ToKeN2000/Health Care

1 Project Title

Building and Using Temporal Bayesian Models in a CPR Setting

Project Acronym

TIMEBAYES

Principal Investigator

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2 Classification

2a) Application area: Health Care
2b) Research cluster: Data and Knowledge Refinement

3 Summary

Health care delivery is a complex and expensive activity where data and knowledge in various forms play an extremely important role. At the heart of care delivery lies a series of decisions about diagnosis, prognosis and treatment. These decisions are based on factual, often temporal, data concerning the patient, employing medical knowledge of disease. With the introduction of computer-based patient record systems (CPR systems) in the near future, huge amounts of temporal data will be collected; it seems mandatory to explore and use these data to help in improving the quality of health care. Integrating decision-support tools with CPR sytems would offer such possibilities. Clearly, introducing CPRs without offering decision-support tools at the same time would be unsatisfactory, as this would imply suboptimal use of the CPR system's capabilities.

In the TIMEBAYES project we aim to extend a CPR's functionality. In particular, the projects will develop methods and tools to utilise the temporal data available in a CPR. As statistics lies at the heart of the science of clinical medicine, the project focuses on building temporal Bayesian (probabilistic) models. In particular, we will investigate methods for the exploitation of medical temporal data, methods for expert-guided temporal model development, and learning temporal Bayesian models from temporal data (both structure and parameter learning). In this context, a clinical information system used within an ICU will be used, as such systems are seen as the best approximation to future CPR systems available at the moment. Finally, the clinical information system at UMCU will be used as an environment to investigate the usefulness of the developed methods and tools in a practical, real-life clinical setting.

4 Composition of the Research Team

Institute for Computer and Information Sciences, University of Nijmegen (KUN) Toernooiveld 1, 6525 ED Nijmegen, The Netherlands	
Name	**Discipline**
Prof.dr Th.P. van der Weide	Computing Science
Dr P.J.F. Lucas	Computing Science (AI)/Medical Informatics/Medicine
OIO – requested	Computing Science (AI)/Applied Mathematics

Institute for Computing and Information Sciences, Utrecht University (UU) Padualaan 14, 3584 CH Utrecht, The Netherlands	
Name	**Discipline**
Prof.dr ir L.C. van der Gaag	Computing Science (Decision-support systems, Bayesian Networks)
Dr S. Renooij	Computing Science (AI, Bayesian Networks)
E.M. Helsper, MSc	Computing Science (AI, Bayesian Networks)
OIO (Dutch acronym for PhD student) – requested	Computing Science (AI, Bayesian Networks)

Mathematical Institute, Utrecht University Budapestlaan 6, 3584 CD Utrecht, The Netherlands	
Name	**Discipline**
Prof.dr R. Gill	Statistics (Analysis of Longitudinal Data, Missing Data)

University Medical Centre Utrecht (UMCU) Department of Infectious Disease and AIDS, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands	
Name	**Discipline**
Prof.dr I.M Hoepelman	Medicine (Infectious Disease)
Dr M.J.M. Bonten	Medicine (Infectious Disease)
K. Schurink, MD	Medicine (Internal Medicine, Infectious Disease)
OIO – requested	Medicine

Harvard Medical School, Harvard University, USA	
Name	**Discipline**
Dr M. Ramoni (consultant)	Medical Informatics (Learning Bayesian Networks from Data)

Department of Biomedical Informatics, Pittsburgh University, USA	
Name	**Discipline**
Prof.dr G.F. Cooper (consultant)	Medical Informatics (Bayesian Networks, causal and temporal Bayesian Networks, Structure Learning)

Eclipsys Limited, Slough, UK	
Name	**Discipline**
Dr Stephen Dent	Clinical Information Systems

The TIMEBAYES project involves people with a background in Bayesian networks and knowledge-based systems, decision-support systems, statistics, machine learning, information systems, medical informatics and medicine; people from industry are involved as well. Consequently, the entire spectrum of research, from theory and medical applications to industry, is covered.

