<table>
<thead>
<tr>
<th><strong>Stefan Sabutsch</strong></th>
<th><strong>Klaus-Peter Adlassnig</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>ELGA GmbH und Präsidet von HL7 Austria</td>
<td>Medizinische Universität Wien und Medexter Healthcare GmbH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Karsten Fehre</strong></th>
<th><strong>Michael Binder</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medexter Healthcare GmbH</td>
<td>Medizinische Universität Wien</td>
</tr>
</tbody>
</table>
Inhalt

• Begrüßung (Sabutsch)

• HL7 und Standards (Sabutsch)

• Klinische Entscheidungsunterstützung (Adlassnig)

• Arden-Syntax und ArdenML (Fehre)

• Anwendungen (Adlassnig)

• Klinische Perspektiven (Binder)

• Verantwortung und Medizinprodukt (Adlassnig)
HL7 - global interoperability standards

- HL7 provides standards for interoperability
  - improve care delivery, optimize workflow, reduce ambiguity and enhance knowledge transfer

- HL7 Standards
  - Version 2.x messaging standard
  - Version 3: specifications based on HL7’s Reference Information Model (RIM)
    - for messaging and documents
  - CDA® (Clinical Document Architecture): a V3 based document markup standard that specifies the structure and semantics of "clinical documents" → CDA implementation guides
  - Vocabulary Standards
  - CTS2 (Common Terminology Services) – services for accessing and managing terminological content
  - ARDEN Syntax
  - ... 

- HL7 Base Standards are licensed – but that license is free (“license at no cost”)


About HL7

• **Health Level Seven International** (HL7), founded in 1987
  • a not-for-profit, ANSI-accredited standards developing organization in healthcare-IT
  • collaborates with other SDO like ISO, DICOM, IHTSDO, IHE, ...
  • headquarter: USA (Ann Arbor, MI)
  • >2.300 members (healthcare providers, government agencies, vendor community, ...)
  • 34 affiliate organizations around the world (18 in Europe)

• **HL7 Austria**
  • Founded in 2007
  • Activities: information source, support, ballots (eg. CDA IG), e-Learning, courses, meetings/conferences, “Austrian interoperability forum”
  • [www.hl7.at](http://www.hl7.at) Twitter [https://twitter.com/HL7_Austria](https://twitter.com/HL7_Austria)
ELGA & Decision Support

• ELGA has (momentary) no decision support mechanisms, but…

• ELGA gives access to a collection of relevant and highly structured and semantic interoperable healthcare documents (HL7 CDA Rel. 2)

• ELGA provides supplemental standardized information for a patient → Local EHR can be completed with downloaded information from ELGA

• The aggregated data pool (local EHR+ELGA) may be used for clinical decision support!
  • Example: ELGA medications, discharge diagnoses, lab results, …
HL7 activities toward clinical decision support standards

- Arden Syntax for Medical Logic Systems, Version 2.10 (May, 2014)
- HL7 Version 3 Standard: Virtual Medical Record for Clinical Decision Support (vMR-CDS) Logical Model, Release 2 (January 2014)
- ...

http://www.hl7.org/implement/standards/index.cfm?ref=nav
Arden Syntax and Health Level Seven (HL7)

- A standard language for writing situation-action rules that can trigger alerts based on abnormal clinical events detected by a clinical information system.

- Each module, referred to as a medical logic module (MLM), contains sufficient knowledge to make a single decision.
  - extended by packages of MLMs for complex clinical decision support

- The Health Level Seven Arden Syntax for Medical Logic Systems, Version 2.9— including fuzzy methodologies—was approved by the American National Standards Institute (ANSI) and by Health Level Seven International (HL7) on 14 March 2013

- Version 2.10---including ArdenML, an XML-based representation of Arden Syntax MLMs---was approved on 6 May 2014
  - continuous development since 1989
**General MLM Layout**
- Maintenance Category
- Library Category
- Knowledge Category
- Resources Category

**Identify an MLM**
**Data Types**

**Operators**
- Basic Operators
- Curly Braces
- List Operators
- Logical Operators
- Comparison Operators
- String Operators
- Arithmetic Operators
- Other Operators

**Control Statements**

**Call/Write Statements and Trigger**
Sample MLM (excerpt)

```plaintext
logic:
  result := new bmiResult; // create an empty result object
  weight := latest of weights; // get the latest weight from the list
  size := call mlmForReadSize with patientID; // get the size of the patient calculated by another MLM
  result.bmi := weight / (size ** 2); // calculation of BMI
  age := currenttime - birth; // calculation of AGE
  // classification - the classification is only valid for patients older than 19
  if the age is less than 19 years then result.classification := null;
  elseif the result.bmi is less than 18.5 then result.classification := localized 'under';
  elseif the result.bmi is less than 25 then result.classification := null;
  else let the result.classification be localized 'over';
  endif;
  result.bmi := result.bmi formatted with localized 'msg'; // construct the localized message
  if (time of weight) is before (currenttime - 6 months) then
    conclude false; //no bmi calculation if the latest measure was 6 months ago
  else
    conclude result.classification is present ; // if there is a classification, execute the action slot
  endif;
::
```
ArdenML: Objectives and applications

• Provide a complete XML schema for Version 2.10 of the Arden Syntax to express MLMs in XML

• Thus, Arden Syntax is now compatible with all other HL7 standards based on XML (HL7 version 3, VmR, and others)

• Further benefit: To be able to use available XML tools
ArdenML: Example

<Library>
  <Purpose>Test</Purpose>
  <Explanation></Explanation>
  <Keywords></Keywords>
</Library>

<Knowledge>
  <Type data driven /></Type>
  <Data></Data>
  <Evoke></Evoke>
  <Logic>
    <Assignment>
      <Identifier var='var1' />
      <Assigned>
        <Value otype='time'>1990-03-15T15:00:00</Value>
      </Assigned>
    </Assignment>
    <Assignment>
      <Identifier var='res1' />
      <Assigned>
        <ReplaceYearWith>
          <Identifier var='var1' />
          <Value otype='number'>2011</Value>
        </ReplaceYearWith>
      </Assigned>
    </Assignment>
    <Assignment>
      <Identifier var='res2' />
      <Assigned>
        <ReplaceYearWith>
          <Identifier var='var1' />
          <List>
            <Value otype='number'>2011</Value>
            <Value otype='number'>2010</Value>
          </List>
        </ReplaceYearWith>
      </Assigned>
    </Assignment>
  </Logic>
</Knowledge>
Cross compilation/transformation of Arden Syntax to/from ArdenML

