Detecting and Eliminating Bacteria UsinG Information Technology

Clinical Advisory Board Meeting #3
22nd of November 2010, Geneva

Today's agenda

13:30	Informal coffee	
14:00	Opening, welcome	Didier Pittet
14:15	Review of 2nd CAB meeting Presentation of DebugIT progress year 3	Dirk Colaert
15:15	Peg Study & relation to DebugIT	Philippe Daumke
15:30	Coffee Break	
15:45	Plenary discussion Supporting public health challenges Policy priorities for further developments	Christian Lovis
17:15	Next steps, feedback	José Verguts
17:35	Farewell	Dirk Colaert
19:30	Informal dinner	Christian Lovis

Welcome to the members of the CAB

Prof. Dr. Didier Pittet
Prof. Dr. Javier Garau
Dr. Hans Rutberg

DebugIT members of the CAB:
Dr. Håkan Hanberger
Prof. Dr. Sten Walther

DebugIT collaborators

Christian Lovis, Les Hôpitaux universitaires de Genève, Clinical lead DebugIT

Dirk Colaert, Agfa HealthCare, Scientific lead DebugIT

José Verguts, Agfa HealthCare, Project Manager DebugIT

Karl A. Stroetmann, Empirica Gesellschaft für Kommunikations- und Technologieforschung mbH

Alexander Dobrev, Empirica Gesellschaft für Kommunikations- und Technologieforschung mbH

Christel Daniel, Institut National de la Santé et de la Recherche Médicale

Philipp Daumke, Averbis GmbH

Rationale for a CAB

- Assure ***clinical validity*** and relevance of project results
- ***Clinical input*** to an IT project
- Open results to the ***wider scientific communities***
- Improve ***visibility***

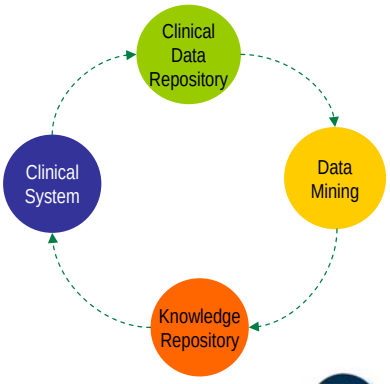
Tasks

- Embed into public health and clinical settings
- identify pertinent clinical research questions
- Advise on the optimal project research process
- Accompany, assess and validate project outputs
- Identify clinical outcome indicators

The debugIT Project (recap)

- the debugIT project
  - collects routinely stored data from clinical systems
  - learns by applying advanced data mining techniques
  - stores the extracted knowledge in repositories
  - applies the knowledge for decision support and monitoring

  - can be used from very low local levels to high strategic global levels



Looking back on the 2nd CAB meeting

Presented by Dirk Colaert

Outcome of CAB#2: Vienna April 2010

- (re-)Confirmation of the relevance of the project
- Importance of
  - monitoring dashboard
    - Early warning by looking at MIC values
    - Various levels of aggregation
    - Compare reality with guidelines
  - decision support
    - Cave overload of information
    - Support for starting the right drug but also for stopping the drug
  - knowledge discovery
    - Literature search: must be easy and intuitive
- Importance of user friendly interface
- Need for global and massive deployment (easy & cheap)

Vienna April 2010

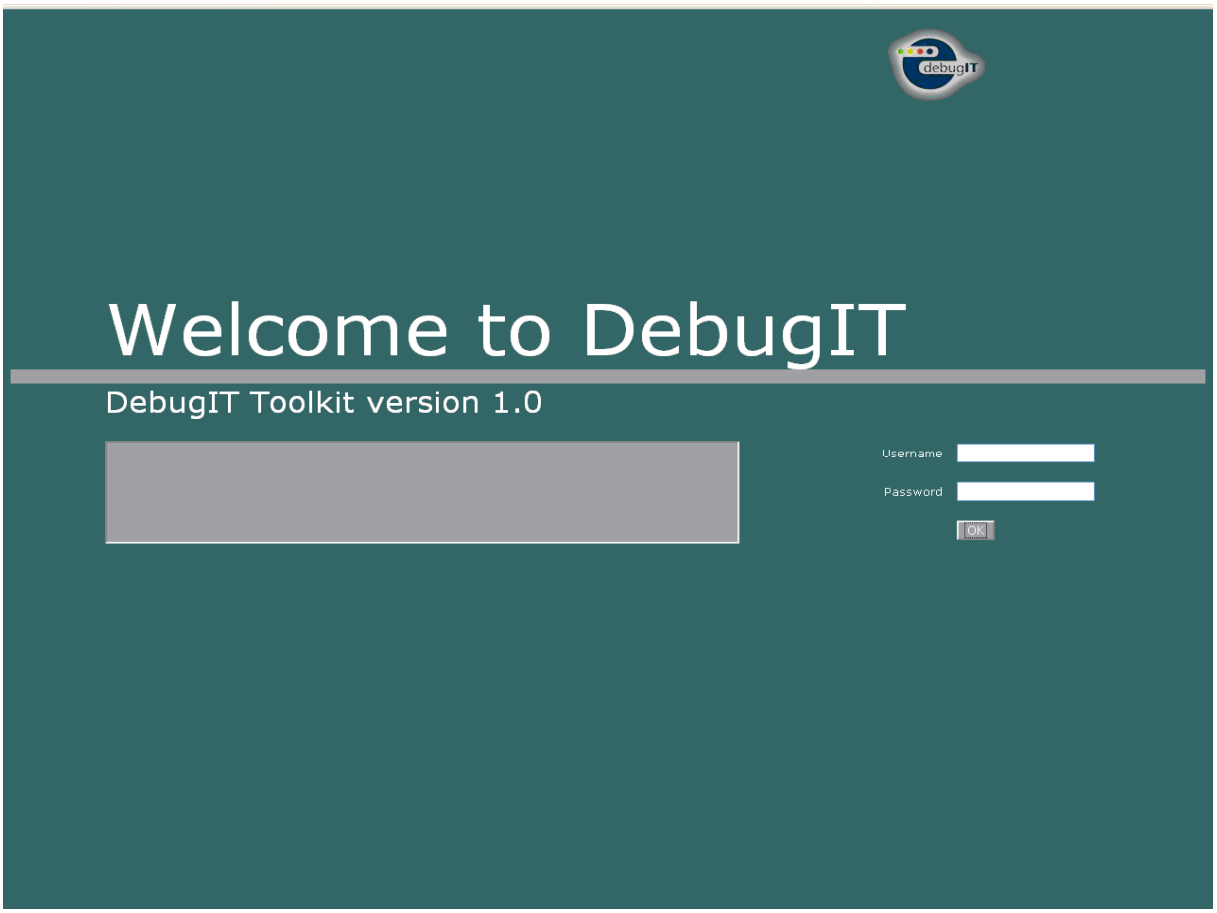
- **Our reaction**
  - Further work on monitoring dashboard & decision support
  - Direct connection to the lab (LIU as proof of concept)
  - Easy, simple, cheap
    - Further automation (less manual interventions)
    - Idea of black box with a limited and fixed set of clinical questions
    - Request to review these questions
  - Exploitation:
    - Planned: contact with ECDC
    - Exploitation plan