UMCU will contribute medical expertise as well as the clinical information-system environment for the research. The clinicians' expertise as well as the Eclipsys information system and the temporal clinical data made available will be used as a basis for actual model construction and use. Utrecht University will contribute expertise in Bayesian-network technology, model building, tool development and statistics. University of Nijmegen will contribute knowledge and experience in adaptive systems, machine learning, Bayesian network technology and medical informatics. Utrecht University and University of Nijmegen will jointly work on the development of the underlying technology needed for the exploitation of temporal data. The team has been put together in a way such as to encourage communication among team members, as their research expertise and interests are partially overlapping. The project team therefore fulfils essential requirements for project coherence. In addition, internationally recognised top researchers in the field of Bayesian networks (in particular structure learning) are involved in the project. Finally, Eclipsys Limited[1], which delivers clinical information systems to health-care organisations, such as UMCU, will act as an industrial partner in the project.

The project will be led by a coordination committee consisting of members from each site; Prof Linda van der Gaag and Dr Peter Lucas will chair this committee.

5 Involved Research Schools

School of Information and Knowledge Systems (SIKS), School for Programming Science and Algorithmics (IPA), School of Infection and Immunity, Mathematical Research Institute.

6 Description of the Proposed Research

6.1 Problem description

As soon as Computer-based Patient Record systems (CPRs[2]) are introduced into clinical practice, huge amounts of biomedical data will be collected and thus become available for exploitation [20, 24, 54]. The main goal of introducing the CPR is to improve the quality, efficiency and cost-effectiveness of the care process. However, it is hard to imagine how this can be brought about without offering CPR-integrated facilities for computer-based medical decision support at the same time. Given the availability of the huge stores of data in future CPRs, it is clearly mandatory to exploit those data in building and using the models underlying these medical decision-support systems.

Biomedical hospital data (clinical data, laboratory data, monitoring data) are collected on a time-scale ranging from days to seconds depending on the care situation. Exploitation of the temporal patterns hidden in the data is expected to be important, as in many instances the temporal patterns convey essential information about what is happening or likely to happen to a patient. *The* **aim** *of the* TIMEBAYES *project is to investigate the construction and use of temporal Bayesian-network models*[3] *in the context of decision-support augmented CPRs.* In particular, the **objectives** of the TIMEBAYES project are:

- to develop methods for the preprocessing of temporal CPR data for the purpose of model building;
- to develop modelling methods for expert-guided temporal Bayesian network construction;
- to develop methods for learning, refining and evaluating temporal Bayesian models based on temporal data;
- to study the requirements for the effective integration of temporal Bayesian models with CPR systems.

6.2 The project's research environment

Cross-health-care, cross-hospital and even cross-ward CPRs do not exist at the moment, and are not expected to be in operation for the next few coming years, even though many countries are investing considerably in creating these systems. Given the advantages linked with the deployment of CPRs in terms of information accessibility, quality and cost control of care, and the provision of

[1]An *i*Soft Group Company, specialised in information systems for the health care; see: `http://www.eclipsys.com`.

[2]Some people speak of Electronic Patient Record systems (EPRs) or Electronic Medical Record systems (EMRs). We follow the terminology of [58], the most recent textbook of medical informatics. We do not see the CPR as a single system, but rather as a collection of possibly heterogenous and distributed information systems, offering a transparent interface to the user.

[3]Also known as dynamic Bayesian networks, or as dynamic probabilistic networks.

decision support it is certain that CPR systems will be in use in the future. The rapid emergence of IT into health care over the last couple of years renders this even more likely.

The success of the TIMEBAYES project is dependent on the availability of a clinical IT environment mirroring the functionality of future CPR systems. Clinical information systems have been in use now for a number of years within Intensive Care Units (ICUs) of in particular (university) hospitals. These systems seem to approximate the characteristics of future CPR systems best. Firstly, because these systems already collect huge amounts of detailed patient data; secondly, because some ICUs have already done away with paper records, so that their systems offer a complete coverage of the clinical history of patients. Thus, the clinical information systems within such ICUs offer almost ideal test-beds for the project's research.