Team effort by Intermountain Hospital, Salt Lake City, Utah, U.S.A., and Medexter Healthcare, Vienna, Austria
Computers in clinical medicine—steps of natural progression

• step 1: patient administration
  • admission, transfer, discharge, and billing

• step 2: documentation of patients’ medical data
  • electronic health record: all media, distributed, life-long (partially fulfilled)

• step 3: patient and hospital analytics
  • data warehouses, quality measures, reporting and research databases, patient recruitment
    ... population-specific

• step 4: clinical decision support
  • safety net, quality assurance, evidence-based
    ... patient-specific
History

- Clay tablets with cuneiform writing from New Babylonian (about 650 B.C.)
  - instructions to medical examination, diagnosis, and prognosis

- “Reasoning Foundations of Medical Diagnosis” by Ledley and Lusted in Science (1959)
  - computer-assisted medical diagnosis and therapy

- medical expert system MYCIN by Shortliffe et al. (Stanford University, 1975)
  - diagnostic and therapeutic proposals for patients suffering from infectious diseases (evaluation JAMA, 1979)
Antimicrobial Selection by a Computer
A Blinded Evaluation by Infectious Diseases Experts

Victor L. Yu, MD; Lawrence M. Fagan; Sharon M. Wraith; William J. Clancey; A. Carlisle Scott, MS; John Hannigan, MS; Robert L. Blum, MD; Bruce G. Buchanan, PhD; Stanley N. Cohen, MD

- An evaluation of a computer-based consultation system called MYCIN was made. Eight independent evaluators with special expertise in the management of meningitis compared MYCIN's choice of antimicrobials with the choices of nine human prescribers for ten test cases of meningitis. MYCIN received an acceptability rating of 65% by the evaluators; the corresponding ratings for acceptability of the regimen prescribed by the five faculty specialists ranged from 42.5% to 62.5%. The system never failed to cover a treatable pathogen while demonstrating efficiency in minimizing the number of antimicrobials prescribed. The study design may be useful in assessing the performance of other computer-based clinical decision-making systems. (JAMA 242:1279-1282, 1979)

DURING the last two decades, many computer programs have been developed to assist physicians in the diagnosis or treatment of a variety of medical disorders. However, to our knowledge, the medical accuracy of these programs has not undergone clinical evaluation by independent experts. We present a comparison of meningitis before the causative agent had been identified.

The computer program, MYCIN, provides advice for the diagnosis of diseases and the treatment of patients with infectious diseases. During the last five years, MYCIN's extensive knowledge base and its therapy-selection process have been therapy, MYCIN takes into account the specific clinical situations (eg, trauma, neurosurgery), host factors (eg, age, immunosuppression), and the possible presence of unusual pathogens (eg, Francisella tularenensis, Candida non-albicans). In selecting antimicrobial therapy, the system considers antimicrobial factors (eg, organism susceptibility, synergistic combinations) and relative contraindications (eg, patient allergies, poor response to prior therapy).

When knowledge about a new area of infectious disease is incorporated into MYCIN's knowledge base, the system's performance is evaluated to determine whether its therapeutic regimens are as reliable as the regimens that an infectious diseases specialist would recommend. An evaluation of the system's ability to diagnose and treat patients with bacterio-
Artificial Intelligence (AI)—applicable to clinical medicine

• **Definition**: AI is the science of artificial simulation of human thought processes with computers.


• It is the decomposition of an entire clinical thought process and its separate artificial simulation—also of simple instances of “clinical thought”—that make the task of **AI in clinical medicine** manageable.

• A functionally-driven science of AI that extends clinicians through computer systems step by step can immediately be established.

  ↓

  artificial-intelligence-augmented clinical medicine
Medical information and knowledge-based systems

patient’s medical data
- symptoms
- signs
- test results
- clinical findings
- biosignals
- images
- diagnoses
- therapies
- nursing data
- standardization
- telecommunication
- chip cards

physician’s medical knowledge
- anatomy
- biochemistry
- physiology
- pathophysiology
- pathology
- nosology
- therapeutic knowledge
- disease management
- subjective experience
- intuition

medical statistics
clustering & classification
data & knowledge mining
machine learning

induction
- many patients
- general knowledge
clinical decision support
medical expert systems

deduction
- single patient
- general knowledge
diagnosis
therapy
prognosis
management

information systems
- telemedicine

knowledge-based systems
- telemedicine

integration

medical knowledge acquisition
by clinicians
+ knowledge engineers
Clinical decision support and quality assurance

patients’ structured medical data

<table>
<thead>
<tr>
<th>diagnostic support</th>
<th>therapy advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>• clinical alerts, reminders, calculations</td>
<td>• drug alerts, reminders, calculations</td>
</tr>
<tr>
<td>• data interpretation, (tele)monitoring</td>
<td>• indication, contraindications,</td>
</tr>
<tr>
<td>• differential diagnostic consultation</td>
<td>redundant medications, substitutions</td>
</tr>
<tr>
<td>– rare diseases, rare syndromes</td>
<td>• adverse drug events, interactions,</td>
</tr>
<tr>
<td>– further or redundant investigations</td>
<td>dosage calculations, consequent orders</td>
</tr>
<tr>
<td>• pathological signs accounted for</td>
<td>• management of antimicrobial therapies, resistance</td>
</tr>
<tr>
<td>• consensus-criteria-based evaluation</td>
<td>• (open-loop) control systems</td>
</tr>
<tr>
<td>– definitions, classification criteria</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>prognostic prediction</th>
<th>patient management guidelines &amp; quality assurance</th>
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</thead>
<tbody>
<tr>
<td>• illness severity scores, prediction rules</td>
<td>• evidence-based reminders and processes</td>
</tr>
<tr>
<td>• trend detection and visualization</td>
<td>• computerized clinical guidelines, protocols, SOPs</td>
</tr>
<tr>
<td></td>
<td>• healthcare-associated infection surveillance</td>
</tr>
</tbody>
</table>

highly-structured medical knowledge
• studies in Colorado and Utah and in New York (1997)
  – errors in the delivery of health care leading to the death of as many as 98,000 US citizens annually

