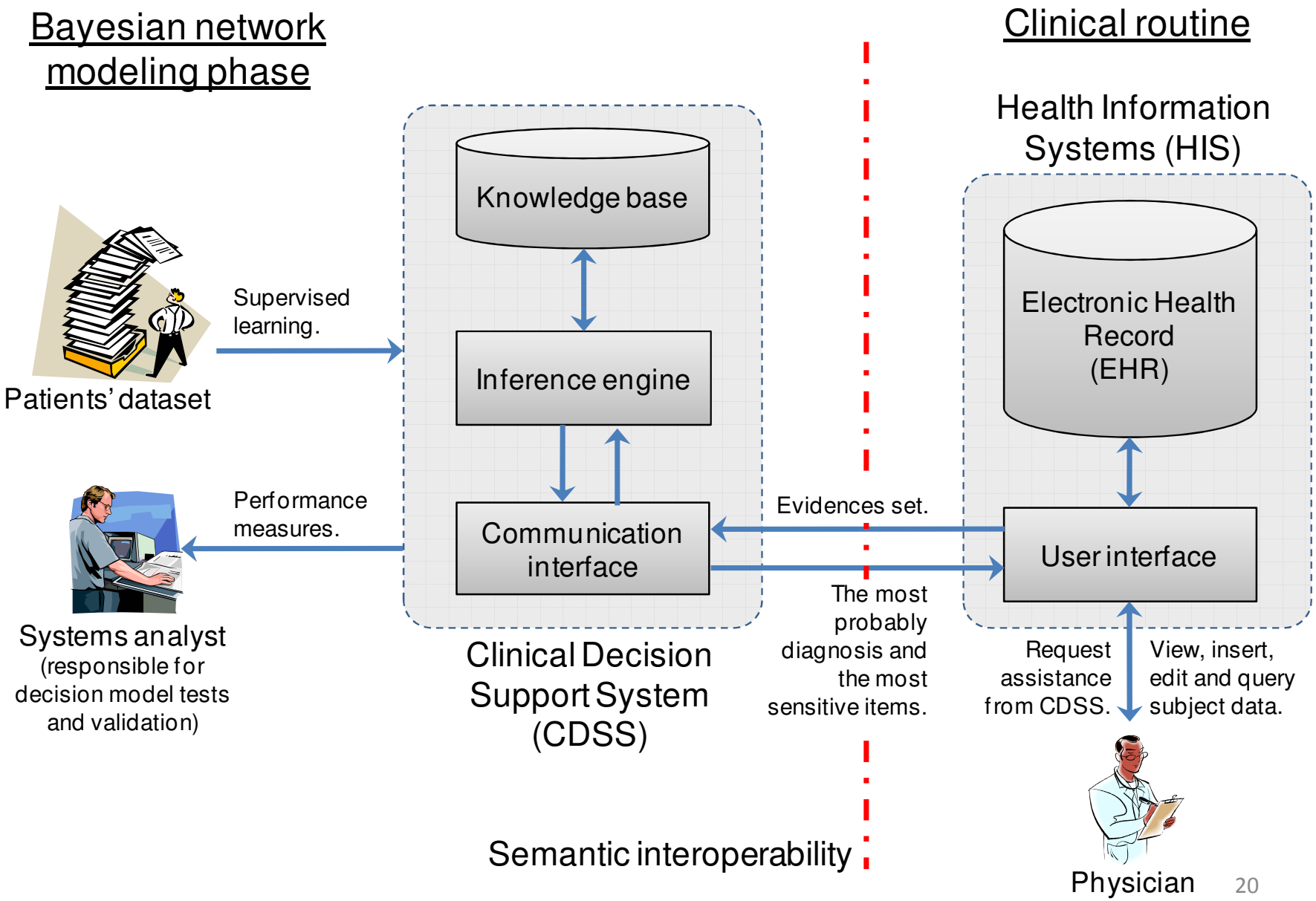
Clinical Decision Support System

- The decision theoretic model was built on a **Bayesian network using a data-driven approach.**
- The Bayesian network structure was built with **the support of a disease domain expert** and a three-level generic structure.
- Probability distribution was estimated using a **supervised learning method and a training base containing real patient cases and normal controls.**
- The **training attributes** are composed of predisposal factors, **neuropsychiatry tests**, patient data, **symptoms** and **signs**.