Progress in last 6 months

Presented by Dirk Colaert

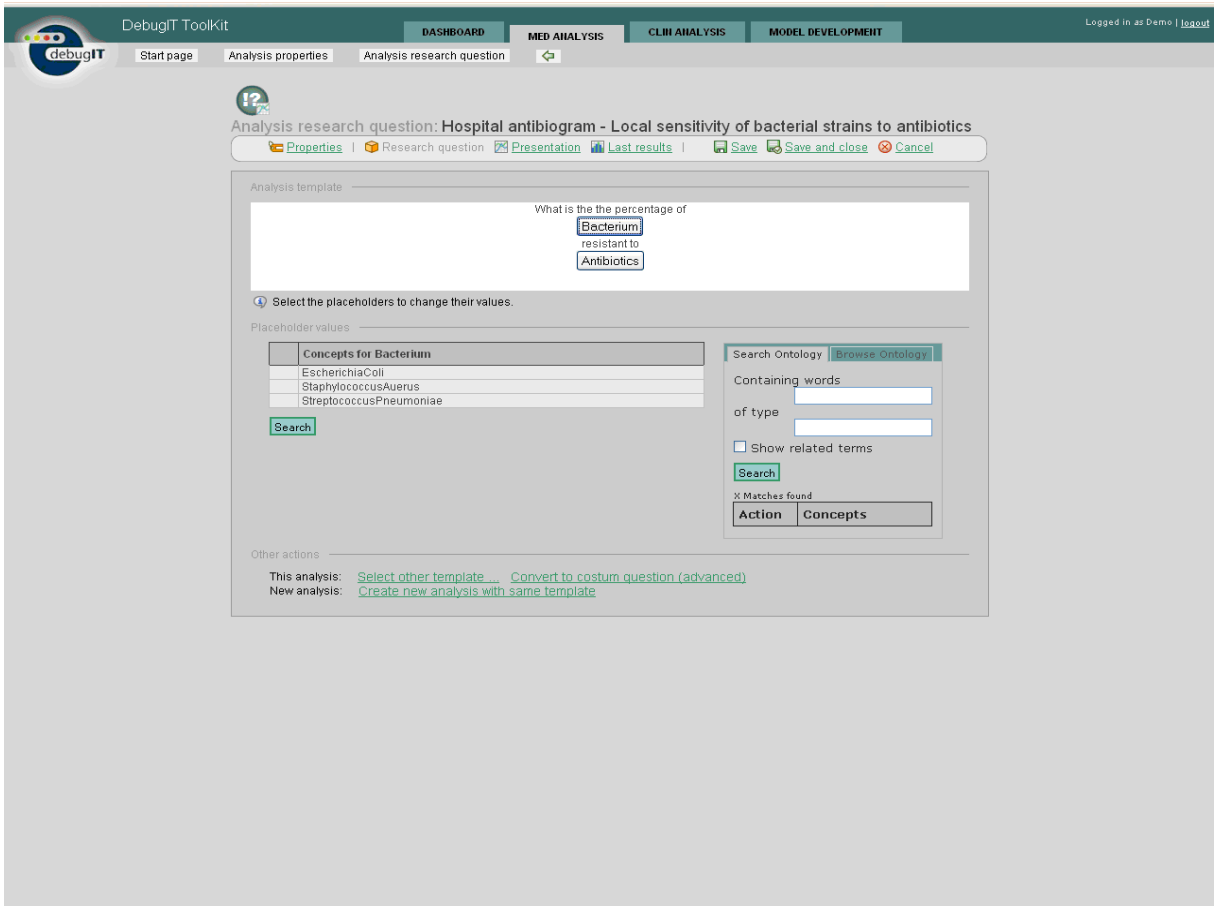
What we achieved since April

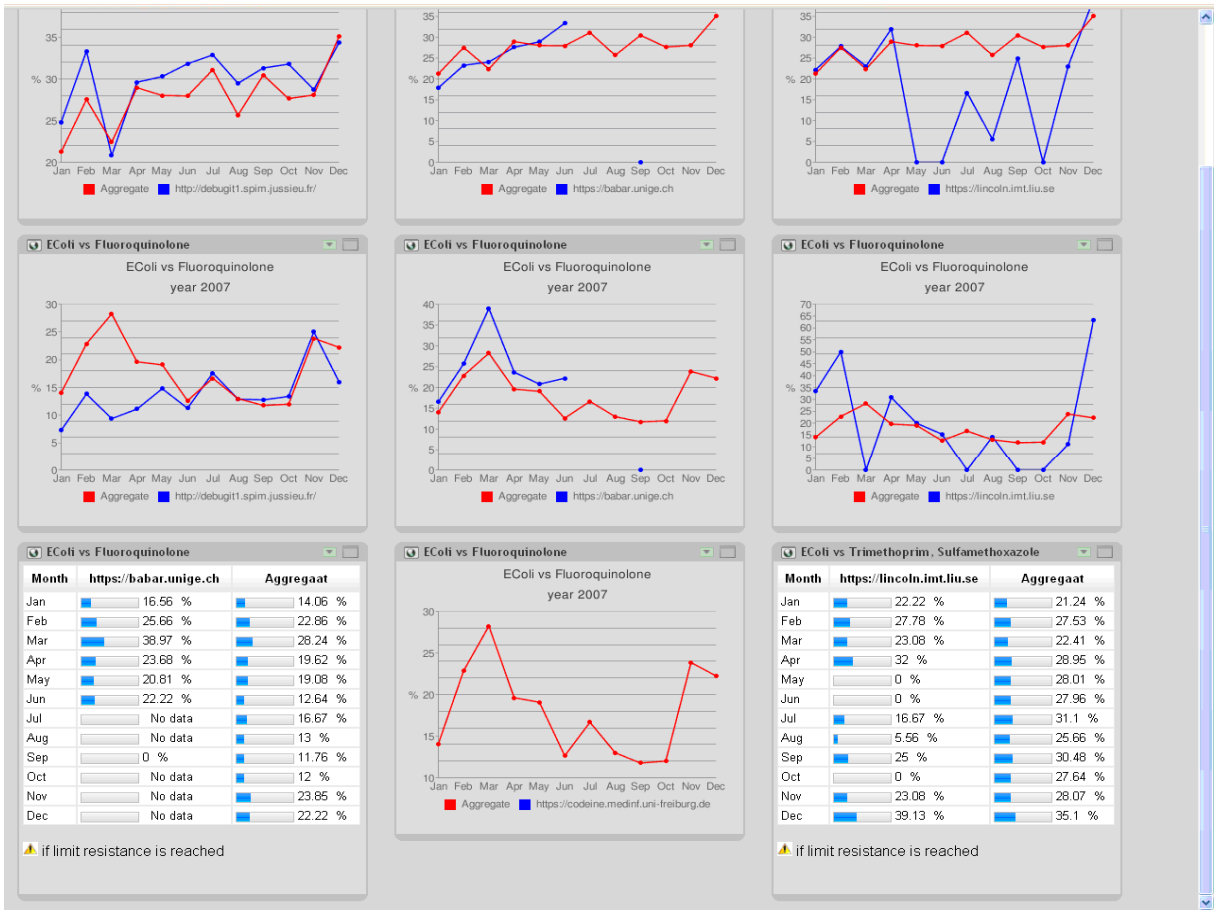
- Closing the loop and automation of the whole cycle
- We defined a set of clinical queries