• causes of errors
  – error or delay in diagnosis
  – failure to employ indicated tests
  – use of outmoded tests or therapy
  – failure to act on results of testing or monitoring
  – error in the performance of a test, procedure, or operation
  – error in administering the treatment
  – error in the dose or method of using a drug
  – avoidable delay in treatment or in responding to an abnormal test
  – inappropriate (not indicated) care
  – failure of communication
  – equipment failure

• prevention of errors
  – we must systematically design safety into processes of care
A “holy grail” of clinical informatics is scalable, interoperable clinical decision support.

according to
Kensaku Kawamoto
HL7 Work Group Meeting,
San Diego, CA, September 2011
Fuzzy Arden Syntax: Modelling uncertainty in medicine

• **linguistic uncertainty**
  - due to the unsharpness (fuzziness) of boundaries of linguistic concepts; gradual transition from one concept to another
  - modeled by fuzzy sets, e.g., fever, increased glucose level

• **propositional uncertainty**
  - due to the uncertainty (or incompleteness) of medical conclusions; includes definitional and causal, statistical and subjective relationships
  - modeled by truth values between zero and one, e.g., usually, almost confirming
Crisp sets vs. fuzzy sets

yes/no decision

\[ U = [0, 120] \]
\[ Y \subseteq U \text{ with } Y = \{ (\chi_Y(x)) \mid x \in U \} \]
\[ \chi_Y : U \to \{0, 1\} \]
\[ \chi_Y(x) = \begin{cases} 
0 & x > \text{threshold} \\
1 & x \leq \text{threshold} 
\end{cases} \quad \forall x \in U \]

gradual transition

\[ U = [0, 120] \]
\[ Y \subseteq U \text{ with } Y = \{ (\mu_Y(x)) \mid x \in U \} \]
\[ \mu_Y : U \to [0, 1] \]
\[ \mu_Y(x) = \begin{cases} 
\frac{1}{1 + (0.04x)^2} & x > \text{threshold} \\
1 & x \leq \text{threshold} 
\end{cases} \quad \forall x \in U \]
Crisp sets vs. fuzzy sets

- "arbitrary" yes/no decisions
  - cause of unfruitful discussions
  - often simply wrong

- "intuitive" gradual transitions
Clinical concepts and relationships between them

\[
\left( S_1 \land S_2 \right) \lor \neg S_3 \rightarrow D
\]
Arden Syntax
What is Arden Syntax?

- ... a language used for representing and sharing medical knowledge.
- ... used for sharing of computerized health knowledge bases across personnel, information systems, and institutions.
- ... organized using modules, while each module, referred to as a Medical Logic Module (MLM), contains sufficient knowledge to make a single decision.
- ... an executable format which can be used by clinical decision support systems.
In Arden Syntax, medical knowledge is arranged within Medical Logic Modules (MLMs)

Each MLM represents sufficient knowledge to make a single clinical decision

One or more MLMs are stored within a file that has the extension “.mlm”

Each MLM is well organized and structured into categories and slots with specific content

An MLM is composed of slots, grouped into the following four required categories: maintenance, library, knowledge, and resources

Categories must appear in the correct order

Within each category is a set of slots that must appear in the correct order, too

```
Arden Syntax – Fundamentals I

• In Arden Syntax, medical knowledge is arranged within Medical Logic Modules (MLMs)

• Each MLM represents sufficient knowledge to make a single clinical decision

• One or more MLMs are stored within a file that has the extension “.mlm”

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• An MLM is composed of slots, grouped into the following four required categories: maintenance, library, knowledge, and resources

• Categories must appear in the correct order

• Within each category is a set of slots that must appear in the correct order, too

```
MLMs are working in close contact with their host system. Ways of interaction are:

- **Input**: By calling an MLM, an input parameter can be committed
- **Curly Brace Expressions**: So called “curly brace expressions” implement a special kind of dynamic interaction between MLMs and host systems
- **Write Statements**: Texts can be written to destinations that are maintained by the host system
- **Output**: Analogous to the input parameter, data can be committed from the MLM to the host system after the execution of the MLM has finished

In order to start the execution of an MLM, an engine is needed that handles communication with the host system and can tell which of the MLMs are available

Ways to start running an MLM:
- **MLM call**: An MLM is directly called
- **Event call**: Any MLM that listens to a specific event is executed
Sample MLM

• Some of the operators and concepts can be seen in the following sample MLM that calculates the body mass index (BMI) of a patient:

```plaintext
maintenance:
title: simple body mass index;;
mlmname: BMI_HowTo;;
arden: Version 2.7;;
version: 1.00;;
institution: Medexter Healthcare GmbH;;
author: Karsten Fehre;;
specialist: ;;
date: 2010-09-09;;
validation: testing;;
library:
purpose: body mass index;;
explanation: calculation of body mass index;;
keywords: BMI, body mass index;;
citations: ;;
links: http://en.wikipedia.org/wiki/Body_mass_index;;
```
Sample MLM (cont.)

// MLM that contains the interface definition "LET get_birth BE INTERFACE {Patient.dateOfBirth}; "

mlmImport := MLM 'interface_birthday_definition';

// include
include mlmImport;

mlmForReadSize := MLM 'read_Size_MLM'; // MLW which can read the current size of the patient from the DB

LET patientID BE argument; // the patient ID is passed to the MLM

LET birth BE CALL get_birth WITH patientID; // call the interface with the passed patient ID

// read all measured weights from the database
LET weights BE READ {SELECT measured_weight FROM DB WHERE patID = patientID };

LET userEvent BE EVENT {getBmi};

// object declaration
bmiResult := object [bmi, classification];

;;
priority: ;;
evoke: 
  userEvent;
  ;;
logic:
result := new bmiResult; // create an empty result object
weight := latest of weights; // get the latest weight from the list
size := call mlmForReadSize with patientID; // get the size of the patient calculated by another MLM
result.bmi := weight / (size ** 2); // calculation of BMI
age := currenttime - birth; // calculation of AGE

// classification - the classification is only valid for patients older than 19
if the age is less than 19 years then result.classification := null;
elseif the result.bmi is less than 18.5 then result.classification := localized 'under';
elseif the result.bmi is less than 25 then result.classification := null;
else let the result.classification be localized 'over';
endif;

result.bmi := result.bmi formatted with localized 'msg'; // construct the localized message

if (time of weight) is before (currenttime - 6 months) then
  conclude false; // no bmi calculation if the latest measure was 6 months ago
else
  conclude result.classification is present ; // if there is a classification, execute the action slot
endif;