Used Bayesian network



Clinical Decision Support System components



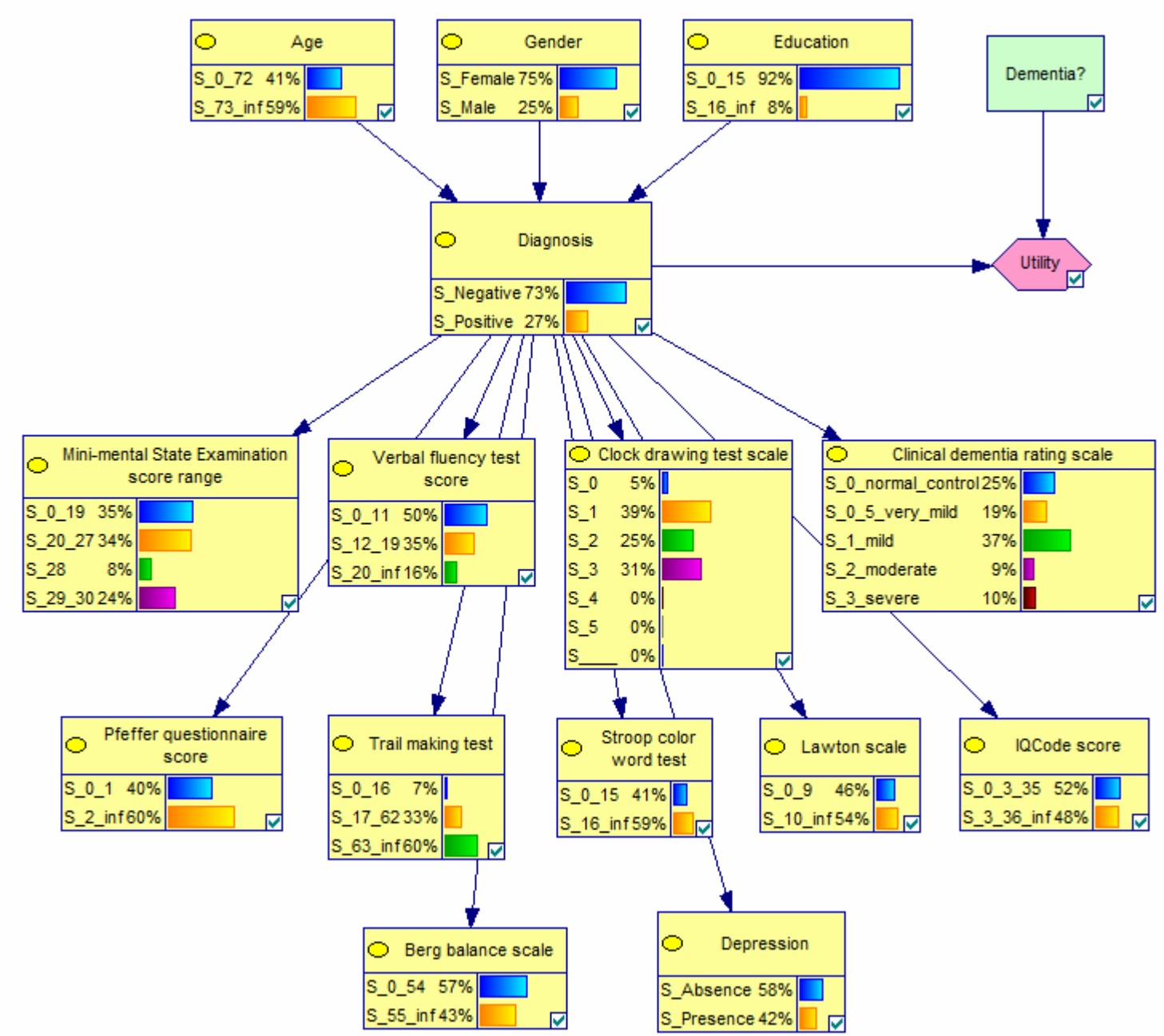
The training database

- Real clinical cases of patients and normal controls from:
  - Duke University Medical Center (USA)

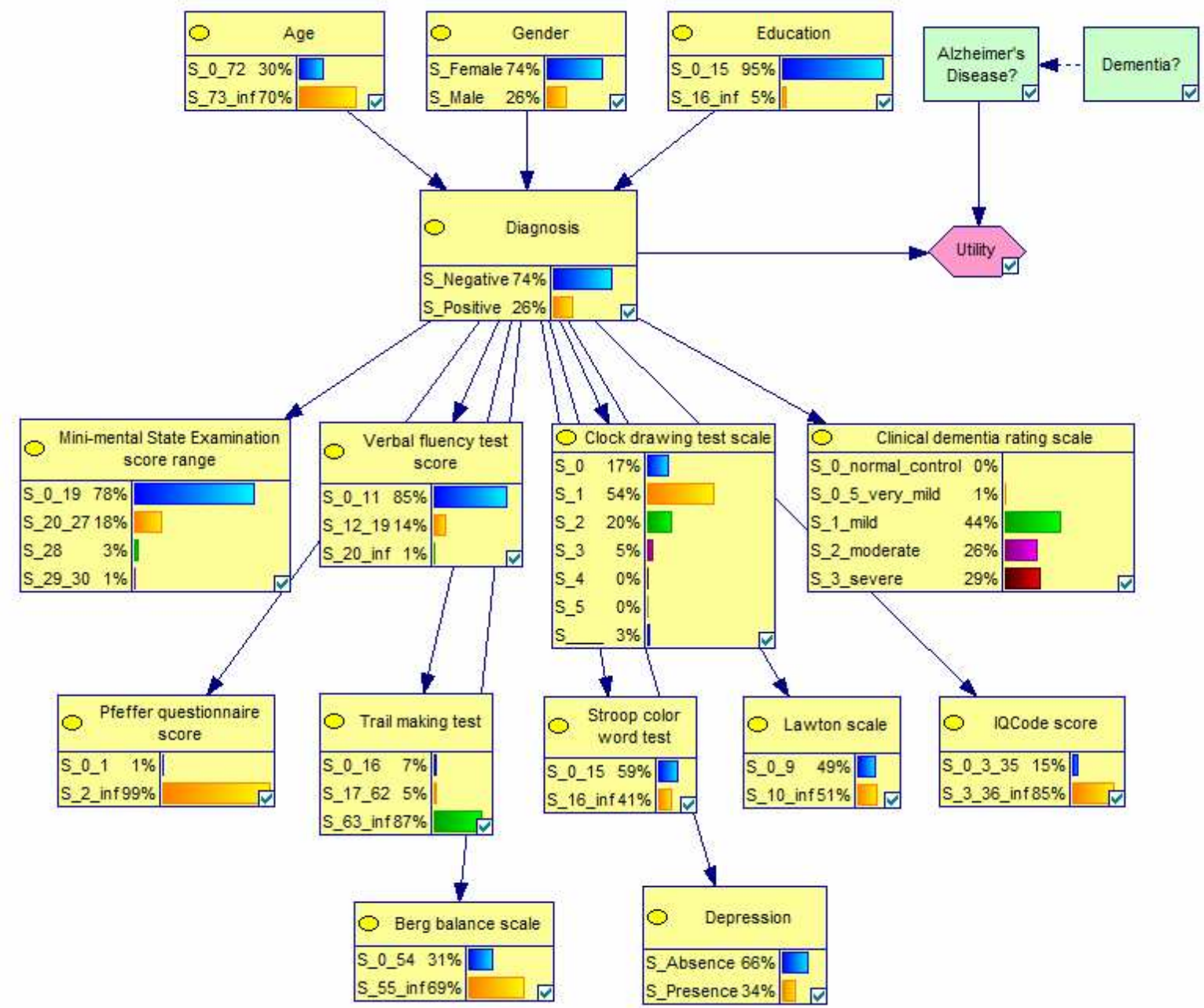
    +
  - Center for Alzheimer Disease and Related Disorder, Institute of Psychiatric of Federal University of Rio de Janeiro (Rio de Janeiro, Brazil).

