Introduction to eHealth
What, why, how?

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Course aims and website

At the end of the two eHealth courses you need to have knowledge of:

▶ The role of biomedical knowledge in medicine and healthcare
▶ Anatomy, physiology and internal medicine of an organ system
▶ Probabilistic techniques for diagnosis and treatment selection
▶ Normative and descriptive techniques for decision analysis
▶ The role of medical image analysis in clinical medicine

You are the Pioneers!!

Website: http://www.ocw.cs.ru.nl/NWI-IPC027
Structure and assessment of the course eHealth1/2

Four themes:

▶ **Theme I:** principles of medicine and healthcare (illustrated by an organ system and disease management) (eHealth 1)

▶ **Theme II:** diagnostic reasoning and decision making (by means of probability and decision theory) (eHealth 1)

▶ **Theme III:** Human factors in clinical decision making (part eHealth 1 and part eHealth 2)

▶ **Theme IV:** role of image analysis in clinical medicine (eHealth 2)

**Assessment:** by means of essays and problems you have to solve (for which you will get a mark)
eHealth 1 – Schedule

▶ Theme I: Principles medicine and clinical decision support:

1. 7 February: Principles of medicine, computing science in healthcare
2. 14 February: Computing Science in healthcare
3. 21 February: anatomy, physiology, internal medicine, treatment
4. 28 February: probability theory and making a diagnosis
5. 7 March: decision support, decision making and treatment
6. 14 March: decision theory and medical applications

▶ Theme II: Human factors in decision making:

7. 21 March: Chapters 2, 3, 4: Intro psychological decision making and heuristics
8. 28 March: Chapters 6 and 7: Causes of associations, risks and uncertainty
eHealth 2 – Schedule

▶ Theme II Human factors in decision making (continued):
  1. 25 April: Chapters 8, 9 and 11: Preferences, trust and real life
  2. 9 May: Groups and intuition

▶ Theme III Medical image analysis:
  3. 16 May: Image construction modalities
  4. 23 May: Medical image processing
  5. 6 June: Computer-aided detection in screening
  6. 13 June: Digital pathology
  7. 20 June: Images and information flow in a hospital
Theme I: Clinical decision support

- Challenging problems
- Highly relevant decisions (every one becomes ill somewhere in life)
- Lots of improvements possible: mistakes, wrong judgements made by medical professionals
- Many research opportunities
Medicine ~ engineering?

Bridge building

Engineering principles

Consequence of failure

Medicine

Clinical principles

Consequence of failure
Context of most eHealth: clinical reasoning

- **signs**
  - diagnostic process
  - test
  - medical knowledge
  - patient data
  - therapy selection
  - therapy
  - disease prediction
  - prognosis
  - patient data
  - therapy
  - disease progress
  - prognosis
Patient and data

- **Clinical data**: symptoms and signs
- **Biosignals**: space-time records (stream) of biological events
  - mechanical
  - chemical
  - electromagnetic
  - acoustic
  - optic
- **Physiological origin**
- **Measured by biosensors**

Nowadays are the data collected at different sites: home, general practice, hospital, specialised units
Interpretation of patient data (including biosignals) in a clinical context:

- Collect uncertain
  - symptoms and signs
  - biosignals
  and interpret them taking into account their mutual dependence

- Clinical knowledge is the context of this interpretation (so needs to be represented)

- Only then, clinical decision support is possible

- Structured joint probability distributions (e.g. Bayesian networks) are perfect for that
Big data and healthcare

Patient and Sensors → Digital Doctor → Patient Data

-Dental and Mouth Sensors
-Blood Transfusion and Renal Dialysis Systems
-Orthopedic Devices
-Fluid-Handling and Drug Delivery Systems
-Hand Grippers
-Neurological and Nerve Transducers
-Tendon and Ligament Transducers
-Guidewire Torque Verification Devices
-Carpal Tunnel Transducers
-Joint Simulators
Problem: bias in big datasets because the data come from different area (e.g. different healthcare areas in the Netherlands)