;;
Sample MLM (cont.)

```java
action:

    write result.bmi || result.classification || "."; // return result

    return result;
    ;
    urgency: ;
    resources:
    default: de;
    ;
    language: en
    'msg' : "The patient's BMI %.1f is not in the normal range and is classified as ";
    'under' : "Underweight";
    'over' : "Overweight"
    ;
    language: de
    'msg' : "Der BMI %.1f des Patienten ist nicht im normalen Bereich und wird klassifiziert als ";
    'under' : "Untergewicht";
    'over' : "Übergewicht"
    ;
end:
```
Arden Syntax – Fundamentals III

- Data types
- Statements, expressions (assignments, loops, variables, constants, objects)
- Operators
  - List operators
  - Logical operators
  - Comparison operators
  - String operators
  - Arithmetic operators
  - Temporal operators
  - Aggregation operators
  - Time and object operators
Primary Time

- In addition to its value part each data value has a **primary time** part and an applicability

- Primary time represents the value part’s time of creation or measurement

- By default, primary time is **null**

- Can be accessed using the **time** operator
  
  \[
  2011-03-15T00:00:00 := 2 \text{ days AFTER} \ 2011-03-13T00:00:00
  \]

- Database query results should contain both, the value and the primary time
  
  - Might be the time when a blood test was drawn from the patient
  - Might be the time when a medication order was placed
  - Which time of a database entry is taken as primary time is left to the used Arden Syntax implementation
A first draft of the standard was prepared at a meeting at the Arden Home-stead, New York, in 1989. Arden Syntax was previously adopted as a standard by the American Society for Testing and Materials (ASTM) as document E 1460, under subcommittee E31.15 Health Knowledge Representation.

- 1992: Arden Syntax version 1.0
- 1998: sponsorship moved to HL7 International (Arden Syntax Work Group)
- 1999: Arden Syntax version 2.0 adopted by HL7 and the American National Standards Institute (ANSI)
- 2014: Arden Syntax version 2.10
## History

<table>
<thead>
<tr>
<th>Version</th>
<th>Year</th>
<th>Important changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>2002</td>
<td>new string operators; reserved word “currenttime” returns the system time</td>
</tr>
<tr>
<td>2.5</td>
<td>2005</td>
<td>object capabilities: create and edit objects; XML representation of MLMs (except logic, action and data slot)</td>
</tr>
<tr>
<td>2.6</td>
<td>2007</td>
<td>UNICODE encoding; additional resources category to define text resources for specific languages; time-of-day and day-of-week data types; “localized” operator to access texts in specific languages</td>
</tr>
<tr>
<td>2.7</td>
<td>2008</td>
<td>enhanced assignment statement; extended “new” operator to allow easy and flexible object instantiation</td>
</tr>
<tr>
<td>2.8</td>
<td>2012</td>
<td>additional operators for list manipulation; operators to manipulate parts of given date and time values; switch statements; keyword “breakloop” for aborting a loop; number of editorial corrections</td>
</tr>
<tr>
<td>2.9</td>
<td>2013</td>
<td>fuzzification: fuzzy data types and fuzzy sets; adjustment of all available operators to be able to handle fuzzy data types</td>
</tr>
<tr>
<td>2.10</td>
<td>2014</td>
<td>XML representation of whole MLMs (including logic, action and data slot)</td>
</tr>
</tbody>
</table>
Fuzzy Arden Syntax
Fuzzy Sets – Background I

- **Crisp** border
  - Defines a **sharp** border
  - Checking if a given measurement is greater or less than the defined crisp border results in either true or false
  - Borderline cases are not detected

- **Fuzzified** border
  - Defines a **gradual** border
  - Checking if a given measurement is greater or less than the defined fuzzified border results in a truth value between 0 and 1
  - Borderline cases are detected
  - Weighted results for borderline cases, all other are as usual
Fuzzy Sets – Background II

• Function that maps a given data value to a truth value between 0 and 1
• A fuzzy set represents a linguistic/clinical concept with fuzzy (non-sharp) boundaries
Fuzzy Sets

- Definition of a fuzzy set
  \[ \text{Fuzzyset}_u := \text{FUZZY SET} (18.5, 0), (19.5, 1), (24, 1), (25, 0); \]
  \[ \text{Fuzzyset}_v := 7 \text{ fuzzified by } 2; \]

- Fuzzy set based on other data types
  \[ \text{Fuzzyset\_duration} := \text{FUZZY SET} (3 \text{ days}, 0), (10 \text{ days}, 1), (20 \text{ days}, 1), (25 \text{ days}, 0); \]
  \[ \text{simple} := \text{2009-10-10 fuzzified by 12 hours}; \]
  \[ \text{complex} := \text{FUZZY SET} (2009-10-10, 0), (2009-10-11, 1), (2009-11-10, 1), (2009-11-11, 0); \]

\[ x \text{ is in } \text{BMI.normal} \]
Fuzzy Sets – Example I

- **Usual** Arden Syntax

  ```plaintext
  fever_limit := 38;
temperature := 37.9;

  message := "patient has no fever";
  IF temperature > fever_limit THEN
      message := "patient has fever";
  END IF
  
  - Result message: “patient has no fever”
  - Borderline case is not detected
  ```

- **Fuzzy** Arden Syntax

  ```plaintext
  fever_limit := FUZZY SET (37.5,0), (38,1);
temperature := 37.9;

  message := "patient has no fever";
  IF temperature > fever_limit THEN
      message := "patient has fever";
  END IF
  
  - Result message: “patient has fever” (with applicability 0.8)
  ```
Arden Syntax contains two types of fuzziness:
- Data types: for explicit calculations e.g., truth value, fuzzy set
- Applicability: for weighting MLM evaluation and weighting of branches

- All simple data types are endowed with information concerning the degree of **applicability**

- Stores a truth value that refers to the degree to which it is reasonable to use the value of a variable

- Default applicability is 1 and the applicability is never null

- Can be accessed using the **applicability** operator

- If-then statements with a condition that evaluates to a truth value [0,1] result in a split of the MLM execution
  - Each branch will be executed under corresponding applicability
  - The applicability is implicit attached to each variable of the branch
Statements – If-Then-ElseIf – Fuzzy Condition

Source

maintenance: [...]
knowledge: [...]
logic:

//define linguistic variable BMI
[...]
myBMI := 24.8;
x := myBMI <= BMI.overweight;
if x then
// this branch is executed
// with applicability 0.8
<then_block>
else
// this branch is executed
// with applicability 0.2
<else_block>
endif;
[...]
end:

Arden Syntax

Fuzzy Arden Syntax
 Statements – If-Then-Aggregate

if x then
  <then_block>
else
  <else_block>
endif AGGREGATE;

- Combination of the variable values in each execution branch according to their applicability
- Aggregations are common in fuzzy control
ArdenML: Objectives and applications

- Provide a complete XML schema for version 2.10 of the Arden Syntax to express MLMs in XML.

