Measuring clinical pathway adherence

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Abstract

As clinical pathway adoption continues worldwide, it is necessary to establish adherence measurement methods in order to understand the difficulties and results of implementation. Adherence measurement literature mostly provides binary measurements of adherence to guidelines regarding individual medical activities over patient groups. The resulting measurements are of limited value in view of the pathways actually followed by individual patients. We develop and test dynamic programming formulations for adherence measurement in clinical pathways - based on partially ordered data in medical records and pathway definitions. With these new methods at hand, we analyze clinical pathway adherence at the Cardiovascular Center of Maastricht University Medical Center.

Introduction

As health care cost are growing from 10 towards 20 percent of GDP in most developed countries [1, 2], the need for cost reduction and efficiency improvement is strongly felt. At the same time, science and technology progress and obedient patients change into demanding customers, increasing the pressure to deliver high quality, customized service. Hence, many health care organizations seek operational innovations that combine high quality with low cost as they have been successfully introduced in other industries. Ford's successful introduction of standardization in the automotive industry brought higher quality and lower cost already in the early 20th century. Since then, many companies and industries have followed, and the operations management discipline has adopted and further developed Ford's seminal ideas. The concepts of Total Quality Management and 6σ are among the most widely adopted successors in the global manufacturing industry. Service industry however has proven to be more unruly. Whereas successful implementation of standardization techniques have taken place in various service industries, ranging from fast food restaurants to health care, other service processes have been concluded to be inappropriate for standardization. By nature, and because of the high degree of customization, service operations often appear to combine badly with standardization. This holds especially for health care processes whose professionals have cynically referred to standardization as 'cookbook medicine' [3].

Canadian Shouldice Hospital adopted a standardized approach for abdominal wall hernia surgery as early as 1945, and has proven to deliver low cost services with faster recovery and fewer complications than comparable organizations that use traditional methods [4]. Shouldice however does not accept every patient but aims to accept just those for which their processes are designed and optimized. This cookbook approach of Shouldice (referred to as the McDonald's approach by Dr. Earl Shouldice, founder of Shouldice Hospital [5]), is not considered to be appropriate for all cure processes, and as will be described shortly, mixed results are being reported in literature.

Scientific literature usually refers to standardized, typically evidence based, health care processes, whether for diagnosis or for treatment, by the term clinical pathways. A common definition of clinical pathways is: 'management plans that display goals for patients and provide the corresponding ideal sequence and timing of staff actions to achieve those goals with optimal efficiency' [6]. We refer to [7]

for a survey that revealed as much as 84 definitions for clinical pathways in the years 2000-2003. Clinical pathways are also akin to clinical guidelines, which can be defined as "systematically developed statements to assist practitioner decisions about appropriate health care for specific clinical circumstances" [8, 9], and for which a wide variety of definitions appears in scientific literature as well. Clinical guidelines can be quite detailed, as is further discussed below, but in principal form generally applicable, evidence based statements. By their operational nature, clinical pathways provide detailed operational procedures within a specific organization, and are therefore less general than clinical guidelines. Below we discuss the modeling of clinical pathways as appropriate for our research purposes in more detail, and address related literature on the modeling of clinical pathways and guidelines.

Although some clinical pathway introductions have brought considerable improvements [10, 11, 12], literature paints a mixed picture [13] - not in the least because of skepticism and difficulties regarding the adherence to the clinical pathways [10, 11, 14]. Hence, decision making on implementing or rejecting clinical pathways should not be taken lightly. Moreover, not withstanding the fact that deviations from the cookbook pathways might address the needs of an individual patient better, deviation from evidence-based pathways might just as well reduce quality of care. Scientific literature on clinical pathways however, hardly addresses in depth analysis of pathway adherence after implementation, or its improvement. We present a model to measure clinical pathway adherence, which is able to cope with variations in pathways and deviations from pathways. Further, we apply it to real life data from the years 2001-2005 at the Maastricht University Medical Centre (MUMC).

The aim of this paper is not to determine whether or when adherence to the pathways is justified, nor to explore the medical consequences. The promise of clinical pathways is to increase the quality of health care while lowering costs, as society requests. Thus, it is worth to implement best practices, yet still to deviate if justified for medical reasons. Consequently, the concept of deviation must be meaningfully defined, and deviations must be systematically measured and reported. The methodology developed in this paper therefore provides a systematic approach to define and measure deviations, building on arguments of medical experts. In doing so, it contributes to the understanding of the pros and cons of clinical pathways, and subsequently to advancing health care quality and efficiency.