Approval of the “Comissão Nacional de Ética em Pesquisa” Brazilian Ministry of Health nº 284/2010.

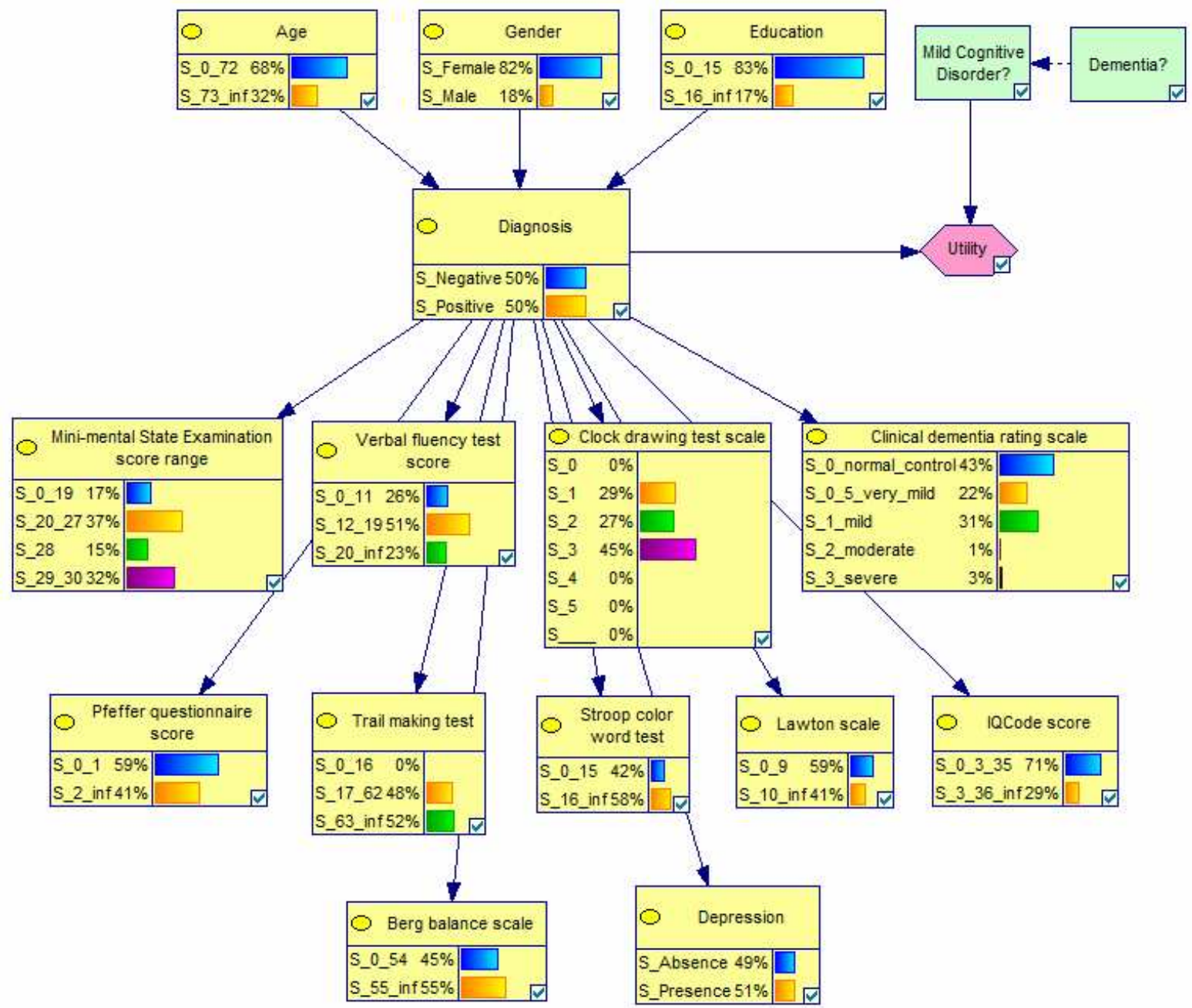
Bayesian network for diagnosis of Dementia