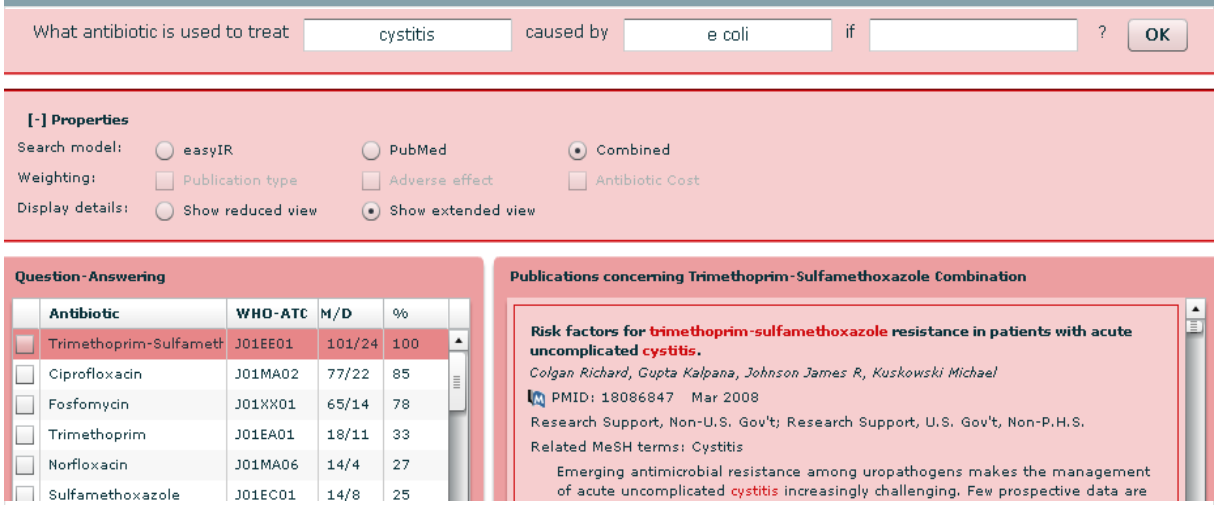
Monitoring Dashboard

Presented by the DebugIT team

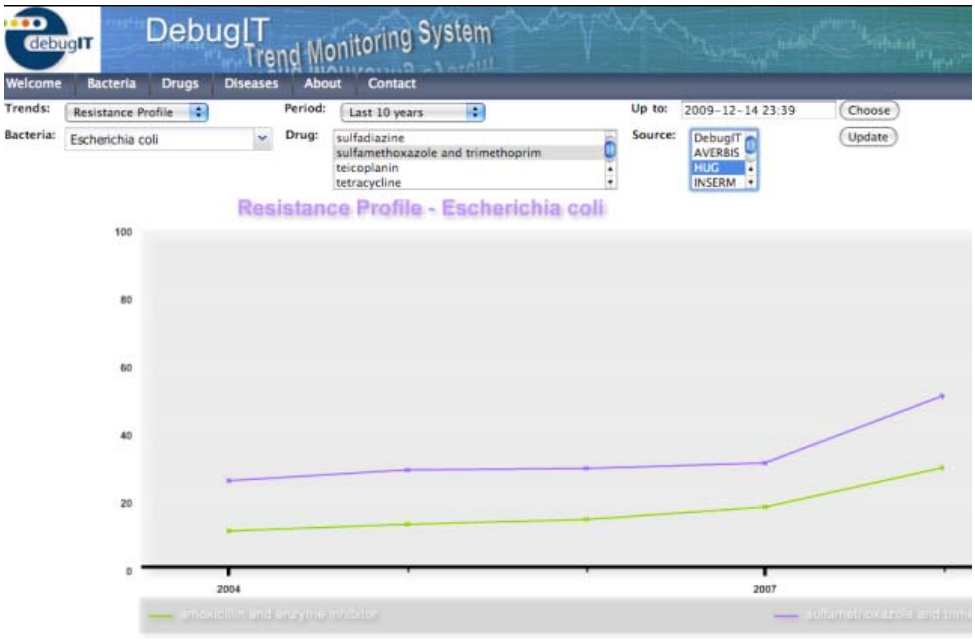

DebugIT ToolKit
DASHBOARD
MED ANALYSIS
CLIN ANALYSIS
MODEL DEVELOPMENT
Logged in as Demo | logout
Start page
Analysis properties
Analysis research question
Analysis research question: Hospital antibiogram - Local sensitivity of bacterial strains to antibiotics
Properties | Research question | Presentation | Last results | Save | Save and close | Cancel
Analysis template
What is the the percentage of
Bacterium
resistant to
Antibiotics
Select the placeholders to change their values.
Placeholder values
Concepts for Bacterium
EscherichiaColi
StaphylococcusAuerus
StreptococcusPneumoniae
Search
Search Ontology
Browse Ontology
Containing words
of type
Show related terms
Search
X Matches found
Action
Concepts
Other actions
This analysis: Select other template ... Convert to costum question (advanced)
New analysis: Create new analysis with same template


Aggregate
http://debugit1.spim.jussieu.fr/
https://babar.unige.ch
https://lincoln.imt.liu.se
EColi vs Fluoroquinolone
EColi vs Fluoroquinolone
year 2007
EColi vs Trimethoprim, Sulfamethoxazole
Month
https://babar.unige.ch
Aggregaat
Jan 16.56 % 14.06 %
Feb 25.66 % 22.86 %
Mar 38.97 % 28.24 %
Apr 23.68 % 19.62 %
May 20.81 % 19.08 %
Jun 22.22 % 12.64 %
Jul No data 16.67 %
Aug No data 13 %
Sep 0 % 11.76 %
Oct No data 12 %
Nov No data 23.85 %
Dec No data 22.22 %
if limit resistance is reached
https://codeine.medinf.uni-freiburg.de
https://lincoln.imt.liu.se
Jan 22.22 % 21.24 %
Feb 27.78 % 27.53 %
Mar 23.08 % 22.41 %
Apr 32 % 28.95 %
May 0 % 28.01 %
Jun 0 % 27.96 %
Jul 16.67 % 31.1 %
Aug 5.56 % 25.66 %
Sep 25 % 30.48 %
Oct 0 % 27.64 %
Nov 23.08 % 28.07 %
Dec 39.13 % 35.1 %
if limit resistance is reached

Text Mining



Trend monitoring across sites

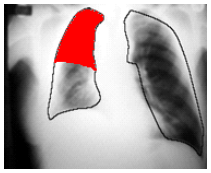


Frequent patterns

#	Support #	Support %	Pattern
5	1069	15.79%	Ts([]); A([], 1-> ["Resistant"])
			Explanation: there is a treatment followed by an antibiogram which indicates that the bug is resistant to the treatment.
8	623	9.2%	A([]); Ts([], 1-> ["Resistant"])
			Explanation: There is an antibiogram followed by a treatment, treatment to which the bug tested in the antibiogram is resistant.
42	508	7.5%	Ts([]); A([], 1-> ["Resistant"]); Ts([], 1-> ["Different"], 2-> ["AntibioticResistance"])
			Explanation: A treatment is followed by an antibiogram to which the bug tested is found to be resistant to the first treatment. The antibiogram is followed by another treatment different from the first one. The relation of the second treatment to the antibiogram can be anything, i.e. Resistant, Sensitive, Intermediate, Not Tested.

