SECTION 1. PUBLISHABLE SUMMARY

1.1 Overall description of the debugIT project

Improving the quality of healthcare and patient safety are priority health policy goals globally. Despite half a century of antibiotic use, re-emerging and new infectious diseases, partially caused by the rise of antimicrobial resistance, have become important problems. This increasing prevalence of resistance results in escalating healthcare costs, increased morbidity and mortality and the (re-) emergence of potentially untreatable conditions. The DebugIT project is developing an IT-framework to allow health care systems to better address these emergent problems and improve their management. In the context of infectious diseases, DebugIT

- detects patient safety related patterns and trends,
- acquires new knowledge through advanced data mining, and
- uses this knowledge for better decision-making on the optimal treatment for infectious diseases,
- thereby improving the quality of healthcare.

The problem: the rapid emergence of resistance among pathogens, the misuse and overuse of antibiotics

Although medical errors are currently under the spotlight, (re-)emerging infectious diseases are also becoming an important challenge. The rapid development of antimicrobial resistance, the spread of nosocomial and other infections are major concerns.

The impact of this phenomenon is most apparent in hospitals. However, community-based practice is not immune, due to the frequency and rapidity of patient transfers between the two sectors and citizen mobility. Hence, epidemics are a regular occurrence and may spread between continents. Examples of such epidemics are methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococci or multiresistant tuberculosis. In addition, as a result of the efforts made in harmonising data on infections and antimicrobial resistance across Europe, it has become clear that a wide variability in preventive practices and outcomes across European countries exists, indicating considerable leeway for improvement.

The DebugIT response

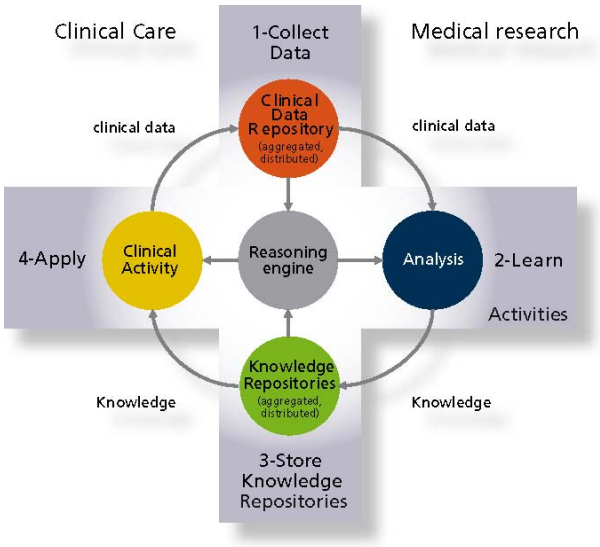
To address the challenges of improving antibiotic therapy and reducing antimicrobial resistance, the DebugIT project will make use of data that are already routinely collected and stored in electronic Clinical Information Systems (CIS) in hospitals and primary care clinics. Today however, this occurs in widely differing systems. The DebugIT challenge is to establish the coherent and systematic exchange of a rich data set, harmonised across the DebugIT sites and their CIS systems. This data set will primarily include information about pathogens and drug treatments.

DebugIT is adopting a multi-stage framework of several distinct steps:

- **Collect Data:** Clinical data is aggregated from across different hospitals, countries, languages and information models, via advanced and commonly agreed data models (minimum data sets), standards and mapping algorithms, organized in a virtualized, decentralized but fully integrated Clinical Data Repository (CDR)
- **Learn:** Advanced data mining techniques on multimodal, multi-source, structured and unstructured data to detect patterns, relevant for patient safety and the better treatment of infectious diseases.
- **Store Knowledge**: This knowledge will be stored, validated, visualized and aggregated together with pre-existing medical and biological knowledge (guidelines, regulations) in a federated knowledge repository to achieve a consolidated view on the required knowledge.
- **Apply:** The new knowledge will be applied to the monitoring of ongoing care activities and outcomes, and may help to predict future outcomes to give additional support to treatment decision on individual patients and for populations. To a lesser extent, due to the rescoping of the project and based on the input of the Clinical Advisory Board, decision support tools will apply the newly generated knowledge and help the clinician to provide improved clinical care (choice, dose and administration of antibiotics for example).