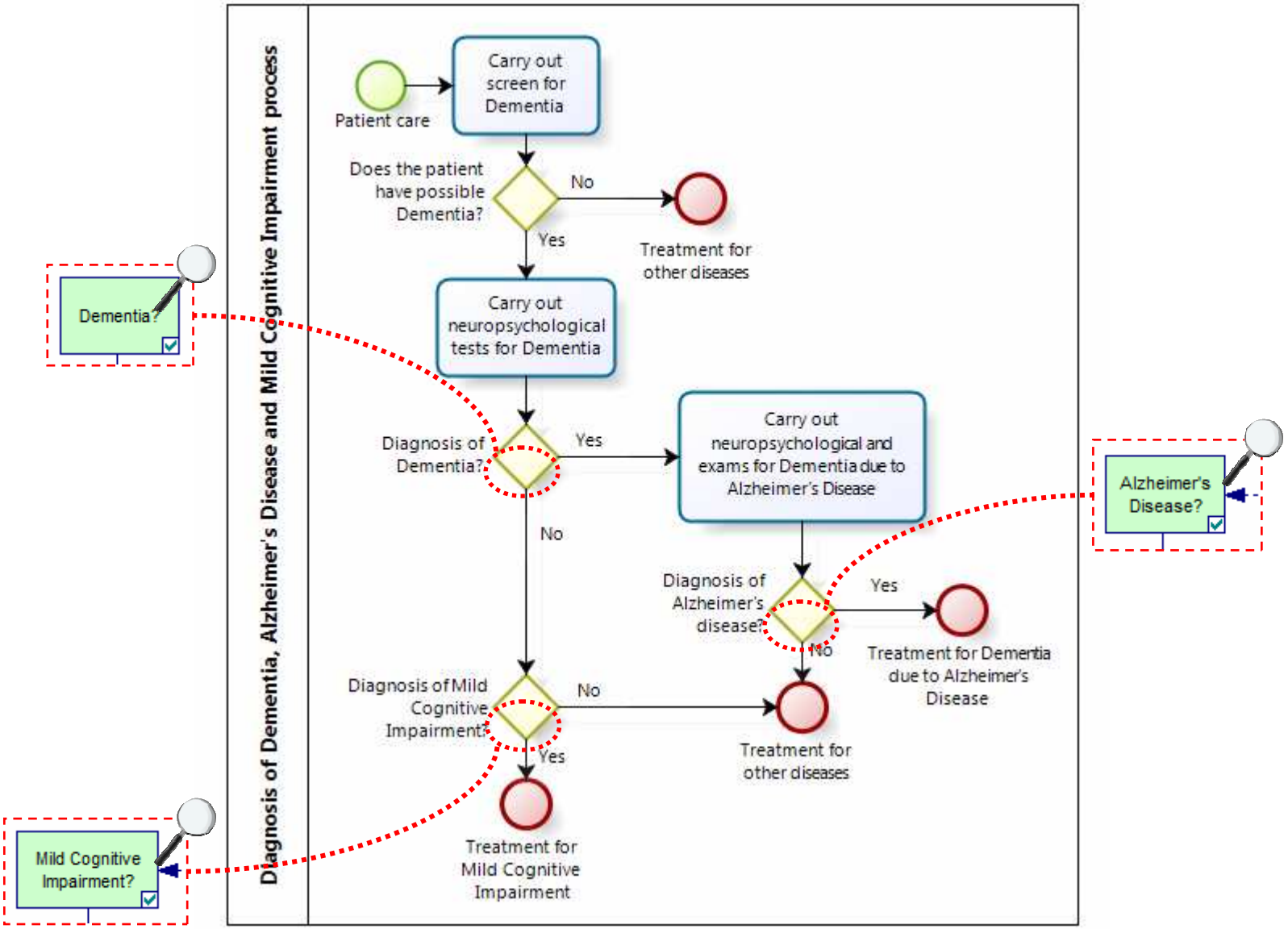
Bayesian network for diagnosis of Alzheimer's Disease