- Thus, Arden Syntax is now compatible with all other HL7 standards based on XML (HL7 version 3, VmR, and others).

- Further benefit: To be able to use available XML tools.
ArdenML: Example

```xml
<Library>
  <Purpose>Test</Purpose>
  <Explanation></Explanation>
  <Keywords></Keywords>
</Library>
<Knowledge>
  <Type>data driven</Type>
  <Data></Data>
  <Evoke></Evoke>
  <Logic>
    <Assignment>
      <Identifier var='var1' />
      <Assigned>
        <Value otype='time'>1990-03-15T15:00:00</Value>
      </Assigned>
    </Assignment>
    <Assignment>
      <Identifier var='res1' />
      <Assigned>
        <ReplaceYearWith>
          <Identifier var='var1' />
          <Value otype='number'>2011</Value>
        </ReplaceYearWith>
      </Assigned>
    </Assignment>
    <Assignment>
      <Identifier var='res2' />
      <Assigned>
        <ReplaceYearWith>
          <Identifier var='var1' />
          <List>
            <Value otype='number'>2011</Value>
            <Value otype='number'>2010</Value>
          </List>
        </ReplaceYearWith>
      </Assigned>
    </Assignment>
  </Logic>
</Knowledge>
```
Cross compilation/transformation of Arden Syntax to/from ArdenML
Integration
How to execute MLMs

- **MLM calls**: When the MLM call statement is executed, the current MLM is interrupted, and the named MLM is called; parameters are passed to the named MLM

  ```
  /* Define find_allergies MLM */
  find_allergies := MLM 'find_allergies';
  (allergens, reactions):= call find_allergies;
  ```

- **Event calls**: When the event call statement is executed, the current MLM is interrupted, and all the MLMs whose evoke slots refer to the named event are executed; parameters are passed to the named MLMs

  ```
  allergy_found := EVENT {allergy found};
  reactions := call allergy_found;
  ```
How to execute MLMs – Arden Syntax Engine

Arden Syntax engine

provide compiled MLMs

Arden Syntax authoring component

Arden Syntax compiler

Arden Syntax IDE
How to execute MLMs – Web Service Interfaces

Arden Syntax server
- SOAP and REST web services
- Arden Syntax engine

Arden Syntax server administration

internet/intranet
- mobile app
- website
- connected to application
- integrated in application

MLM/event calls

Arden Syntax authoring component

provide compiled MLMs

Arden Syntax compiler

Arden Syntax IDE
How to execute MLMs – Web Service Usage
How to get data into MLMs

- MLM and event calls
  - Provide data to an other MLM
  - Read data provided to the actual MLM
  - Return data to calling MLM or instance

- Curly brace expressions
  - Read data from external data sources
  - Write data to external data sources
  - Call external applications or interfaces
How to get data into MLMs – Curly Brace Expressions
Types of Integration I

I. MLM/event calls together with data
   - through web-services (intranet/Internet)
Types of Integration II

MLM/event calls
- through web-services

Data access from inside MLMs
- through server connector as
  + ... {web-services}
  + ... {SQL statements}
  + ... {...}
Data warehouse + Arden Syntax server = autonomous CDS system
- data provided through HL7/XML/batch/... communication
- full process control (MLM triggering)
- additional analytics, reporting, benchmarking
- full legal control (legal obligation to retain data, burden of proof)
Clinical decision support with Arden Syntax

• CDS platforms
  - based on Arden Syntax and Fuzzy Arden Syntax
    * with data (sometimes) and knowledge services center and extended interoperability (web services, XML data interfaces, libraries, HL7)
  - integrated into or interconnected with
    - PDMSs (ICCA by Philips, MetaVision by iMDsoft)
      * Monitoring, reporting, and benchmarking of ICU-acquired infections (ICUs and NICUs)
    - ICM (by Dräger)
      * ICU decision support modules (Universitätsklinikum Erlangen)
    - i.s.h.med HIS and Soarian HIS (by Siemens AG)
      * dosing of immunosuppressive drugs for kidney transplant patients
      * prediction of metastases in melanoma patients
      * standard operating procedures for chemotherapy treatment of melanoma patients
      * hepatitis serology test interpretation
    - medico//s HIS (by Siemens AG)
      * laboratory-based clinical reminders
    - Epic
      * clinical decision support
    - VistA HIS (by Department of Veterans Affairs)
      * service-oriented, standards-based CDS (clinical reminders and patient report cards)
    - Monitoring adverse drug events (project with Salzburger Universitätsklinikum)
    - Teleiatros, iPhone, iPad
      * remote CDS, mHealth
<table>
<thead>
<tr>
<th>Datum</th>
<th>Status / Patient</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011-12-14</td>
<td>62354</td>
<td>(Stat. 62354) no data</td>
</tr>
<tr>
<td>2011-12-13</td>
<td>62354</td>
<td>(Stat. 62354) no data</td>
</tr>
<tr>
<td>2011-12-12</td>
<td>62354</td>
<td>(Stat. 62354) no data</td>
</tr>
<tr>
<td>2011-12-11</td>
<td>62354</td>
<td>(Stat. 62354)</td>
</tr>
<tr>
<td>2011-12-10</td>
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</tr>
<tr>
<td>2011-12-09</td>
<td>62354</td>
<td>(Stat. 62354)</td>
</tr>
<tr>
<td>2011-12-08</td>
<td>62354</td>
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</tr>
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<td>2011-12-05</td>
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</tr>
<tr>
<td>2011-12-04</td>
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</tr>
<tr>
<td>2011-12-03</td>
<td>62354</td>
<td>(Stat. 62354)</td>
</tr>
</tbody>
</table>