Three of four ICUs within UMCU use a full-fletched clinical information system sold by the Eclipsys Limited (`http://www.eclipsys.com`); this system collects temporal information covering the entire history of the patient. The Eclypsis system uses modern relational database technology as its back-end, allowing easy access to data for research purposes through an SQL interface. The ICU's clinicians can access patient information using workstations through a graphical user interface as a front-end. The Eclipsys clinical information system will be used as a real-life test-bed in the TIMEBAYES project. In particular, we will investigate the use of temporal data and models in handling a number of clinical problems in the ICU related to infectious disease. Management of infectious disease in ICUs is generally seen as a major clinical problem, due to the following facts: (1) patients in the ICU are seriously ill and therefore contract infections easily [9], (2) there are huge costs involved in prescribing antibiotics in the ICU (a significant portion of a hospital's budget is normally spent on antibiotics), and (3) the development of bacterial resistance to antibiotics is due to suboptimal prescription practice in ICUs. The development of infections in hospital patients is a relevant, real-life example of a process involving time. This is due to the fact that patients become colonised by hospital bacteria once they enter the hospital [11]; these bacteria are much more likely to be pathogen and resistant to antibiotics than the common bacteria with which people are normally colonised [1, 10].

In summary, the project will focus on problems which are clinically significant and difficult, warranting the deployment of decision-support tools [25].

6.3 Project structure

In Section 6.4, the various topics investigated within the project are described in detail. The project has been organised in such way as that each single topic is covered by more than one project partner instead, as is often the case, by one partner. However, there is always at most one partner for which the topic is seen as the *primary topic*. The partner mentioned as being primarily responsible will carry out most of the work, with the assistance of secondary partners. This set-up was chosen in order to ensure close collaboration across the project. The PhD students (OIOs) supervised by institutes for which the topics are the primary ones, are expected to devote most of their thesis work to those topics.

6.4 Methods

There are various interrelated aspects of the exploitation of temporal data in building Bayesian-network decision-support models that will be addressed in the proposed research. The project intends to explore the entire spectrum of topics, from the preprocessing of data to the development of explicit temporal Bayesian models in collaboration with domain experts and the learning of such models completely from data. The project also tackles the problems linked to the specific nature of medical temporal data as available within clinical information systems. Below, the various issues and their associated methods are discussed in detail.

6.4.1 Preprocessing of temporal CPR data

Clinical information systems as well as future CPR systems contain huge quantities of temporal patient information. In the field of time-series analysis, which studies methods for the analysis of temporal data, it is often assumed that the data can be represented as a series $\{\mathbf{y}(t_i) \mid i = 1, \ldots, n\}$, where $\mathbf{y}(t_i) = [y_1(t_i), \ldots, y_m(t_i)]$ is a vector with components $y_j(t_i)$ representing observations, or when $\mathbf{y}(t_i)$ is a statistical variable, summarising observations, at time point $t_i \in \mathbb{R}$ [21, 35, 58]. For practical purposes, time series are normally assumed to be finite, which in fact corresponds to data-collection practice within ICUs. Nonetheless, temporal data collected within ICUs or hospitals in general cannot be described easily in terms of such time series. The reasons for this are twofold: (1) the data collected vary from numerical laboratory and monitoring data to categorical data and narrative descriptions; (2) the time point t_i at which individual data items $y_j(t_i)$ are observed varies considerably; the latter may be interpreted as a time-related missing data problem. The overall consequence is that it is not possible to view the task of analysing clinical temporal data as seeking a mathematical model in terms of simple vectors $\mathbf{y}(t_i)$.

Based on what is mentioned above, there is a clear need for the development of systematic methods to interpret and transform temporal, clinical data in such way that the resulting data can be used effectively to build, refine and evaluate temporal Bayesian-network models.