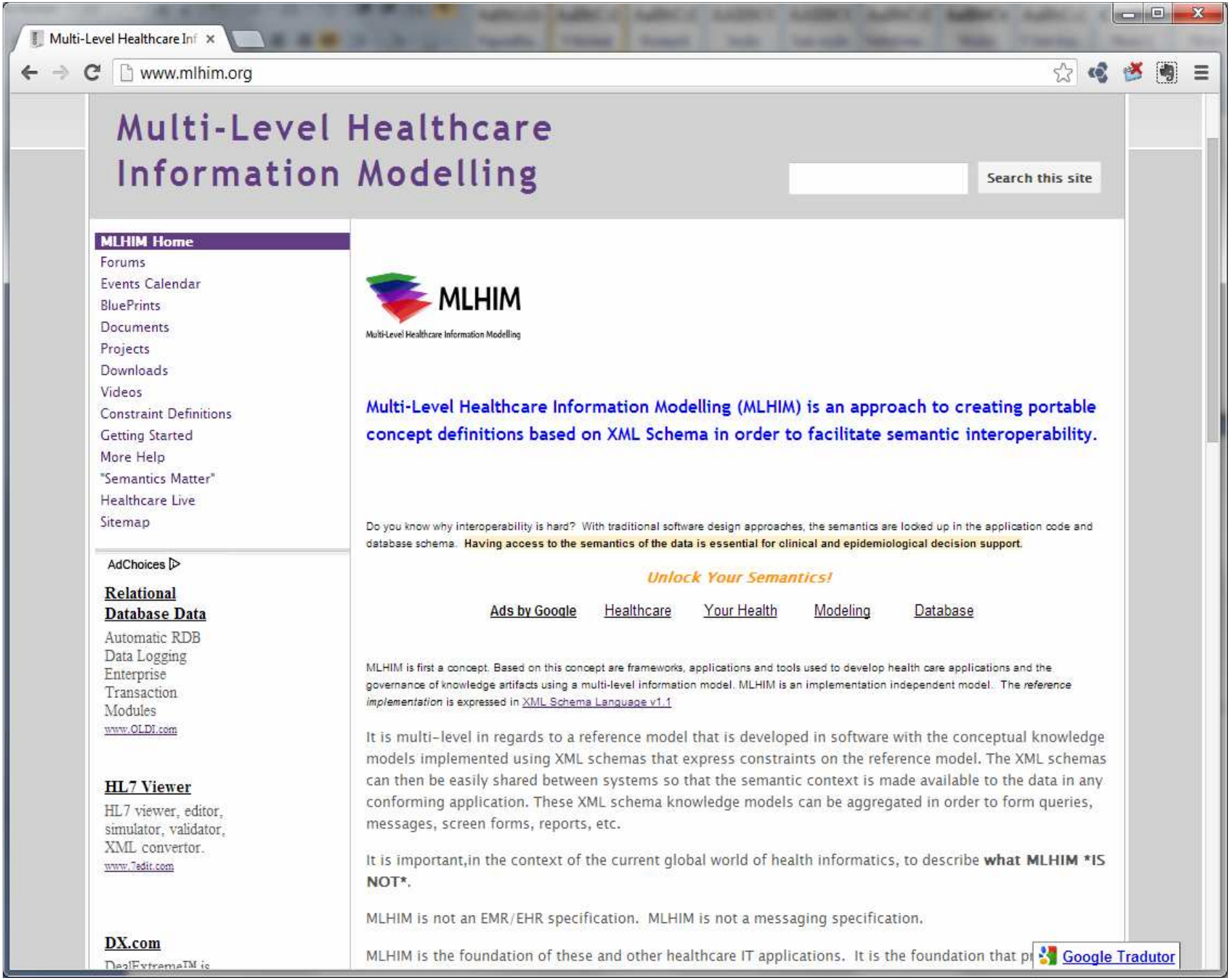


Bayesian network for diagnosis of Mild Cognitive Impairment

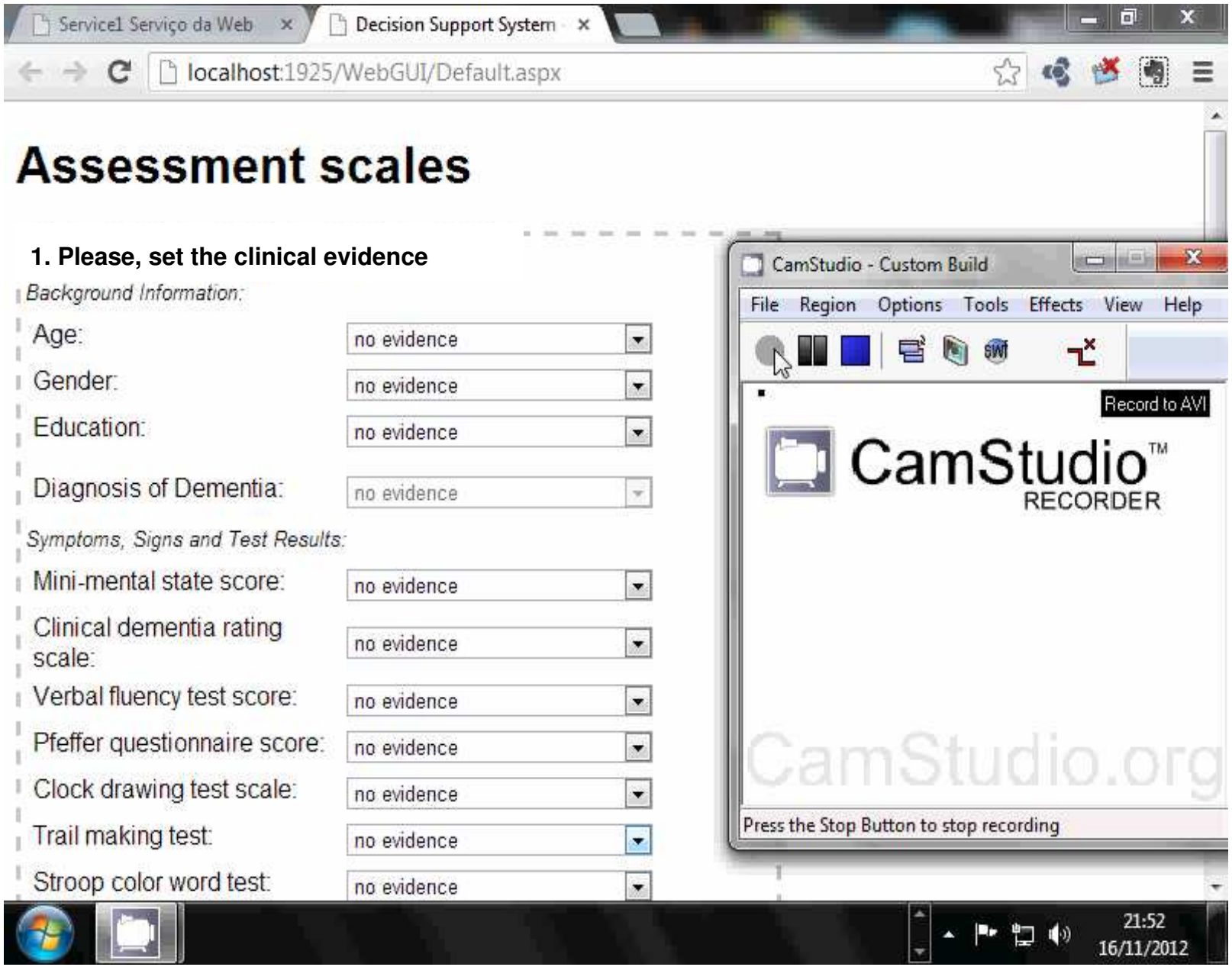


Relationship between decision points considering diagnostic process

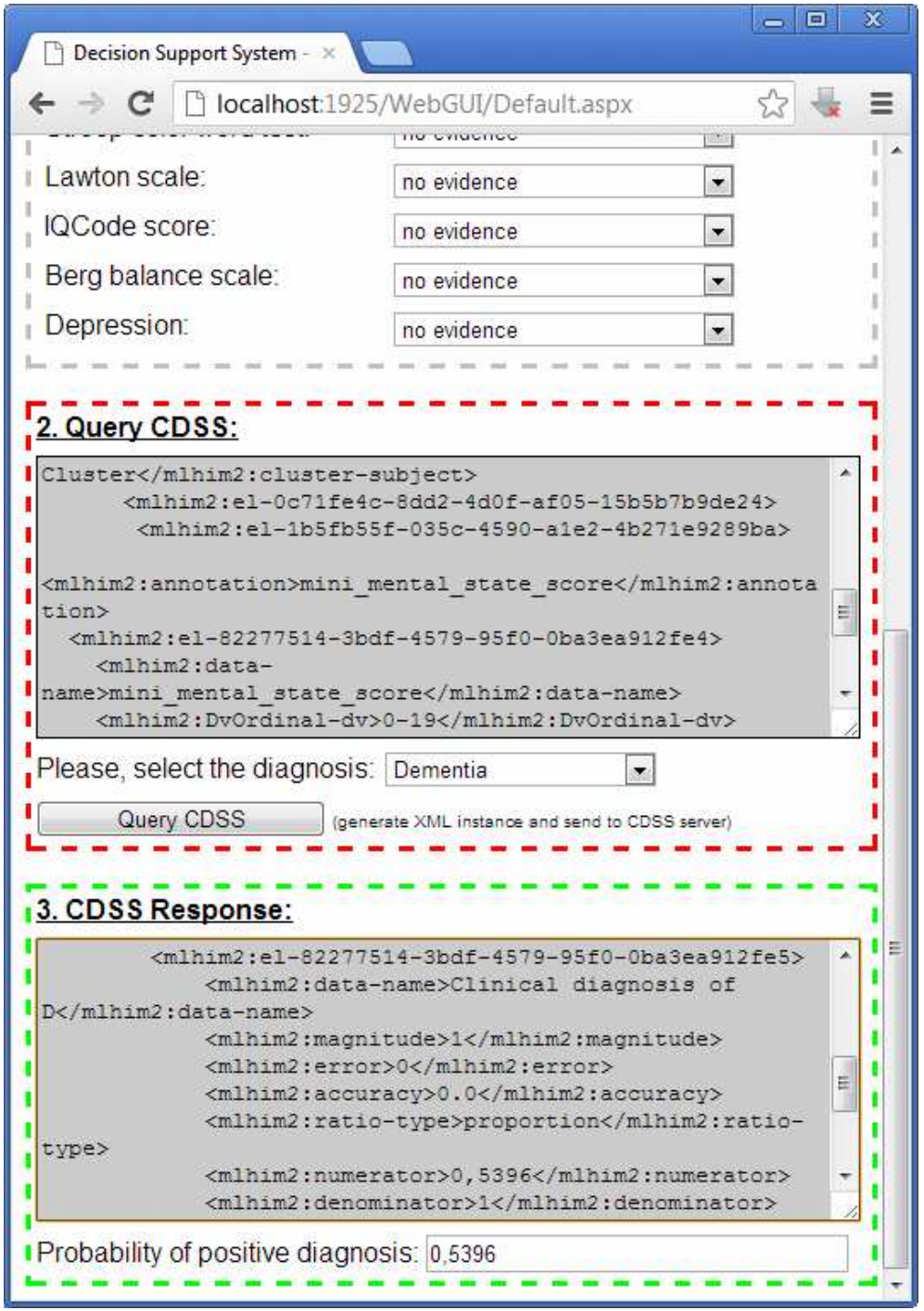



Multi-Level Healthcare Inf
www.mlhim.org
Multi-Level Healthcare Information Modelling
Search this site
MLHIM Home
Forums
Events Calendar
BluePrints
Documents
Projects
Downloads
Videos
Constraint Definitions
Getting Started
More Help
"Semantics Matter"
Healthcare Live
Sitemap
AdChoices
Relational Database Data
Automatic RDB Data Logging Enterprise Transaction Modules
www.OLDI.com
HL7 Viewer
HL7 viewer, editor, simulator, validator, XML convertor.
www.7edit.com
DX.com
MLHIM
Multi-Level Healthcare Information Modelling
Multi-Level Healthcare Information Modelling (MLHIM) is an approach to creating portable concept definitions based on XML Schema in order to facilitate semantic interoperability.
Do you know why interoperability is hard? With traditional software design approaches, the semantics are locked up in the application code and database schema. Having access to the semantics of the data is essential for clinical and epidemiological decision support.
Unlock Your Semantics!
Ads by Google
Healthcare
Your Health
Modeling
Database
MLHIM is first a concept. Based on this concept are frameworks, applications and tools used to develop health care applications and the governance of knowledge artifacts using a multi-level information model. MLHIM is an implementation independent model. The reference implementation is expressed in XML Schema Language v1.1
It is multi-level in regards to a reference model that is developed in software with the conceptual knowledge models implemented using XML schemas that express constraints on the reference model. The XML schemas can then be easily shared between systems so that the semantic context is made available to the data in any conforming application. These XML schema knowledge models can be aggregated in order to form queries, messages, screen forms, reports, etc.
It is important,in the context of the current global world of health informatics, to describe what MLHIM *IS NOT*.
MLHIM is not an EMR/EHR specification. MLHIM is not a messaging specification.
MLHIM is the foundation of these and other healthcare IT applications. It is the foundation that p
Google Tradutor