Image & data mining

- If we can do this:

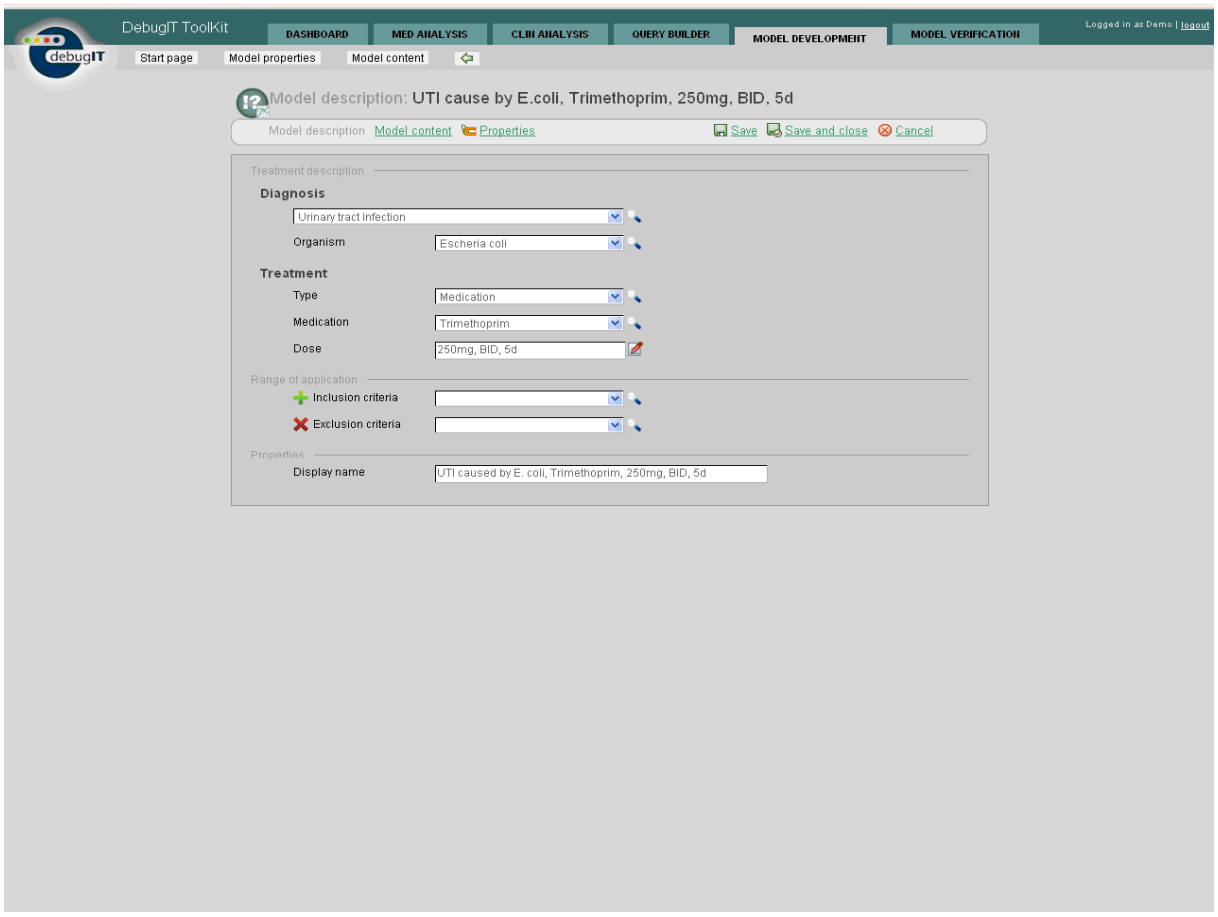


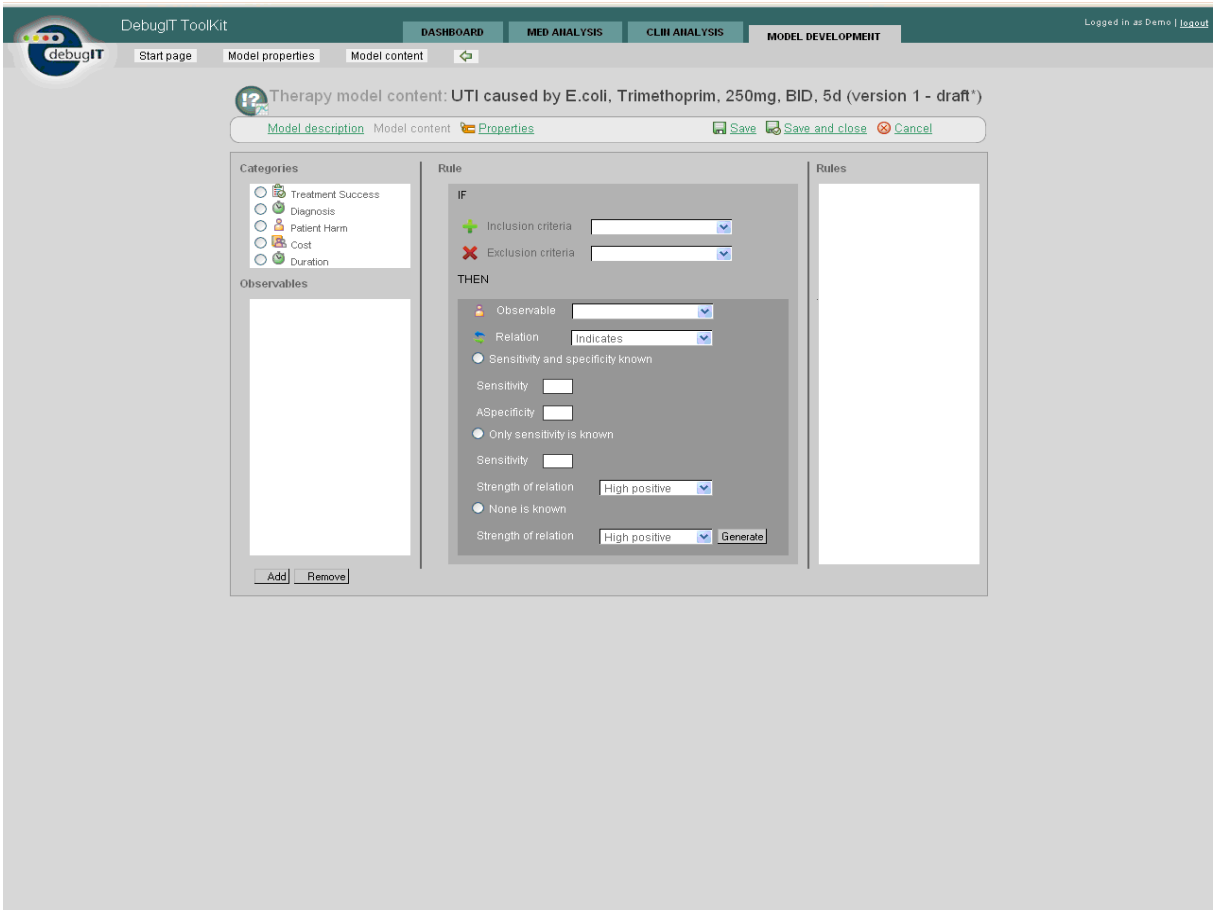
- Lung consolidations?
  - Left, Right, Both, None
- Extent of consolidations?
  - Left 0%
  - Right 45%