Statistical solution: multilevel regression (to model variation of outcomes between various groups):

- multilevel linear regression:
  \[ P(O_k \mid e, l) \sim \mathcal{N}(\mu, \Sigma) \text{ with} \]
  \[ \mu = \mathbb{E}[O \mid e, l] = \beta_k e = (\delta_k + \gamma_k l)^T e \]

- multilevel logistic regression:
  \[ P(O_k \mid e, l) \sim \mathcal{B}(n, p) \text{ with } \logit(\mathbb{E}[O_k \mid e, l]) = (\delta_k + \gamma_k l)^T e \]
Multimorbidity and big data

Multilevel regression often used for the analysis in multimorbidity (patients with multiple diseases)

**single disease**
- environment
- characteristics
- genetics
- disease
- pathophysiology
- signs
- symptoms
- laboratory results

**multiple diseases**
- environment
- characteristics
- genetics
- disease A
- pathophysiology X
- sign 1
  - symptom 1
- laboratory results 1
- pathophysiology Y
  - sign 2
  - symptom 2
- laboratory results 2
- pathophysiology Z
  - sign 3
  - symptom 3
- laboratory results 3
Multimorbidity and time

- Model-based analysis of healthcare data
- Temporal patterns
Decision support: its computerisation is not easy

► Early academic attempts, e.g.:
  ► Diagnosis of disorders in internal medicine (e.g., gastrointestinal, rheumatoid, endocrine disorders): INTERNIST-I (1975–1985)

► Commercial AI attempts:
  ► Quick Medical Reference (QMR) – based on INTERNIST-I (discontinued 2001)
  ► DXplain (1984–) –
    http://lcs.mgh.harvard.edu/projects/dxplain.html
  ► Recently (2013-) from Poland: DxMate (https://dxmate.com) and in Polish:
    http://doktor-medi.pl/
Why failure?

- Focus on diagnostic systems: after entering set of findings ⇒ differential diagnosis
- First generation programs: immature technology, PhD projects
- Don’t offer the support clinicians want to have
- Computational infrastructure too primitive until 2000
- Clinicians had little computer literacy until ±1995
- No integration with electronic patient record systems (still not generally available)
- Bad computer interface
Do clinicians need ‘support’?

- Obstetric clinics at Vienna General Hospital mid 1800s
- Doctors (1st clinic) versus midwives (2nd clinic):

- Ignaz Semmelweis (1818–1865): infection after child birth can be drastically cut by hand washing
Hand hygiene in the intensive care unit: prospective observations of clinical practice

Pol Arch Med Wewn, 2008; 118 (10): 543-547

Ismael A. Qushmaq, Diane Heels-Ansdell, Deborah J. Cook, Mark B. Loeb, Maureen O. Meade

Abstract. INTRODUCTION: Adherence to hand hygiene recommendations in the intensive care unit (ICU) is variable and moderate, at best. OBJECTIVES: To measure adherence to hand hygiene recommendations among ICU clinicians in a prospective observational study in 6 multidisciplinary ICUs among 4 hospitals. . . . RESULTS: The rate of adherence to current recommendations was 20%. . . .
2002 Centers for Disease Control and Prevention Guidelines for the prevention of intravascular catheter-related infections:

- Wash your hands before inserting a central venous catheter
- Clean the skin with chlorhexidine
- Use of full-barrier precautions during CVC insertion
- Avoid the femoral site
- Remove unnecessary central venous catheters

⇒ We can investigate compliance
Example: NICE DM2 guideline

DM2 GL: ORAL GLUCOSE CONTROL THERAPIES (2):
Thiazolidinediones (glitazones)

► **R40** If glucose concentrations are not adequately controlled (to HbA1c <7.5% or other higher level agreed with the individual), consider, after discussion with the person, adding a thiazolidinedione to:
  ► the combination of metformin and a sulfonylurea where insulin would otherwise be considered but is likely to be unacceptable or of reduced effectiveness because of:
    ► employment, social or recreational issues related to putative hypoglycaemia
    ► barriers arising from injection therapy or . . .
  ► a sulfonylurea if metformin is not tolerated
  ► metformin as an alternative to a sulfonylurea where . . .