Involvement of partners:

- primary topic: UU
- secondary topic: KUN and UMCU

6.4.2 Modelling methods for the development of temporal Bayesian models

One of the strongest features of the Bayesian network formalism is that it supports representing both qualitative and quantitative knowledge [50, 39, 26, 55, 56, 57]. At a practical level this means that suitably encoded knowledge from clinical experts can be used to guide the search for temporal models in learning, for example by utilising particular fragments of a temporal Bayesian model that are clinically obvious, but may nonetheless be difficult to learn from data. The advantage of temporal Bayesian networks in comparison to for example Markov process models are twofold [19]: (1) it is possible to introduce arbitrary (in)dependence models as dictated by the characteristics of the domain; (2) fast special-purpose Bayesian network reasoning algorithms exist, that are able to exploit the independences modelled in the network (even though Bayesian network inference is NP hard in general [13]). Models developed with the help of clinical experts can also be used as references for comparison with automatically learnt models.

Basically, the problem of developing Bayesian networks for problems involving time amounts to solving two subproblems. Firstly, to model the temporal statistical relationships between statistical variables; secondly, to model the atemporal relationship between statistical variables. In both cases, the modelling is essentially done in terms of statistical dependence and independence, but the semantics of the two types of relationship are different.

The research described in [7, 18, 19, 53, 4] offers a starting point for the proposed research. The TIMEBAYES project will in particular focus on methods for developing temporal Bayesian network models that take into account the special temporal characteristics of CPR data. Furthermore, methods of sensitivity analysis of temporal Bayesian networks, based on previous work on sensitivity analysis of atemporal Bayesian networks by the principal investigator, will be extended [15, 17, 34, 28, 31]. When used to predict the likelihood of future events, we call these models *prognostic* [6, 44].

Within the research team there is significant experience in building Bayesian networks for the medical domain (e.g. [36, 42, 41, 51, 2, 4]). Experience built up in the ICEA project (see Section 6.6) is particularly useful in dealing with the problem domain of infectious disease management in the ICU.

Involvement of partners:

- primary topic: UU
- secondary topic: KUN and UMCU

6.4.3 Learning temporal Bayesian models

Learning a Bayesian network can be separated into two tasks, *structure learning*, i.e. identifying the topology of the network, and *parameter learning*, i.e. determining the associated conditional probability distributions for a given network topology. As the number of possible Bayesian-network structures for a given set of statistical variables is exponentially large, it is necessary to use heuristic methods to construct a Bayesian network automatically using medical data. Learning temporal Bayesian networks from data is even more difficult, as it involves learning both temporal and atemporal structure.

A frequently used procedure for Bayesian-network structure construction from data is the K2 algorithm [14]. Given a database D, this algorithm searches for the Bayesian network structure G that maximises the probability $\Pr(G \mid D)$. K2 is a greedy heuristic. It starts by assuming that a node lacks parents, after which in every step it adds incrementally that parent whose addition most increases the probability of the resulting structure. K2 stops adding parents to the nodes when the addition of a single parent cannot increase the probability. The K2 algorithm is a typical *search & scoring method*, i.e. local search is guided by a scoring function. Other search & scoring methods include the MDL algorithm [37], and the CB algorithm [59].

A learning method which takes an entirely different approach is *dependency analysis* [12]. In this method, conditional independence relationships play an important role. The collection of conditional independence statements represented in a Bayesian network also imply other conditional independence statements using the independence axioms [16, 27, 50].

The literature on heuristic structure discovery of Bayesian networks indicates that most methods developed thus far do an acceptable job when lots of data are available, ignoring temporal relationships among data. The aim of this part of research within TIMEBAYES is to extend existing structure-learning algorithm to cope with temporal data and the characteristics of medical datasets [45]. This research will also include dealing with missing temporal data.