**BSI-3 (KISS)**

- UND: 100 % DoC
- imp. keine Blutkultur: ja
- imp. kein Erreger in nicht-Blut: ja
- Anbahnung für 5 Tage: ja
- 2 Labor- und klin. Anz. f. Sepsis (KISS): 100 % DoC

**2 Labor- und klin. Anz. f. Sepsis (KISS)**

- MIND: 2 VON: 100 % DoC
- pathol. Körpertemperatur: ja
- **neue Hyperglykämie (KISS)**: 100 % DoC

**neue Hyperglykämie (KISS)**

- UND: 100 % DoC
- NICHT: 100 % DoC
  - Hyperglykämie (KISS) (t-1d)
  - Hyperglykämie (KISS): 100 % DoC

**Hyperglykämie (KISS)**

- maximale Glukose: 178 mg/dl

**maximale Glukose**

- imp. Glukose: 69 mg/dl
- imp. Glukose: 154 mg/dl
- imp. Glukose: 178 mg/dl
- imp. Glukose: 160 mg/dl
Moni output

Section of Moni screenshot for one ICU: Colors indicate patients with infection episodes, where change in color means change in data-definition compatibility.
**Arden Syntax—integration of software**

Data warehouse + Arden Syntax server = autonomous CDS system
- data provided through HL7/XML/batch/... communication
- full process control (MLM triggering)
- additional analytics, reporting, benchmarking
- full legal control (legal obligation to retain data, burden of proof)
First study:

⇒ 99 ICU patient admissions; 1007 patient days

<table>
<thead>
<tr>
<th>HAI episodes correctly / falsely identified or missed by Moni-ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>episode present “gold standard” (n= 19)</td>
</tr>
<tr>
<td>episode present “Moni-ICU”</td>
</tr>
<tr>
<td>episode absent “Moni-ICU”</td>
</tr>
</tbody>
</table>

Time expenditure for both surveillance techniques

<table>
<thead>
<tr>
<th>Time spent</th>
<th>conventional surveillance</th>
<th>Moni-ICU surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>time spent</td>
<td>82.5 h (100%)</td>
<td>12.5 h (15.2%)</td>
</tr>
</tbody>
</table>

Second study:

⇒ 93 ICU patient admissions; 882 patient days; 30 HAI episodes over complete or partial duration of stay; 76 stays with no HAI episodes

<table>
<thead>
<tr>
<th>gold standard</th>
<th>Moni-ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>I+</td>
<td>26</td>
</tr>
<tr>
<td>I-</td>
<td>1</td>
</tr>
</tbody>
</table>

HAI episodes correctly / falsely identified or missed by Moni-ICU

sensitivity = 87%
• 3 false-negative pneumonias + 1 false-negative CVC-related infection due to missing microbiology

specificity = 99%
• 1 false-positive CVC-related infection because of a present concomitant leukemia (with leukocytosis)

Two different hyperglycemia definitions
Regel zur Interpretation von klinisch relevanten Befunden (Regelprämissen bilden Äquivalenzklassen)

REGEL 103:

WENN eine der folgenden 100 Kombinationen zutrifft

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>anti-HBs</th>
<th>anti-HBc</th>
<th>IgM-anti-HBc</th>
<th>HBeAg</th>
<th>anti-HBe</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>●</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>- ●</td>
</tr>
<tr>
<td>+</td>
<td>●</td>
<td>+</td>
<td>- ●</td>
<td>+</td>
<td>- ●</td>
</tr>
</tbody>
</table>

DANN

Das gleichzeitige Auftreten von HBe-Antigen und Anti-HBs-Antikörpern ist im natürlichen Verlauf einer Hepatitis-B-Virusinfektion ein seltenes Ereignis. Diese Befundkonstellation ist entweder auf (a) zirkulierende HBsAg-anti-HBs-Immunkomplexe, (b) auf eine Koinkidenz einer Hepatitis-B-Virusinfektion mit einer Hepatitis-B-Impfung oder Injektion von HBV-Hyperimmunglobulin oder (c) eine Reinfektion mit einem Hepatitis-B-Virus mit unterschiedlichem HBsAg-Subtypus zurückzuführen. Blut und Sekrete (Speichel, Sperma, Muttermilch) solcher Patienten sind als infektös anzusehen.
## Test Results

### Proteindiagnostik

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ergebnis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>61.5 ***</td>
</tr>
</tbody>
</table>

### Hormone

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ergebnis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>3.00</td>
</tr>
</tbody>
</table>

### Infektionsserologie

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ergebnis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-Antikörper</td>
<td>Negativ</td>
</tr>
</tbody>
</table>

### Hepatitis-Serologie

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ergebnis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HAV-IgM</td>
<td>Negativ</td>
</tr>
<tr>
<td>Anti-HAV</td>
<td>Positiv</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Negativ</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Negativ</td>
</tr>
<tr>
<td>Anti-HBc (quant.)</td>
<td>4.2 U/l</td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>Negativ</td>
</tr>
</tbody>
</table>

### Medizinischer Kommentar / Interpretation


Anti-HBs Titer: 1 Units/Liter

## Hepatitisserologie Diagnostik

<table>
<thead>
<tr>
<th></th>
<th>Hep A</th>
<th>Hep B</th>
<th>Hep C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HAV</td>
<td>Negativ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM anti-HAV</td>
<td>Positiv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAV</td>
<td>Grenzwertig</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Positiv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBs Tit</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbsAg</td>
<td>Positiv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Negativ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM anti-HB</td>
<td>Negativ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbeAg</td>
<td>Positiv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Nicht gemessen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>Positiv</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV RNA</td>
<td>Grenzwertig</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Ergebnisse

**Hepatitis A**

Der Befund enthält Widersprüche, da definitionsgemäß bei Vorliegen von IgM anti-HAV-Antikörpern auch der Gesamtkörper Anti-HAV positiv sein müßten.


**Hepatitis B**

Das gleichzeitige Auftreten von HBe-Antigen und Anti-HBs-Antikörpern ist im natürlichen Verlauf einer Hepatitis-B-Virusinfektion ein seltenes Ereignis. Diese Befundkonstellation ist entweder auf (a) zirkulierende HbsAg-Anti-HBs-Immunkomplexe, (b) auf eine Koinzidenz einer Hepatitis-B-Virusinfektion mit einer Hepatitis-B-Impfung oder Injection von HB-Hyperimmunglobulin oder (c) eine Infektion mit einem Hepatitis-B-Virus mit unterschiedlichem HbsAg-Subtyp zurückzuführen. Blut und Sekrete (Speichel, Sperma, Muttermilch) solcher Patienten sind als infektiös anzusehen.