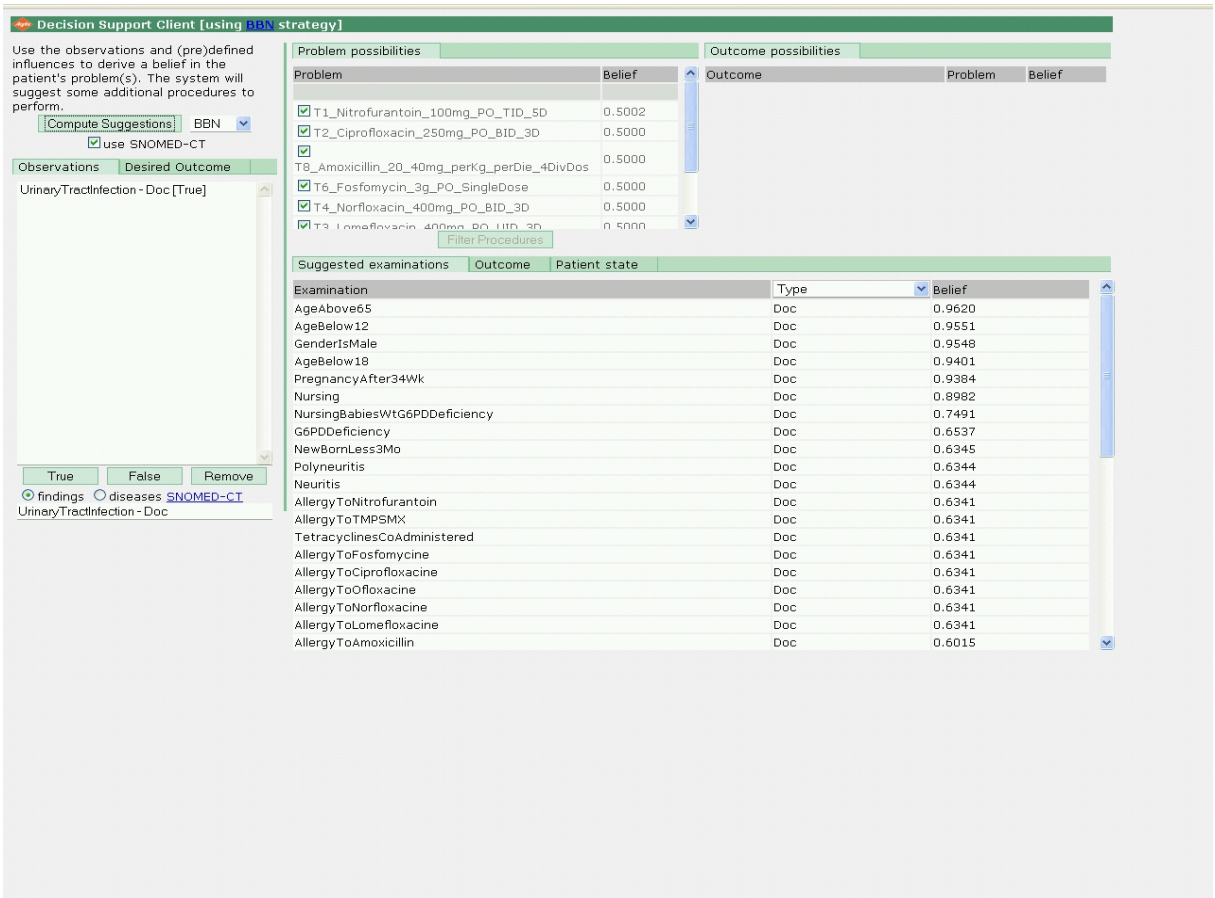
- Can we prevent adverse events ?
  - If the patient is under antibiotic treatment and the consolidations increase,
    - the infection possibly progresses
    - alert for possible mistreatment
- Can we answer some clinical questions ?
  - Are there differences between laboratory and image evidences as an infection progresses/treated?
  - What kinds of bacteria produce similar image evidences?

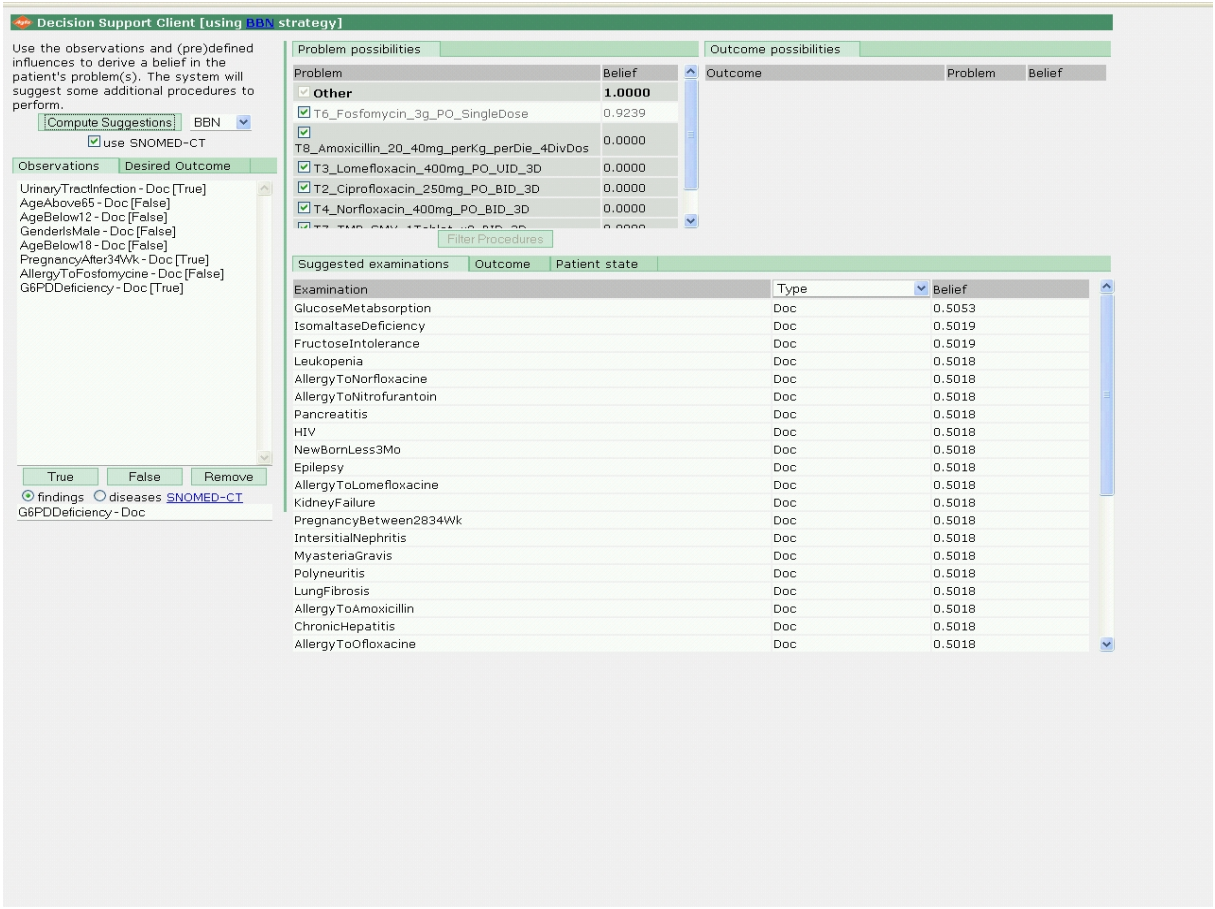
Decision support

Presented by the DebugIT team




DebugIT ToolKit
DASHBOARD
MED ANALYSIS
CLIN ANALYSIS
MODEL DEVELOPMENT
Logged in as Demo | logout
Start page
Model properties
Model content
Therapy model content: UTI caused by E.coli, Trimethoprim, 250mg, BID, 5d (version 1 - draft*)
Model description
Model content
Properties
Save
Save and close
Cancel
Categories
Treatment Success
Diagnosis
Patient Harm
Cost
Duration
Observables
Rule
IF
Inclusion criteria
Exclusion criteria
THEN
Observable
Relation
Indicates
Sensitivity and specificity known
Sensitivity
ASpecificity
Only sensitivity is known
Sensitivity
Strength of relation
High positive
None is known
Strength of relation
High positive
Generate
Rules
Add
Remove