Involvement of partners:

- primary topic: KUN
- secondary topic: UU and UMCU

6.4.4 Requirements for the effective integration of temporal Bayesian models with CPR systems

The ultimate aim of the TIMEBAYES project is to develop methods and tools that offer insight into the requirements for integrating decision-support systems with CPRs. To achieve this aim, it is necessary to investigate the suitability of those methods and tools in the context of an actual CPR system and a particular clinical field. We have selected the management of infectious disease in the ICUs of the University Medical Centre Utrecht (UMCU) to act as an example field in TIMEBAYES, for the following reasons: (1) the development of infectious disease in the patient is a temporal process, so that models underlying decision support need to be temporal in nature; (2) clinical information systems as used in UMCU's ICUs can be seen as forerunners of future CPRs and contain temporal data; (3) deciding on optimal treatment of infectious disease is hard for medical doctors not specialised in infectious disease, and is seen as an appropriate area for decision-support systems; (4) there is much expertise on infectious disease in the UMCU's Department of Infectious Disease and AIDS, to be utilised in the modelling process.

The TIMEBAYES project will develop a number of prognostic, temporal Bayesian network models in the area of infectious disease, using expert knowledge from the UMCU's infectious disease specialists, and temporal data from the ICU's clinical information system (Eclipsys). Finally, Eclipsys will be used as an environment to study the embedding and use of Bayesian-network decision-support tools by clinicians [44, 4].

Before one uses a suggested prognostic model it is important to have an indication whether the model will work well for populations different from the one used to develop the model. There are many studies reporting on model validation, certainly the lack thereof [60]. One may distinguish between laboratory evaluation and clinical evaluation [6, 61]. A *laboratory evaluation* usually focuses on the performance of the model. Relevant questions in a laboratory evaluation are whether the model passes the appropriate statistical tests, usually on a new data set, and whether it is the best model given the available factors. In a *clinical evaluation* one is interested in the question whether the model is satisfactory for its *clinical purpose*. It is possible to have a statistically but yet not clinically valid model and vice versa. Both laboratory and clinical evaluation of the developed models will be undertaken in the project.

Involvement of partners:

- primary topic: KUN
- secondary topic: UU and UMCU

6.5 Relevance

The effective exploitation of data in future CPRs in order to support, improve and guarantee quality of patient care is the single most important issue related to the CPR. This warrants research into the underlying fundamental methods for the exploitation of temporal medical data. Such research would normally involve evaluating the effectiveness of the developed methods and tools in a practical, clinical setting, using empirical research methods. To our knowledge no research groups have so far undertaken such a systematic study. The TIMEBAYES project intends to close this research gap. More in general:

(1) The TIMEBAYES project will develop novel methods and techniques for the utilisation of temporal data in the process of building models underlying decision-support systems. The expected research results will contribute to research in statistical model building using Bayesian network technology.

(2) The TIMEBAYES project aims at developing methods, techniques, and concrete models which have the potential for contributing to quality improvement of the care delivery process. This will provide insight into the role that the CPR can play in such a setting.

(3) The TIMEBAYES project will investigate the integration of decision-support capabilities within the CPR such that the CPR can function as a clinical problem-solving instrument. This will result in the formulation of the desired CPR design specifications concerning the form, contents and quality of data within the CPR.

Due to its explicit attention to the development of decision-support instruments for care quality improvement, the TIMEBAYES project is also broadly relevant to the community at large. The principles behind the instruments and the instruments themselves should be accessible to other medical centers. By the involvement of the medical field (UMCU) and industry (Eclipsys) it is ensured that the outcome of the project will be of value to both areas.

There is a global tendency in organisations to seek *integral* solutions to problems. This tendency, which is certainly sensed in health care, means that integrated instruments for solutions are sought instead of many local instruments for solving partial problems. It is hence important to study the implications of the integration of decision-support within the CPR on the CPR's structure and content and view decision-support as an integral part of the CPR instead of assuming a CPR structure which is isolated from its functions. The TIMEBAYES project contributes to this 'integral solution' point of view.