DebugIT will allow healthcare providers and decision makers to take appropriate actions at various levels in the healthcare system, including policy, point-of-care, service management, and subsequently influence the

future development of our health systems. Integration of DebugIT tools into existing CIS will enable the recording of activities and results and thus make sure the necessary data are generated for a next cycle of learning.
Throughout this process, DebugIT will pay strong attention to privacy concerns, taking into account the various legal and ethical frameworks that must be met across Europe.



Expected outcomes

DebugIT will contribute to achieving world-leading levels of patient safety with fewer medical errors and optimised medical interventions. The learn-predict-prevent approach embodied in the knowledge base and the decision support system of DebugIT will contribute to effective and automated risk prediction. Further expected outcomes are:

- Clinical Information Systems (CIS) of participating European hospitals, industry and their clients are updated with DebugIT knowledge
- New knowledge will be made available at a global level, preferably through a European or global Disease Control Centre/Public Authority, and/or through Open Source services
- New, advanced ICT applications and innovations will be marketed in the following domains: virtualization of Clinical Data Repository information, advanced multimodal data mining techniques on text, image and distributed storage, use of machine reasoning related to real, point of care patient data
- A distributed Medical Knowledge Repository integrated with domain knowledge coming from external sources (guidelines and scientific evidence)
- Innovative and user friendly knowledge representation paradigms for both clinicians and IT experts

Feeding DebugIT results into applications

Real world examples of applications benefiting from DebugIT research include

- Computerised Physician Order Entry (CPOE) systems, integrated with, e.g., drug data bases and/or clinical decision support systems,
- Adverse Drug Event (ADE) reporting solutions, and hospital-wide Clinical Information Systems (CIS), Health Database Systems, or Electronic Health Record (EHR) Systems, and
- Integration of knowledge translation and decision support into hospital systems.

Above all, the DebugIT project is a good example of how to achieve **Translational and Evidence Based Medicine**:

- clinical information is used to support medical research and to enhance medical knowledge,
- the new evidence – the outcome of the research - is used to support clinical care.

Although the DebugIT project is focusing on infectious diseases, its translational framework will be suitable for many other clinical problems, providing a solution to increase patient safety and enhance the quality of care.

1.2 Progress in year three

In the scheme below the overall timing and project orientation is listed:

- Year 1: investigation and requirements
- Year 2: design, prototyping, closing the loop
- Year 3: automatization and deploying
- Year 4: exploitation

During year three we focused on finishing the technical development and glue the different pieces together. Based on the input of the Clinical Advisory Board we limited the set of clinical questions to be answered by the system to a set of bacterial resistance related questions.

1.2.1 Scientific approach

The scientific approaches and choices are based on the investigations in year 1 to 3 and can be summarized as follows:

- Ontology engineering: we follow a dual approach. We build a DebugIT Core Ontology (DCO), capturing the concepts of the medical domain of infectious diseases. This ontology is based on the high level concepts of BioTop and is made in OWL-DL. The purpose of DCO is to describe the domain in a comprehensive and complete way. Besides DCO we are building a set of so called *operational* ontologies. These are ontologies with a domain of discourse more directed to the actual implementation and usage of the system: These ontologies formalize domains such as query building, statistics, analysis, evidence classes, reasoning, etc…. These ontologies reuse existing ontologies as much as possible and use OWL Full formalization. We use a couple of techniques to seamlessly connect the operational ontologies with the domain ontologies.
- The interoperability platform heavily counts on the sparql technology. Sparql stands for Semantic protocol and RDF query language and means on the semantic level what sql means for querying relational databases. We argue that ultimately semantic interoperability can only be achieved by formalizing the clinical data and raising them up to the semantic layer as soon as possible. This is exactly what we do by building sparql endpoints on top of the individual clinical information sources. This also considerably facilitates aggregation of clinical data across clinical sites.
  In year three of the project we came across some interesting scientific findings with regard to the nature of the semantic interoperability problem. (First Order Logic problem, scalability issues with top down mapping rules, …).
- Beyond the classical endeavor to find powerful clinical analysis and data mining algorithms we face the challenge of the consolidation of multimodal data mining (structured text, free text, images, …) and integrating the data mining “machinery” into the system.
- The decision support uses knowledge extracted by the clinical analysis. Different approaches are used (Bayesian belief networks, fuzzy cognitive maps, …) and part of the work is making a reasoning framework that can cope with different decision support approaches. This is done by making specific build-in’s in the reasoning framework. We use (and contribute to) the open source Euler reasoning engine. With regard to the Euler reasoner we made some very relevant scientific and technical progress (coherent logic, relation between induction, abduction deduction).
- Population monitoring is build around an “i-google”-like parametrizable dashboard, where individual visualization portletsc called gadgets, showing the results of sparql queries, can be dragged in, according to each user’s needs and preferences.
- Above all, in a complex project like the DebugIT project the challenge is to integrate all the different modules and technologies in a smoothly way in order to create a comprehensive framework with consistent behavior and functionalities. Also here we rely on sparql: many of the interactions between the different modules will be based on a request-result scenario formalized with sparql. This means that the communication between the different pieces of the total solution happens through a so called knowledge bus: formalized and ontology based communication.