Decision Support Client [using BBN strategy]
Use the observations and (pre)defined influences to derive a belief in the patient's problem(s). The system will suggest some additional procedures to perform.
Compute Suggestions
BBN
use SNOMED-CT
Observations
Desired Outcome
UrinaryTractInfection - Doc [True]
True
False
Remove
findings
diseases
SNOMED-CT
UrinaryTractInfection - Doc
Problem possibilities
Problem
Belief
T1_Nitrofurantoin_100mg_PO_TID_5D 0.5002
T2_Ciprofloxacin_250mg_PO_BID_3D 0.5000
T8_Amoxicillin_20_40mg_perKg_perDie_4DivDos 0.5000
T6_Fosfomycin_3g_PO_SingleDose 0.5000
T4_Norfloxacin_400mg_PO_BID_3D 0.5000
Filter Procedures
Outcome possibilities
Outcome
Problem
Belief
Suggested examinations
Outcome
Patient state
Examination
Type
Belief
AgeAbove65 Doc 0.9620
AgeBelow12 Doc 0.9551
GenderIsMale Doc 0.9548
AgeBelow18 Doc 0.9401
PregnancyAfter34Wk Doc 0.9384
Nursing Doc 0.8982
NursingBabiesWtG6PDDeficiency Doc 0.7491
G6PDDeficiency Doc 0.6537
NewBornLess3Mo Doc 0.6345
Polyneuritis Doc 0.6344
Neuritis Doc 0.6344
AllergyToNitrofurantoin Doc 0.6341
AllergyToTMPSMX Doc 0.6341
TetracyclinesCoAdministered Doc 0.6341
AllergyToFosfomycine Doc 0.6341
AllergyToCiprofloxacine Doc 0.6341
AllergyToOfloxacine Doc 0.6341
AllergyToNorfloxacine Doc 0.6341
AllergyToLomefloxacine Doc 0.6341
AllergyToAmoxicillin Doc 0.6015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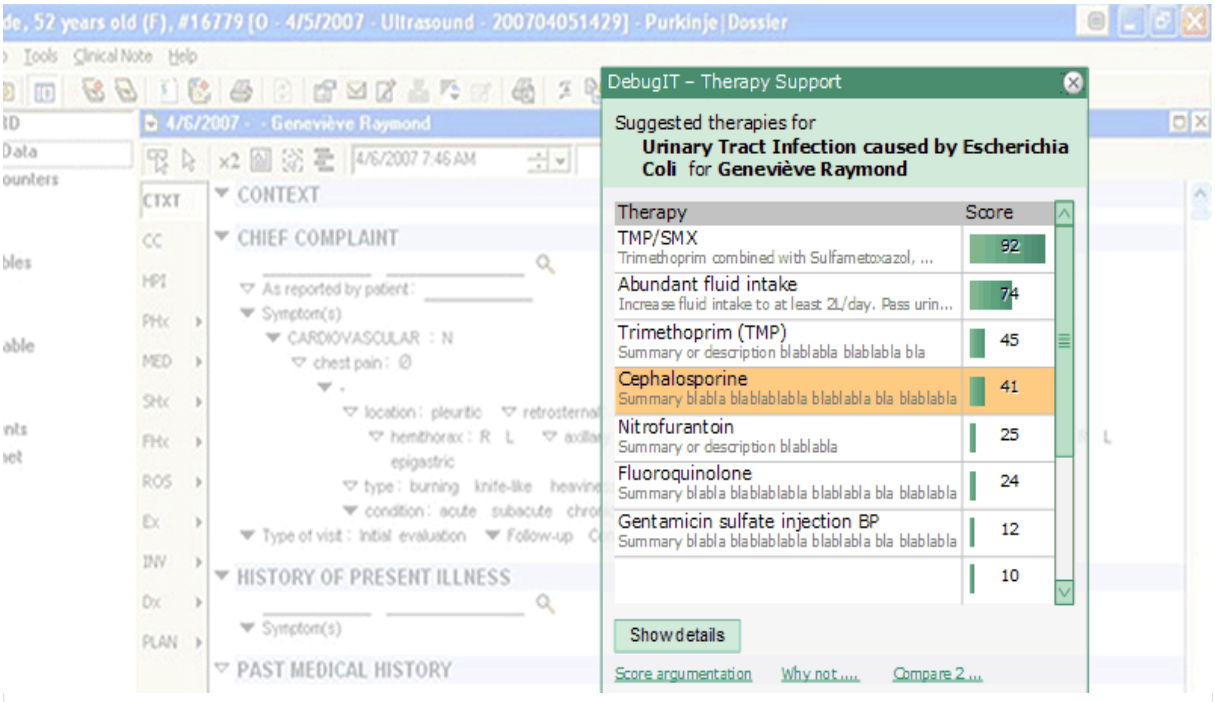
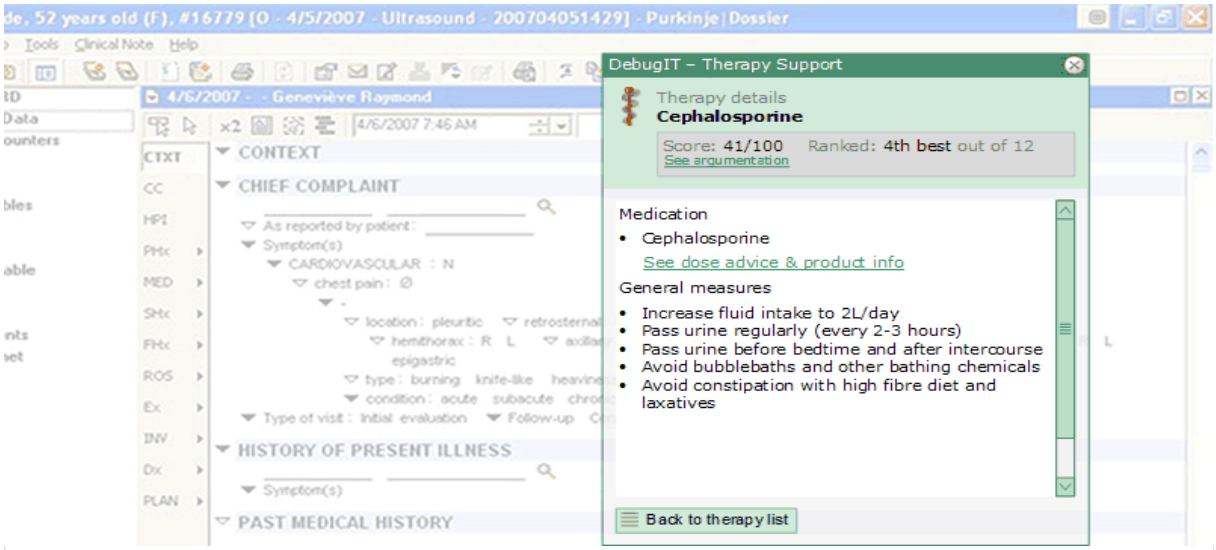
Use the observations and (pre)defined influences to derive a belief in the patient's problem(s). The system will suggest some additional procedures to perform.
Compute Suggestions
BBN
use SNOMED-CT
Observations
Desired Outcome
UrinaryTractInfection - Doc [True]
AgeAbove65 - Doc [False]
AgeBelow12 - Doc [False]
GenderIsMale - Doc [False]
AgeBelow18 - Doc [False]
PregnancyAfter34Wk - Doc [True]
AllergyToFosfomycine - Doc [False]
G6PDDeficiency - Doc [True]
True
False
Remove
findings
diseases SNOMED-CT
G6PDDeficiency - Doc
Problem possibilities
Problem
Belief
Other 1.0000
T6_Fosfomycin_3g_PO_SingleDose 0.9239
T8_Amoxicillin_20_40mg_perKg_perDie_4DivDos 0.0000
T3_Lomefloxacin_400mg_PO_UID_3D 0.0000
T2_Ciprofloxacin_250mg_PO_BID_3D 0.0000
T4_Norfloxacin_400mg_PO_BID_3D 0.0000
Filter Procedures
Outcome possibilities
Outcome
Problem
Belief
Suggested examinations
Outcome
Patient state
Examination
Type
Belief
GlucoseMetabsorption Doc 0.5053
IsomaltaseDeficiency Doc 0.5019
FructoseIntolerance Doc 0.5019
Leukopenia Doc 0.5018
AllergyToNorfloxacine Doc 0.5018
AllergyToNitrofurantoin Doc 0.5018
Pancreatitis Doc 0.5018
HIV Doc 0.5018
NewBornLess3Mo Doc 0.5018
Epilepsy Doc 0.5018
AllergyToLomefloxacine Doc 0.5018
KidneyFailure Doc 0.5018
PregnancyBetween2834Wk Doc 0.5018
IntersitialNephritis Doc 0.5018
MyasteriaGravis Doc 0.5018
Polyneuritis Doc 0.5018
LungFibrosis Doc 0.5018
AllergyToAmoxicillin Doc 0.5018
ChronicHepatitis Doc 0.5018
AllergyToOfloxacine Doc 0.5018