6.6 Related Research and Collaboration

Both Dr Peter Lucas and Prof. Linda van der Gaag have experience in building Bayesian-network based systems for clinical problems in collaboration with clinicians [2, 29, 41, 4]. Dr Peter Lucas, formerly at the University of Aberdeen, has recently joined the Information Systems group at the University of Nijmegen, which is lead by Prof.dr Th.P. van der Weide, and will bring in expertise in medical informatics, medical AI (logical reasoning in medicine), Bayesian networks and decision theory. He has 18 years experience in dealing with the methodological questions which arise in research in medical decision support. He is collaborating with most researchers mentioned above, and also with the clinicians at UMCU in the context of the ICEA project. His contacts in the medical field cover a broad area [36, 40, 41, 4], from treatment selection in cancer using modern decision-theoretic techniques [41] to advice in pacemaker reprogramming [43] and Bayesian-network learning [45]. Linda van der Gaag is an internationally recognised expert in the foundations of Bayesian networks. Her research covers methods that guide the process of building Bayesian networks, such as sensitivity analysis [15, 17, 34, 28, 31], methods for probability assessment [22, 23, 2], Bayesian-network structure [32], algorithms for Bayesian networks [8], and evaluation [29].

There exists collaboration of Utrecht University and University of Nijmegen with the group of Prof.dr Steen Andreassen of Aalborg University in the ICEA project (optimal treatment of infectious diseases, see below), with Prof.dr Gregory Cooper of the Department of Biomedical Informatics, University of Pittsburg, with Prof.dr Finn V. Jensen, also Aalborg University, in the field of Bayesian-network and decision theory, and with the group of Dr Marek Druzdzel of the Decision Sciences Laboratory, Pittsburgh University, in the evaluation of diagnostic systems. There also exist good contacts with the British medical informatics society, in particular Prof.dr John Fox, Prof.dr Jeremy Wyatt and Prof.dr Peter Hammond.

Prof.dr Richard Gill is an expert statistician in the area of the statistical analysis of longitudinal data and in statistical methods for dealing with missing data. He has experience with applying statistics to the medical field. He is involved in the project in order to help with statistical issues.

Dr Marc Bonten is project leader of the ICEA project [4]. This project can be seen as a precursor to the TIMEBAYES project. The ICEA project team is working on a Bayesian network model of ventilator-associated pneumonia, within the ICU environment of UMCU, using traditional knowledge acquisition techniques. Dr Bonten is an internationally recognised expert in the area of infectious disease and has close international contacts with many researchers in this field [1, 9, 10, 11]. Novel in the TIMEBAYES project in comparison to the ICEA project, which is now nearly finished, is the exploitation of temporal ICU data using machine-learning methods. However, the TIMEBAYES project will definitely profit from the expertise which was built up during ICEA.

Dr Marco Ramoni and Prof Greg Cooper are experts in Bayesian network structure-learning methods, and will be as such advise the project team on algorithmic aspects of this part of the research. Dr Steve Dent will be involved in the project as a representative of Eclipsys Limited.

6.7 Embedding in ToKeN2000, Relation to ICZ

The proposed project belongs the Data and Knowledge Refinement theme of ToKeN2000, investigated in a clinical setting. The links from the proposed to the topic of the CPR, a necessary requirement of the ToKeN2000/Health Care, are clearly present in this project. The CPR can even be seen as the greatest common divider of the subprojects.

There are close contacts with ICZ's 'Terminology and Semantics' project via Dr Ameen Abu-Hanna of the Department of Medical Informatics, AMC. We also intend to develop links with ICZ's 'Proper' project, which is led by Dr Huibert Tange of the Department of Medical Informatics, University of Maastricht. The latter project is in particular appropriate for TIMEBAYES, as it focuses on the relationship between medical guidelines and the CPR, which complements to the research that will be carried out in the TIMEBAYES project.