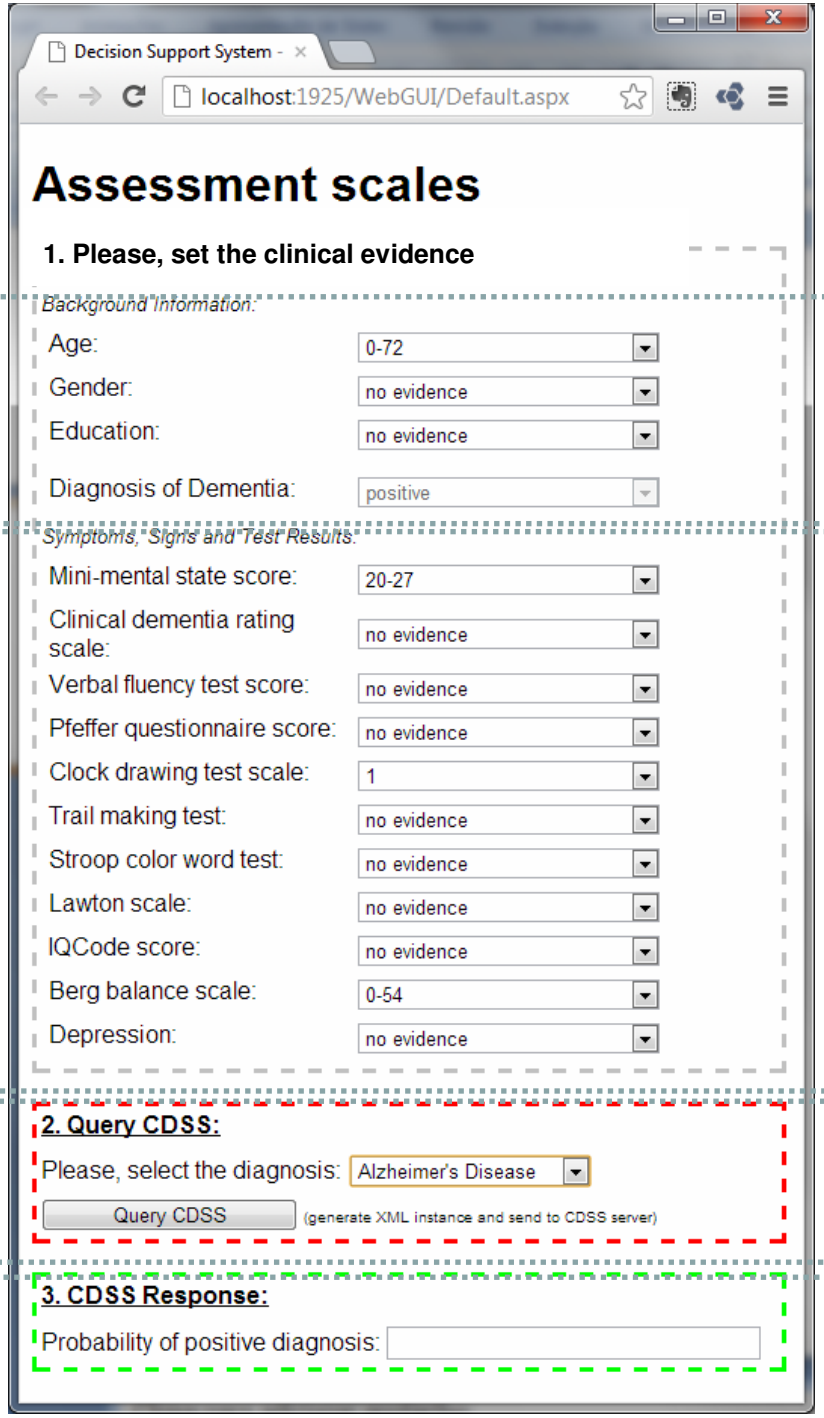
Interface


Service1 Serviço da Web
Decision Support System
localhost:1925/WebGUI/Default.aspx
Assessment scales
1. Please, set the clinical evidence
Background Information:
Age:
Gender:
Education:
Diagnosis of Dementia:
Symptoms, Signs and Test Results:
Mini-mental state score:
Clinical dementia rating scale:
Verbal fluency test score:
Pfeffer questionnaire score:
Clock drawing test scale:
Trail making test:
Stroop color word test:
no evidence
CamStudio - Custom Build
File Region Options Tools Effects View Help
Record to AVI
CamStudio™
RECORDER
CamStudio.org
Press the Stop Button to stop recording
21:52
16/11/2012

Interface


Decision Support System -
localhost:1925/WebGUI/Default.aspx
Lawton scale:
no evidence
IQCode score:
no evidence
Berg balance scale:
no evidence
Depression:
no evidence
2. Query CDSS:
Cluster</mlhim2:cluster-subject>
<mlhim2:el-0c71fe4c-8dd2-4d0f-af05-15b5b7b9de24>
<mlhim2:el-1b5fb55f-035c-4590-a1e2-4b271e9289ba>
<mlhim2:annotation>mini_mental_state_score</mlhim2:annotation>
<mlhim2:el-82277514-3bdf-4579-95f0-0ba3ea912fe4>
<mlhim2:data-name>mini_mental_state_score</mlhim2:data-name>
<mlhim2:DvOrdinal-dv>0-19</mlhim2:DvOrdinal-dv>
Please, select the diagnosis:
Dementia
Query CDSS
(generate XML instance and send to CDSS server)
3. CDSS Response:
<mlhim2:el-82277514-3bdf-4579-95f0-0ba3ea912fe5>
<mlhim2:data-name>Clinical diagnosis of D</mlhim2:data-name>
<mlhim2:magnitude>1</mlhim2:magnitude>
<mlhim2:error>0</mlhim2:error>
<mlhim2:accuracy>0.0</mlhim2:accuracy>
<mlhim2:ratio-type>proportion</mlhim2:ratio-type>
<mlhim2:numerator>0,5396</mlhim2:numerator>
<mlhim2:denominator>1</mlhim2:denominator>
Probability of positive diagnosis:
0,5396