**Hepatitis C**

Es besteht eine reaktive oder chronisch persistierende oder eine früher abgelaufene Hepatitis-C-Virusinfektion. Die Bestimmung von HCV RNA bringt zusätzliche Information. Das Blut solcher Personen ist hinsichtlich Hepatitis C als infektiös anzusehen.

Zur Kontrolle des nicht eindeutig negativen oder positiven Befundes wird neuerliche Material einsendung empfohlen.
Interpretation of hepatitis serology test results

Hepaxpert/Interpretation
Knowledge-based interpretation of hepatitis A, B, and C serology

Input of test results

Hepatitis A serology
- Anti-HAV: [ ] positive [ ] negative [ ] borderline [ ] not tested
- IgM anti-HAV: [ ] positive [ ] negative [ ] borderline [ ] not tested
- HAV-RNA: [ ] positive [ ] negative [ ] borderline [ ] not tested

Hepatitis B serology
- HBsAg: [ ] positive [ ] negative [ ] borderline [ ] not tested
- anti-HBs: [ ] positive [ ] negative [ ] borderline [ ] not tested
- anti-HBc: [ ] positive [ ] negative [ ] borderline [ ] not tested
- IgM anti-HBc: [ ] positive [ ] negative [ ] borderline [ ] not tested
- HBeAg: [ ] positive [ ] negative [ ] borderline [ ] not tested
- anti-HBs titre: [ ] not tested [ ] not available

Hepatitis C serology
- anti-HCV: [ ] positive [ ] negative [ ] borderline [ ] not tested
- HCV-RNA: [ ] positive [ ] negative [ ] borderline [ ] not tested

Interpretation

Hepatitis A serology
- Anti-HAV: positive
- IgM anti-HAV: negative
- HAV-RNA: negative
- Positive results for total anti-HAV antibodies in combination with negative results for IgM anti-HAV antibodies indicate immunity to the hepatitis virus A and exclude the possibility of a recent hepatitis A. An infant born either natural or through an infected mother or a patient who may have been infected by active vaccination or passively acquired inoculations.

Hepatitis B serology
- HBsAg: positive
- Anti-HBs: negative
- Anti-HBc: negative
- IgM anti-HBc: negative
- HBeAg: negative
- Anti-HBs titre: negative
- Positive results for HBsAg and negative results for anti-HBs antibody and anti-HBc indicate a past infection of hepatitis B or chronic infection. The presence of anti-HBs antibodies suggests a recent exposure to hepatitis B or vaccination against hepatitis B. The persistence of anti-HBs antibodies over time is an indicator of protection against hepatitis B.

Hepatitis C serology
- anti-HCV: positive
- HCV-RNA: positive
- Positive results for anti-HCV and positive results for HCV-RNA indicate chronic hepatitis C infection. Blood and secretions (saliva, semen, breast milk) of the patient are to be considered infectious.

Important Notice
- This triaging physician alone is responsible for the patient’s diagnosis and therapy. Therefore, contact a doctor at all times. Only the doctor will be able to interpret the Hepaxpert interpretation with the full clinical picture of the patient.
Arden-Syntax-Server and MLMs at Universitätsklinikum Erlangen

Dr. Ixchel Castellanos
Interdisziplinäre Operative Intensivmedizin, Anästhesiologische Klinik

and

Dipl.-Inform. Stefan Kraus
Lehrstuhl für Medizinische Informatik
Patient ****** hat einen BMI von 30,1.

Patient hat Adipositas Grad I (E66.00).

HINWEIS: Diagnose E66.00 wurde noch nicht codiert!
Patient ******* | ISH-Aufnahmenummer: ******* | Bettnummer: Batt 10 (4/2) | Organeinheit: AN

MLM: ICM_ANIONENLUECKE

Die Anionenlücke von ******* beträgt 4 mmol/l.

Berechnungsgrundlage

Letzter Natriumwert: 153 (Alter: 3 Stunden 31 Minuten)
Letzter Chloridwert: 127 (Alter: 3 Stunden 31 Minuten)
Letzter HCO3-Wert: 22 (Alter: 3 Stunden 31 Minuten)

Verwendete Formel: Anionenlücke = Natrium - Chlorid - HCO3

Anionenlücke sollte bei verwendet Formel zwischen 8 und 16 liegen.
Antwort von Medexter-Engine

Aktuell ist keine Procalcitoninmessung erforderlich.

Patient hat 39 Procalcitoninwerte.
Die letzte Procalcitoninmessung erfolgte am 05.07.2011 um 09:00 Uhr und ergab den Wert 0.08. Die letzte Procalcitoninmessung liegt also 7 hours 29 minutes 34. seconds zurück.

Es wurden 13 vermeidbare Messungen gefunden: (4, 7, 9, 11, 13, 16, 18, 20, 22, 24, 26, 28, 31)
Das Einsparpotential liegt bei 182 Euro

Regression über alle Werte -0.03
Regression über die letzten beiden Werte 0
Trend: Veränderung pro Stunde 0

<table>
<thead>
<tr>
<th>#</th>
<th>Wert</th>
<th>Zeitstempel</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.22</td>
<td>29.05.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>2</td>
<td>1.80</td>
<td>30.05.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>3</td>
<td>0.97</td>
<td>31.05.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>4</td>
<td>0.65</td>
<td>01.06.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>5</td>
<td>0.36</td>
<td>02.06.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>6</td>
<td>0.17</td>
<td>04.06.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>7</td>
<td>0.42</td>
<td>05.06.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>8</td>
<td>0.33</td>
<td>08.06.2011 um 09:00 Uhr</td>
</tr>
<tr>
<td>9</td>
<td>0.2</td>
<td>08.06.2011 um 09:00 Uhr</td>
</tr>
</tbody>
</table>
Use Case: Hypoglycemia

• Hypoglycemia may seriously harm
• If patient is unconscious, it is difficult to notice
• The PDMS should actively notify the physician:

  If glucose is less than 50mg/dl,
  then send an SMS message to the physician.

by Stefan Kraus
Use Case: Hypoglycemia

DATA:
LET glucose BE READ {...glucose...};
LET physician_DECT BE DESTINATION {sms:26789};