de, 52 years old (F), #16779 [0 - 4/5/2007 - Ultrasound - 200704051429] - Purkinje | Dossier
Tools
Clinical Note
Help
4/6/2007 - - Geneviève Raymond
CONTEXT
CHIEF COMPLAINT
HISTORY OF PRESENT ILLNESS
PAST MEDICAL HISTORY
DebugIT – Therapy Support
Suggested therapies for
Urinary Tract Infection caused by Escherichia Coli for Geneviève Raymond
Therapy
Score
TMP/SMX
Trimethoprim combined with Sulfametoxazol, ...
92
Abundant fluid intake
Increase fluid intake to at least 2L/day. Pass urin...
74
Trimethoprim (TMP)
Summary or description blablabla blablabla bla
45
Cephalosporine
Summary blabla blablablabla blablabla bla blablabla
41
Nitrofurantoin
Summary or description blablabla
25
Fluoroquinolone
Summary blabla blablablabla blablabla bla blablabla
24
Gentamicin sulfate injection BP
Summary blabla blablablabla blablabla bla blablabla
12
10
Show details
Score argumentation
Why not ....
Compare 2 ...



Clinical questions

- 1) What percentage of Escherichia coli cases cultured from urine samples is resistant to the combination of trimethoprim/sulfametoxazol (TMP/SMX) or trimethoprim over a period x in ward/hospital/community y?
- 2) What percentage of Escherichia coli cases cultured from urine samples is resistant to fluoroquinolones over a period x in ward/hospital/community y?
- 3) What is the % of empirical antibiotic therapies confirmed by an antibiogram?
- 4) What is the percentage of culture-based antibiotic therapies confirmed by an antibiogram?
- 5) What is the % of antibiogram-based antibiotic therapies compliant with the antibiogram? (Assumed: did physician decided to give something else than tested sensitive AB?

Clinical questions

- Pneumonia in steps (LIU):
  - 6) step 1: Select all episodes of care having a diagnose of pneumonia and divide them in “Bacterial”, “Viral” and “other”.
  - 7) step 2: Dividing Bacterial pneumonia in modest and severe.
    - = clinical decision based on the clinical findings needed e.g.: “reason for admission”
    - LIU available: type of clinic/ward as a proxy: general hospital ~ modest; intensive care (ICU) ~ severe
    - See also criteria for modest and severe -> rules
  - 8) step 3: Dividing the group Bacterial pneumonia in community acquired and hospital acquired.
    - needed e.g.: “reason for admission”; patient from home: community acquired; patient from other ward/ICU or other hospital: hospital acquired
    - Cave 'colonisation' instead of infection
  - 9) step 4: Describing the bacterial distribution in the two/four groups in step 3.
    - four groups: modest community, modest hospital, severe community, severe hospital
    - distribution table for each bacteria found
    - extended with sampling site, starting with blood and airways
      - blood: anywhere from circulating blood. Note: sample from “around the central venous catheter (CVC)” usually represents the skin and not the blood stream.
      - Airways: nasopharynx, sputum, tracheal, broncoscopic and similar.Note: mouth is usually not considered representing the airways.
  - 10) step 5: Finding the main culture/antibiogram for each bacterial pneumonia considering bacterial pneumonia as the main reason for this episode of care, we only want to study the result of cultures from airways or blood taken within the first 24 hours from admission. -> rule
  - 11) step 6: Comparing antibiogram from the main culture in step 5 with guidelines' recommended treatment, for four groups of step 4
    - Note: recommendation depending on modest/severe and the source of the bacteria community/hospital acquired.
  - 12) step 7: Describing severity of pneumonia with clinical information. Note: different types of info needs to be simultaneously

Clinical questions

- Public health
  - 13) What is the evolution of the prevalence of bacterium x infection during period y in ward/hospital/community z, with which sample type taken?
    - prevalence: number of infected individuals in a population, divided by the total number of individuals in that population, on a certain moment
    - Assuming: prevalence of bacterium x = infection, not colonisation
  - 14) Evolution intime of the previous
  - 15) What is the AB used
    - in which type of antibiotic treatment (empirical/culture-based/ABG-based) of bacterium x infection,
    - in which type of place (ward/hospital/community),
    - with which sample type taken?
  - 16) as 13) + 14) + 15)
  - 17) as 14) + 15)
- Hospital infection control
  - 18) same as 13) for ward/hospital
  - 19) same as 14) for ward/hospital
  - 20) same as 15) for ward/hospital
  - 21) as 18) + 19) + 20)
  - 22) as 19) + 20)
  - 23) What percentage of patients
    - with which infection,
    - with which sample type taken,
    - get which AB in which type of antibiotic therapy, during which period?
  - 24) What percentage of antibiotic therapies changed,
    - for which infection,
    - with which sample type taken,
    - during which period?
    - Assuming: AB changed
  - 25) What percentage of antibiotic therapies changed from AB x to AB y?
    - Note: project result could be: "this data should be in EHR in structured format“

Clinical questions

- Image mining:
  - 26) What is the percentage of cases of bacterial pneumonia, after antibiotic treatment, in a period of 2002-2009, showing a decrease of lung consolidation on RX thorax of more than 50%?
  - 27) What is the evolution of resistance to <AB1..n> (of <BUG 1..n>) during period <t> (at location <locations1..n>) (in sample <SAMPLE 1..n>)?
- MIC related
  - 28) Can a resistance be predicted by following MIC values
- Decision support:
  - 1) How to treat lower urinary tract infections caused by Escherichia coli?
  - 2) Is AB conform ABG?
  - 3) What is preferred AB in certain type of antibiotic treatment for certain infection, having certain sample?
  - 4) What is preferred AB in certain type of antibiotic treatment in case of certain symptoms?
  - 5) What are 'usual' bacteria found in certain sample?

Questions for the CAB

- Relevant clinical questions ?
- Relevant pathologies, bacteries ?
- Relevance of image mining ?
- Local versus global data sets ?
- Acceptance by clinicians ?!
  - How to motivate physicians to use it ? (comparison between own results and peers ?)
  - How can we deal with poor quality and structure of the data ?
  - Visualization hints ?
  - How to include into daily practice ?
  - How intrusive should it be ?