Interface



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2

3

4

- Selection of factor for the patient.
- Selection of symptoms, signals, and results of tests
- Selection of diseases
- Results

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Considerations:

- ***TP:*** *Disease patients correctly classified as diseased;*
- ***TN:*** *Healthy patients correctly identified as diseased;*
- ***FP:*** *Healthy patients incorrectly classified as healthy;*
- ***FN:*** *Disease patients incorrectly identified as healthy.*

- **Sensitivity:** *measures the proportion of positive cases which are correctly identified as positive;*
- **Specificity:** *measures the proportion of negative cases which are correctly identified as negative;*
- **Accuracy:** percentage of correct classification.

- **Area under Receiver Operating Characteristic** - ROC **curve : Sensitivity x (1- Specificity)**
- *F1* measure

Cont.

$$\textit{Sensibility or True Positive Ratio: } TPR = \frac{TP}{TP + FN}$$

$$\textit{Specificity or True Negative Ratio : } TNR = \frac{TN}{TN + FP}$$

$$\textit{Precision : } TP = \frac{TP}{TP + FP}$$

$$F_1 = 2 \cdot \frac{Precision \cdot Recall}{Precision + Recall}$$

$$MSE = \frac{1}{n} \sum_{i=1}^{n} [y_i - P(x = 1)]^2$$

$$MXE = \frac{1}{n} \sum_{i=1}^{n} - y_i \cdot \log[P(x = 1)] - (1 - y_i) \cdot \log[1 - P(x = 1)]$$

Results: Dementia

Performance measures and results obtained for each fold considering the proposed Bayesian network for Dementia (D)

Fold	AUC	F_1	TPR	TNR	TP	FP	TN	FN	MSE	MXE
1	0.93	0.89	0.91	0.63	41	6	10	4	0.11	0.20
2	0.94	0.93	0.93	0.82	42	3	14	3	0.09	0.18
3	0.91	0.94	0.98	0.71	44	5	12	1	0.09	0.21
4	0.89	0.89	0.89	0.71	40	5	12	5	0.15	0.32
Av (St)	**0.92 (0.02)**	**0.91 (0.03)**	**0.93 (0.04)**	**0.72 (0.08)**	-	-	-	-	**0.11 (0.03)**	**0.23 (0.06)**

[b] Av (St) = average (standard deviation).Fold = sub set used for Cross Validation. AUC = area under ROC (Receiver Operating Characteristics), Best result = 1.F_1 Best result = 1. TPR = Best result =1. TNR Best result = 1. MSE Best result = 0 (zero). MXE Best result = 0 (zero).

Results: AD

Performance measures and results obtained for each fold considering the proposed Bayesian network for Alzheimer's disease (AD)

Fold	AUC	F_1	TPR	TNR	TP	FP	TN	FN	MSE	MXE
1	0.74	0.82	0.88	0.18	30	9	2	4	0.16	0.21
2	0.77	0.86	0.94	0.27	32	8	3	2	0.15	0.20
3	0.88	0.85	0.97	0.17	32	10	2	1	0.14	0.17
4	0.80	0.86	0.97	0.09	33	10	1	1	0.15	0.22
Av (St)	**0.80 (0.06)**	**0.85 (0.02)**	**0.94 (0.04)**	**0.18 (0.07)**	-	-	-	-	**0.15 (0.01)**	**0.20 (0.02)**

[b] Av (St) = average (standard deviation).Fold = sub set used for Cross Validation. AUC = area under ROC (Receiver Operating Characteristics), Best result = 1.F_1 Best result = 1. TPR = Best result =1. TNR Best result = 1. MSE Best result = 0 (zero). MXE Best result = 0 (zero).

Results : MCI

Performance measures and results obtained for each fold considering the proposed Bayesian network for mild cognitive impairment (MCI) [b].

Fold	AUC	F_1	TPR	TNR	TP	FP	TN	FN	MSE	MXE
1	1.00	0.94	1.00	0.89	8	1	8	0	0.04	0.04
2	0.95	0.77	0.63	1.00	5	0	8	3	0.19	0.57
3	1.00	0.84	1.00	0.73	8	3	6	0	0.08	0.09
4	0.96	0.94	1.00	0.89	8	1	8	0	0.06	0.26
Av (St)	**0.98 (0.03)**	**0.87 (0.08)**	**0.91 (0.19)**	**0.86 (0.14)**	**-**	**-**	**-**	**-**	**0.09 (0.07)**	**0.24 (0.2)**

[b] Av (St) = average (standard deviation).Fold = sub set used for Cross Validation. AUC = area under ROC (Receiver Operating Characteristics), Best result = 1.F_1 Best result = 1. TPR = Best result =1. TNR Best result = 1. MSE Best result = 0 (zero). MXE Best result = 0 (zero).

Final remarks

- We have constructed the structure of Bayesian network, data-driven base of clinical cases.
- The patients are assisted by Center for Treatment of Alzheimer's (CDA), Federal University of Rio de Janeiro (UFRJ).
- The clinical concepts of Bayesian network are modeled using MLHIM (Multilevel Healthcare Information Model).
- The decision model is represented by a graphical diagram, which facilitates its ongoing review.
- Modeling of a network decision based on Bayesian network and influence diagram is feasible and consistent.

- As future work, we intend to improve the database of clinical cases.

Thank you!

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www.ic.uff.br/~aconci