► **R41** Warn a person prescribed a thiazolidinedione about the possibility of significant oedema and advise on the action to take if it develops.

► **R42** . . .
Which decision support is best?

Protocols and guidelines:
- Evidence based (reflect scientific evidence)
- Have been shown to have a positive effect on quality of care
- Non-interactive, often very lengthy textual documents (with fixed structure)
- Are hard to personalise

Decision-support systems:
- Interactive
- Offer one or more problem solving modes
- Relationship to scientific evidence?
- Integration with clinician’s work flow?
The probabilistic approach

- Management (diagnosis, treatment, prognosis) can be formalised: **meta-model**, e.g.,
  - What is a diagnosis?
  - What is a prognosis, etc.

- Medical knowledge is also modelled (**object model**)

- Deployment of:
  - standard probabilistic methods (e.g. Bayes’ rule)
  - probabilistic graphical models, in particular Bayesian networks
Example: VAP in the ICU

- Problem: diagnosis and antimicrobial treatment of patients with ventilator-associated pneumonia (VAP)
- About 15-20% of ICU patients develop VAP
- Mortality rate: up to 40%
- Up to 50% of used antibiotics in ICUs are prescribed for airway infections
Probabilistic model pneumonia

- hospitalisation
- colonisation
- aspiration
- mechanical ventilation
- immunological status
- symptoms signs, lab
- side effects
- antimicrobial therapy
- organism susceptibility
- coverage
- susceptibility
- coverage
- side effects
- antimicrobial therapy
- organism susceptibility
- coverage
- susceptibility
- coverage
Prediction

\[ \text{Pr(pneumonia)} = 1.0 \quad \text{or} \quad \text{Pr(pneumonia)} = ? \]
Integration with ICU

- PHP Module
- Apache HTTP Server
- Web Browser
- CPR
- Reasoning System
- Bayesian Network

- SQL
- Data
- Variable–value pairs
- Variable–value–probability triples

DHTML
Decision-making for patient

Patient enters signs and symptoms, and makes measurements

► Smartphone’s software interprets these data

► mHealth (mobile health)
History of mobile health

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1905</td>
<td>1st electrocardiogram sent via telephone</td>
</tr>
<tr>
<td>1970s</td>
<td>&quot;Telehealth&quot;</td>
</tr>
<tr>
<td>1990s</td>
<td>&quot;eHealth&quot;</td>
</tr>
<tr>
<td>2004</td>
<td>&quot;mHealth&quot;</td>
</tr>
<tr>
<td>2011</td>
<td>124 mln. mHealth users</td>
</tr>
<tr>
<td>2012</td>
<td>≈ 247 mln. mHealth users</td>
</tr>
</tbody>
</table>

### Definitions

**Telehealth**
Healthcare service delivery where physicians examine patients at a distance where information (e.g., voice, an image, a medical record, commands to a surgical robot) is exchanged using electronic means of communication.

**eHealth**
Health services and information delivered or enhanced through the Internet and related technologies.

**mHealth**
The practice of medicine and public health supported by mobile devices.
Telehealth around 1900

- Electrocardiogram was also be recorded a a distance (telehealth, not mobile health!)
- Terminology waves still the same
mHealth for hypertension in pregnancy

Around 15% of the first-time pregnant women develop high blood pressure (hypertension)

Around half of them develop associated problems, such as presence of protein in the urine leading to the pregnancy syndrome of preeclampsia:

- a major cause of maternal and neonatal mortality and morbidity
- 15 to 20% of maternal mortality in developed countries
- frequent out-patient clinic visits
- cure via delivery
Temporal Bayesian network