6.8 Exploitation of Research Results

The models and software that come out of the research will be used within the UMCU, as part of the Eclipsys clinical information system. It is likely that other university hospitals will follow. Furthermore, research results of the TIMEBAYES project will be published as they emerge in national and international journals and conference proceedings. The results will lead to three PhD theses.

7 Work Programme

The overall planning of the TIMEBAYES project will be as follows:

I. *Orientation phase (mid 2002–end 2002)*

II. *Development phase (beginning 2003–end 2004)*

III. *Experimentation and refinement phase (beginning 2005–end 2005)*

IV. *Evaluation and finalisation phase (beginning 2006–mid 2006)*

There will be close collaboration between the computing science/medical informatics and the clinical partners during the entire course of the project.

I. *Orientation phase (mid 2002–end 2002)*:

- setting up the coordination committee and arranging regular meetings.
- study of relevant literature on preprocessing of data, time-series analysis, modelling Bayesian networks, integrating decision support systems.
- inventory of clinical requirements with respect to support of care decisions in the context of a CPR.
- selection of an appropriate clinical domain, in collaboration with the UMCU's clinicians.
- examining temporal aspects and patterns of ICU data.
- identification of the most promising methods and techniques.

II. *Development phase (beginning 2003–end 2004)*:

- development of methods and tools for temporal-data preprocessing.
- development of Bayesian-network models for the selected domains in collaboration with UMCU's clinicians.
- development of extensions to Bayesian-network structure learning algorithms, in order to deal with temporal clinical data.
- design of an architecture for a workbench for care-decision support, with capabilities of integration with a CPR.
- design and development of the components of the architecture.

III. *Experimentation and refinement (beginning 2005–end 2005)*:

- learning temporal models from clinical information-system data.
- integration of temporal models into the architecture of the workbench.
- evaluation of temporal Bayesian-network models using ICU data.
- refinement of the workbench and models.
- formulation of the first set of requirements for the CPR with respect to integration capabilities.

IV. *Finalisation and evaluation (beginning 2006–mid 2006)*:

- setting up an evaluation framework.
- evaluation of final functionality of models and workbench by clinicians
- requirements with respect to functional architecture, structure and content of the CPR for exploiting temporal data.
- writing of PhD theses.

8 Expected Use of Instrumentation

Two fast workstations have to be bought for the computing science OIOs; one PC has to be bought for the medical OIO. We also intend to buy a standard, commercial Bayesian network package (Hugin) which will be used in the research for initial experimentation. In addition, the Ideal package, our own package which offers standard Bayesian network construction primitives in addition to probabilistic inference methods and methods for evaluation, will be deployed. However, neither Hugin nor Ideal are able to handle temporal Bayesian networks. Either Hugin or Ideal will be extended in the project with such functionality.

9 Requested Budget

Three junior researchers (OIOs) are requested: two will be appointed in Utrecht and one in Amsterdam. The first junior researcher will perform research concerning the integration of care-decision models into the CPR; the second junior researcher will investigate the potentials of the CPR for the exploitation of data for model construction and evaluation. All junior researchers are expected to write a PhD thesis.

OIOs		Amount	
Salary	3 × 129,897 Euro	389691 Euro	
Benchfee	3 × 4,538 Euro	13614 Euro	
Travel	3 × 3,000 Euro	9000 Euro	
Equipment (2 Workstations)	2 × 2,000 Euro	4000 Euro	
(1 PC)	1,000 Euro	1000 Euro	
		———————	+
		407305 Euro	
Matching	3 supervisors,	136101.67 Euro	
	218.12 Euro per day	———————	+
Total		544407 Euro	

10 Publications

Five Most Significant Publications of Research Team

[1] M. Bonten, M. Hayden, C. Nathan, J. van Voorhis, M. Matushek, S. Slaughter, T. Rice, R. Weinstein. Epidemiology of colonisation of patients and environment with vancomycin-resistant enterococci. *The Lancet* 1996; 348: 1615-1619

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11 Signature

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Applicant