LOGIC:
IF LATEST glucose IS LESS THAN 50 THEN
  CONCLUDE true;
ENDIF;

ACTION:
WRITE „Warning...“ AT physician_DECT;

by Stefan Kraus
Use Case: Hypoglycemia

Event monitors are "tireless observers, constantly monitoring clinical events"

(George Hripcsak)

by Stefan Kraus
Implementation

three-step approach

• awareness by clinicians, technicians, and administration; willingness to invest in evidence-based care, quality measures, legal confidence

• form a CDS governance committee (clinicians and technicians, backed by administration)

• demand and install specific CDS solutions and/or a general CDS tool for enterprise-wide knowledge authoring
Clinical perspectives
Regulatory affairs—I

- stand alone software
  - **Meddev 2.1/6**: Guidelines on the qualification and classification of stand alone software used in healthcare within the regulatory framework of medical devices (MDs) (January 2012)
Regulatory affairs—II

- MDD 93/42/EEC

Article 1, Paragraph 2a (art. 1.2a of MDD):
Medical device (MD) means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, ... intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment, or alleviation of disease
- ...
Medical device certification

intended use

classification of software using MDD 93/42/EEC

- application of risk management to medical devices
  ISO 14971
- application of usability engineering to medical devices
  EN 62366:2008
- quality management system for medical products
  ISO 13485
- medical device – software life cycle processes
  EN 62304
- ...

conformity assessment procedure
  - notified body (e.g., TÜV Austria)

CE marking
Clinical medicine

- History data
- Symptoms
- Signs
- Laboratory test results
- Biosignals
- Images
- Genetic data

- Differential diagnosis
- Test results
- Findings

- Symptomatic therapy
- Medication history

- Examination

- Subspecialities

- Clinic

- Medical guidelines

- Prognosis
Clinical medicine: high complexity

• sources of medical knowledge
  – definitional
  – causal
  – statistical
  – heuristic

• layers of medical knowledge
  – observational and measurement level
  – interpretation, abstraction, aggregation, summation
  – pathophysiological states
  – diseases/diagnoses, therapies, prognoses, management decisions

• imprecision, uncertainty, and incompleteness
  – imprecision (=fuzziness) of medical concepts
    * due to the unsharpness of boundaries of linguistic concepts
  – uncertainty of medical conclusions
    * due to the uncertainty of the occurrence and co-occurrence of imprecise medical concepts
  – incompleteness of medical data and medical theory
    * due to only partially known data and partially known explanations for medical phenomena

• "gigantic" amount of medical data and medical knowledge
  – patient history, physical examination, laboratory test results, clinical findings
  – symptom-disease relationships, disease-therapy relationships, ...
  – terminologies, ontologies: SNOMED CT, LOINC, UMLS, ...

specialization, teamwork, quality management, computer support
Clinical medicine: hidden treasures

• holistic diagnosis
  – knowledge and intuition, symptomatic vs. causal therapy, medication history
  – patient’s non-formalizable/non-digitizable data

• probable vs. possible diagnoses
  – interpretation of findings, suspected diagnosis, clinical diagnosis, pathological diagnosis
  – pattern matching, most probable diagnosis, sensitivity, specificity, prevalence

• terminology in context
  – not every diagnostic term is a diagnosis
  – psychology: cold, flu, malaria, ...
Moni-ICU: surveillance of healthcare-associated infections
Moni-NICU: (surveillance of and) alerts for healthcare-associated infections
Differential diagnosis of rheumatic diseases
Clinically-oriented interpretation of hepatitis serology test results

### Hepaxpert/Interpretation
Knowledge-based interpretation of hepatitis A, B, and C serology

#### Input of test results

<table>
<thead>
<tr>
<th>Hepatitis A serology</th>
<th>anti-HAV</th>
<th>IgM anti-HAV</th>
<th>HAV-RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>borderline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>not tested</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hepatitis B serology</th>
<th>HBsAg</th>
<th>anti-HBs</th>
<th>anti-HBc</th>
<th>IgM anti-HBc</th>
<th>HBeAg</th>
<th>anti-HBe</th>
<th>anti-HBs titre</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
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<table>
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<th>Hepatitis C serology</th>
<th>anti-HCV</th>
<th>HCV-RNA</th>
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</tbody>
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### Hepaxpert/Interpretation
Knowledge-based interpretation of hepatitis A, B, and C serology

#### Interpretation

**Hepatitis A serology**

- **anti-HAV**: positive indicates recent infection. Negative results may be due to infection, vaccination, or falsely positive results.
- **IgM anti-HAV**: positive indicates recent infection. Negative results may be due to infection, vaccination, or falsely positive results.
- **HAV-RNA**: positive indicates active infection. Negative results may be due to infection, vaccination, or falsely positive results.

**Hepatitis B serology**

- **HBsAg**: positive indicates active infection. Negative results may be due to infection, vaccination, or falsely positive results.
- **anti-HBs**: positive indicates immunity. Negative results may be due to infection, vaccination, or falsely positive results.
- **anti-HBc**: positive indicates past infection. Negative results may be due to infection, vaccination, or falsely positive results.
- **IgM anti-HBc**: positive indicates recent infection. Negative results may be due to infection, vaccination, or falsely positive results.
- **HBeAg**: positive indicates high viral load. Negative results may be due to infection, vaccination, or falsely positive results.
- **anti-HBe**: positive indicates low viral load. Negative results may be due to infection, vaccination, or falsely positive results.
- **anti-HBs titre**: levels above 100 IU/l indicate immunity.

**Hepatitis C serology**

- **anti-HCV**: positive indicates active infection. Negative results may be due to infection, vaccination, or falsely positive results.
- **HCV-RNA**: positive indicates active infection. Negative results may be due to infection, vaccination, or falsely positive results.

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### Important Notice

The attending physician alone is responsible for the patient's diagnosis and therapy. Therefore, contact a doctor at all times. Only the doctor will be able to sign the Hepaxpert Interpretation with the full clinical picture of the patient.
Arden Syntax software: generic technology platform for clinical decision support
Clinical reality and software artefacts: a sociotechnical, interdependent system

Clinical reality
↓
decision and responsibility

software artefacts
↓
information and risk

PATIENT

substitution

support
- reminders
- uncertainties

- depth
- computational power

certification of both clinicians and software ⇒ best care through best quality