- **Risk factors**: Age, (family) history of hypertension, diabetes, etc.
- **Laboratory measurements**: from 10 checkups at 12, 16, 20, 24, 28, 32, 36, 38, 40 and 42 weeks of pregnancy
- **VascRisk**
- **Vascular and renal functions**
- **Risk of PE** at future time-points
# Prognostic prediction

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Patient A: Not-preeclamptic</th>
<th>Patient B: Preeclamptic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>26-30</td>
<td>36-40</td>
</tr>
<tr>
<td>Smoking</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Obese</td>
<td>obese</td>
<td>normal</td>
</tr>
<tr>
<td>Chronic HT</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Parity-HistoryPE</td>
<td>parous-yes</td>
<td>parous-yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Per control</th>
<th>12 wk</th>
<th>16wk</th>
<th>20wk</th>
<th>24wk</th>
<th>12 wk</th>
<th>16wk</th>
<th>20wk</th>
<th>24wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>Other</td>
<td>Other</td>
<td>Other</td>
<td>Other</td>
<td>Other</td>
<td>Other</td>
<td>Other</td>
<td>Other</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>127-129</td>
<td>118-120</td>
<td>121-123</td>
<td>121-123</td>
<td>124-126</td>
<td>118-120</td>
<td>118-120</td>
<td>136-138</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>76-79</td>
<td>68-71</td>
<td>72-75</td>
<td>76-79</td>
<td>64-67</td>
<td>72-75</td>
<td>64-67</td>
<td>80-83</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>n/a</td>
<td>6.7</td>
<td>n/a</td>
<td>6.2</td>
<td>7.5</td>
<td>n/a</td>
<td>7.4</td>
<td>7.4</td>
</tr>
<tr>
<td>Creatinine</td>
<td>n/a</td>
<td>58-61</td>
<td>n/a</td>
<td>46-49</td>
<td>50-53</td>
<td>n/a</td>
<td>n/a</td>
<td>62-65</td>
</tr>
<tr>
<td>Protein/Creatinine</td>
<td>n/a</td>
<td>0</td>
<td>n/a</td>
<td>0</td>
<td>0</td>
<td>n/a</td>
<td>n/a</td>
<td>0.3-0.6</td>
</tr>
</tbody>
</table>

\[
P_{PRIOR}(PE) = 0.0014 \quad 0.0076 \quad 0.05 \quad 0.16 \\
P_{CURR}(PE) = 0.003 \quad 0.008 \quad 0.08 \quad 0.18 \\
Rel. change = 1.23 \quad 0.11 \quad 0.60 \quad 0.13 \\
|
| 1.36 | 4.71 | 2.80 | 4.93 |

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What does it look like? – Advice to the patient

The patient gets immediate feedback ...

Current status

Prognostic chart

Measurement analysis
Medical imaging
Breast cancer detection

- national breast cancer screening programme
- decision-making under uncertainty
- interpretation of image features in terms of probabilistic graphical models
- from single- to multi-view interpretation
Singleview CAD system

- Region features: contrast, size, location, margin, spiculation, etc.
- Advantage: a good detection rate per image
- Shortcoming: unsatisfactory performance at a patient level because views are treated independently
Multiview interpretation

Mediolateral oblique view

Craniocaudal view

View–A

View–B

A

B

L

L

L

L

A

B

L

L
Multiview Bayesian network

\[ A_i / B_j = (x_1, x_2, \ldots, x_n) \]

\[ a) \text{ RegNet} \]

\[ b) \text{ ViewNet} \]

- Interpretation of regions of interest (real-valued feature vector): logistic regression
- Combination of region and view information: causal independence
What do you need to work in healthcare?

- You need to be a computing or information scientist
- You need sufficient knowhow about what healthcare professionals do:
  - knowledge about making diagnoses, treating patients
  - knowledge of methods used in medicine and healthcare
  - a tiny bit of knowledge of human biology and diseases
Next week

- Computing Science in healthcare