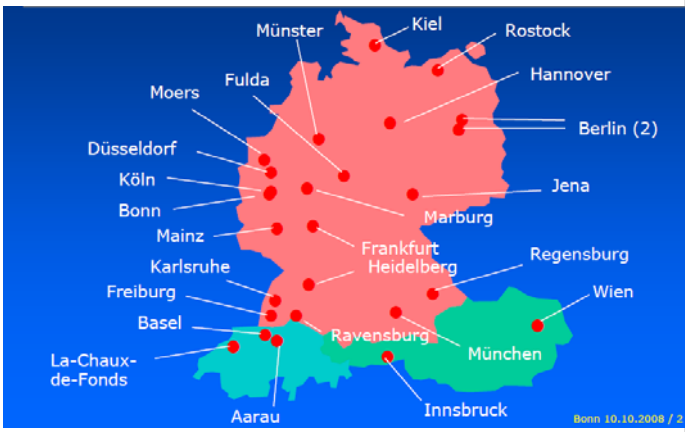
averbis
medical language technology

Highlights from the PEG study 2007
Relation to DebugIT

Dr. med. Philipp Daumke

PEG resistancy study 2007

- Since 1975
- 26 laboratories
- 240 isolates per lab
  - 30 Staph. Aureus
  - 30 coag. neg. Staph.
  - 30 Entercoccus
  - 20 Strep. pneumoniae
  - 80 Enterobacteriaceae
  - 30 Pseud. aerug.
  - 20 Acinetobacter baum. & Steno-trophomonas maltophilia
- 5.908 bugs in total
- Materials
  - Wounds (25,9%)
  - Urine (17,7%)
  - Resp. Tract (19,9%)
  - Blood (12,3%)
- Origin
  - Ambulant (17,2%)
  - Gen. Ward (56,2%)
  - ICU (24,2%)
  - Not sp. (2,5%)



Methods

- Microdilution (DIN EN ISO 20776-1), Microtitration plate from Merlin GmbH, CAMHB als test medium (from Becton Dickinson)
- 30 antibiotics and 6 antibiotics/β-lactam inhibitor combinations
- Quality control:
  - Control stems
  - MIC checks in a reference laboratorium
- Evaluation: EUCAST reference figures
- Detection of ESBL (extended spectrum beta-lactamase)-prod. stems according to criteria of Clinical Laboratory Standards Institute (CLSI)

Results (2004 → 2007)

Fluorchinolon (Ciprofloxacin)
- E.coli: 22,3% → 26,4%
- Staph. Aureus: 23,2% → 27,7%
- Pseudomonas aeruginosa: 22,3% → 18%

ESBL (extended spectrum beta-lactamase) producing:
- E.coli 5,1% → 10,3%
- Klebsiella pneumoniae 7,3% → 10,3%

Staph. aureus
- MRSA 17,5% → 20,3%
- Resistent to Erythromycin and Gentamicin 3% ↓
- Glycopeptids (Vanc., Teicoplanin) 0%

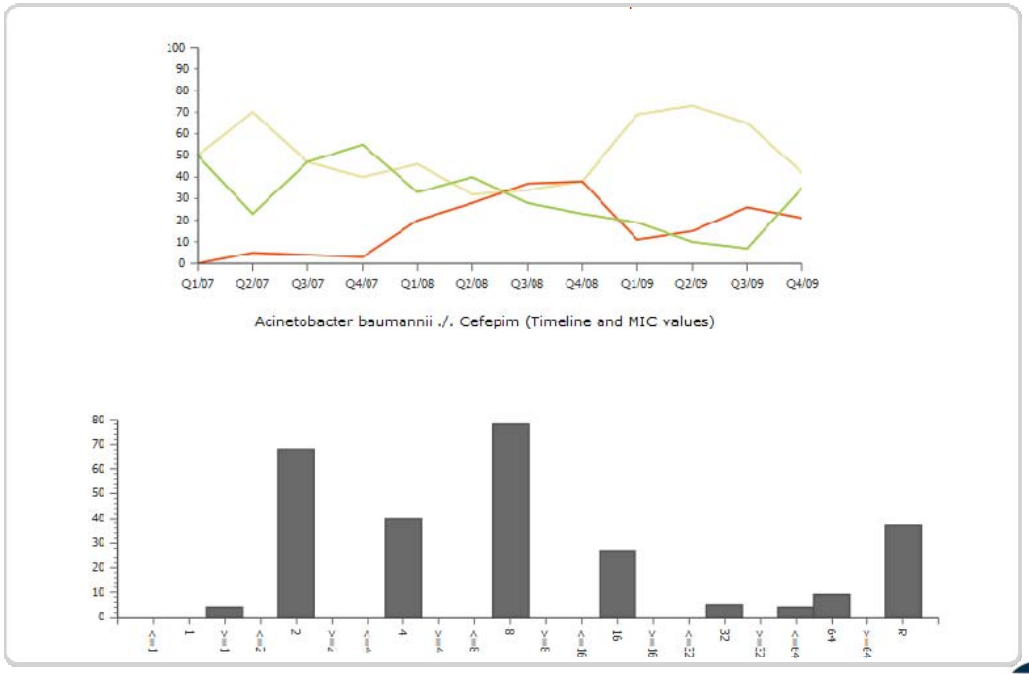
Staph. Epidermidis 15,4% Teicoplanin-intermed., 2,1% resistant

Glycopeptids
- Enterococcus faecium 10,8% (Vanc.), >50% Teicoplanin (VanA phenotype)

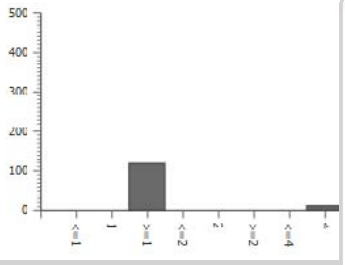
What we currently have in DebugIT - Data

Partner	Bacteria	Drugs	Results	Period	MICs
Averbis	479	71	1156599	1/07-12/09	+
Gama	3	3	2504	5/2010	-
HUG	248	96	726391	1/04-6/08	-
INSERM	291	8170	2447317	1/01-2/10	-
IZIP	-	-	-	-	-
LIU	55	65	61773	1/05-2/10	-
Teilam	20	222	288	8/06-1/10	-

MIC values from Freiburg



Citrobacter freundii ./. Ceftazidim (Timeline and MIC values)



MHK (mg/l)	0.25	0.5	1	2	4	8	16	32	64	%-S	%-I	%-R
absout	33	6	3	2	4	3	3	4	23	51.9	11.1	37.0
kumuliert %	40.7	48.1	51.9	54.3	59.3	63.0	66.7	71.6	100.0			

Grenzwert(e): EUCAST (v 2.0)

Averbis vs. PEI

Open issues & Next steps

- Methodological issues
  - Different data (time periods, test methods, reference values)
  - No live data
  - Unknown data quality, no quality control
- Technical issues
  - Performance of D2R server
  - Coherent mappings to DCO (ddo2dco mappings)
- Next steps
  - Work on open issues above?
  - Reproducing PEG results?
  - Systematically identifying local resistancy changes (alert system)?
  - Defining requirements with ECDC?

Today's agenda

13:30	Informal coffee
14:00	Opening, welcome
14:15	Review of 2nd CAB meeting
	Presentation of DebugIT progress year 3
15:15	Peg Study & relation to DebugIT
15:30	**Coffee Break**
15:45	Plenary discussion
	Supporting public health challenges
	Policy priorities for further developments
17:15	Next steps, feedback
17:35	Farewell
19:30	Informal dinner

Supporting public health challenges
Policy priorities for further developments

Plenary discussion

Moderated by Christian Lovis

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Next steps, feedback

José Verguts, Agfa HealthCare

Feedback, next steps

First feedback

Review of deliverable(s)?

Next meeting: when-where-format

Farewell… informal dinner

19:30

The DebugIT Consortium

Remuneration

- ***Travel and accommodation*** costs for participation at Board or Committee meetings will be reimbursed as a lump sum
- ***Review of deliverables*** will be remunerated with a lump sum, depending on the scope and size

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