1.2.2 Achievements

A brief overview of the scientific achievements so far follows below:

- DebugIT Core Ontology and Operational Ontologies: work in progress and still expanding
- Sparql endpoint based interoperability platform: all endpoints are operational, although not covering the whole Clinical Data Repository
- Aggregation is now implemented such that we can look at the different clinical systems as one virtual Clinical Data Repository
- Extraction of data from production database into research database (HL7-RIM or OpenEHR based). Currenlty in most sites, these are one-time snapshots.
- Text mining, Image mining, finding resistance profiles, solving temporal relations
- Automation of the whole cycle.
- Knowledge repository and authoring tool: extended prototype
- Formalization of bayesian belief network, fuzzy cognitive maps, ran by the same engine, formalization of guidelines

- i-Google-like web application for monitoring
- Several forms of decision support connected to the CIS (HUG, Agfa), but not yet in production environnement.
- In relation to Semantic Interoperability a fundamental scientific output, fully explained in the relevant deliverables can be summarized by the following statements:
    - Semantic Interoperability requires a set of top down mapping rules with disjunctions in the conclusion.
    - This means that we have to solve a First Order Logic problem
    - Declaring top down mapping rules is not scalable because the rules must be changed whenever a new source needs to be connected
    - A solution is to declare mapping rules bottom-up and rewrite them ad hoc to top-down rules.

1.2.3 Clinical Advisory board

Important events in the determination of the clinical approach was the organization of the Clinical Advisory Board (CAB) meetings in Helsinki, Vienna and Geneva. Based on the input from the clinicians we slightly changed the clinical focus: we gave the population wide monitoring more priority than the patient specific decision support. However, both are still in scope.

In 2010 we had a second and third Clinical Advisory Board. Once more, the board strongly confirmed the high clinical relevance of the project and the need for monitoring data + decision support. The board advised to not enlarge the scope of the project too quickly and stick to resistance measuring. Therefore, some potential extensions, such as looking at operational data and finding some resistance inducing patterns will be out of scope.

The board suggested investigating a massive European-wide deployment of the system and collaboration with the ECDC – European Centre of Disease Control.

Finally the board suggested looking at the MIC value (Minimal Inhibitory Concentration). This is a quantitative measure of resistance, available in the microbiology lab, as opposed to the qualitative description that is sent to the clinician. It would allow the DebugIT system to even predict when resistance is about to occur, because an increase of the MIC value could be detected earlier than the statistical significant increase of the number of antibiograms labelled as ‘resistant’. This opinion is not shared by all experts. People at the European Center of Disease Controle told us that an increasing MIC value would also be measurable via the resistance percentages of the antibiograms. To be continued …

Because of the CAB recommendations we decided to:

- even more focus primarily on resistance monitoring and less on decision support,
- to limit the amount of clinical questions we try to solve within the scope of the project. We will not make a system able to launch “any” question (so to speak), but pre-package the system with a fixed list of clinical questions. The list was discussed and validated during the CAB meeting in 2010.

1.2.4 Conclusion and next steps

The project now (Dec. 2010) has closed the full circle: collect clinical data, analyze and store it and use it for individual decision support and population based monitoring in the clinical context. The clinical work will then again produce new information and the cycle can start again.

So far we did the whole round trip with real but exported data from the local CDR’s, resulting in a graph in the monitoring dashboard, showing resistance percentages of specific bacteries. We still need to work on the connection to an on-line data source and on packaging the systems for easy deployment in the hospital. Further we will focus on a limited but relevant set of clinical questions, as suggested by the Clinical Advisory Board.
We will now fin alize the technical implementation and start deployment and clinical validation as soon as possible.

Consortium

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