Literature

Different authors have coined different definitions for the related concepts of clinical pathways, critical pathways, and critical paths. Originally [6], clinical pathways have been typically developed for high volume, low cost treatment processes. Nevertheless, many applications [15, 16, 17] fall in the domain of diagnosis processes, such as diagnosis of myocardial infarction, stroke and deep venerous thrombosis, domains that are closely related to the case study under consideration in subsequent sections. Various authors [15, 16] stress the importance and difficulty of collecting and processing variance data, as understanding and managing variance is necessary to realize the promise of clinical pathways. Delaney et al [17] for instance report better results when restricting the pathway implementation to patients younger than 70 and surgeons who are experienced with the system.

Evidence [10, 11, 12] confirms that clinical pathways enable to improve quality and efficiency simultaneously, or to improve one without adversely affecting the other. Marrie et al. [12] conclude from a study on a critical pathway for community-acquired pneumonia that efficiency has increased without affecting the well-being of patients adversely. Likewise, Macario et al. [10] report a decrease in average hospital costs for knee replacement surgery from $21709 to $17618. On the quality side, Panella et al. [11] report various implementations and that heart failure in-patient mortality rates reduced from 17 percent to below 5 percent in of these implementations. However, several studies deliver negative results and report implementation problems because of resistance to cooperate. Literature surveys have lead to the conclusion that 'the results of the reported studies should be interpreted with caution' [13] and that results of implementing clinical pathways are heterogeneous in various respects, varying from mortality to length of stay, and 'find no evidence that care pathways provide significant additional benefit over standard medical care in terms of major clinical outcomes' [18].

Despite the mixed findings in scientific literature, a recent survey [19] by the European Pathway Association reveals that experienced professionals rank improvement of quality of care and efficiency of care among the most important features of clinical pathways. Moreover, they report that in many participating countries the percentage of patients that receive pathway-based treatment is expected to rise from 15 percent or less to between 40 and 80 percent within the next five years. Improvement of evidence-based care serves as another important objective in the survey results, and defining and measuring indicators for evidence-based medicine is one of the main international trends [16, 19].

Stressing the correlation with quality of care, Caminiti et al. [4] explicitly address adherence to evidence based clinical pathways, and report results on a wide scale study. Their results reveal improvements in adherence (e.g. on cerebral ischemic stroke), but at the same time demonstrate that even after a thorough implementation approach, the adherence appears to leave much room for improvement (e.g. for cesarean sections). They conclude that the ability and willingness to change plays an important role in the adherence to clinical pathways.

Lack of adherence, which generates unnecessary health care expenses of 100 billion dollars in the US [20] has received considerable attention in the literature both from a viewpoint of therapy adherence by patients and from the perspective of guideline adherence by medical professionals. Different modules to measure adherence have been reported, some of which take a binary approach with respect to the adherence to certain pathways, protocols, treatments, or other medical activity. Milchak et al. [21] thoroughly research treatment adherence per patient as measured by an algorithm that calculates a numerical adherence score by weighing a set of binary scores on 22 different criteria. For various reasons [22, 23, 24], the data required to measure whether the actual cure or care treatment is according to the prescribed guidelines (pathways or other) is often incomplete or incorrect. Sometimes information is collected using self-assessment by patients or medical professionals, sometimes from handwritten medical records, and/or from a set of partially integrated IT systems. The low quality of the data makes adherence measurement difficult, yet several practical studies reveal that adherence can indeed be quite poor. The many successfully completed IT implementations have not yet reduced the need for adequate information technology to support quality assessment and improvement in health care [25].

Gardetto et al.[26] and Rood et al. [27] proposed software systems to assist medical professionals in delivering care according to the prescribed pathway as defined by a flow chart, and report improvements in adherence as well as in medical outcomes. In addition, software systems that send reminder messages to medical professionals when treatment is required according to evidence based pathways have been developed and studied with respect to reminder adherence [28]. A formal language (QUIL) to define pathways and adherence, taking complicating issues such as temporal parameters, acceptable alternative and patient-specificity into account is proposed by Advani et al [29]. QUIL does not allow modeling the (partial) orders in pathway structures and patient record structures that we encountered in our research project, and which we believe are of importance to pathway adherence measurement.

The literature on modeling clinical guidelines, by contrast, provides descriptions of elaborate formal modeling languages and software systems such as the Arden Syntax, ASBYR, EON, GLIF, PROforma [30, 31, 32]. These modeling languages support a variety of 43 flow structures [30], of which only the relatively small sets of basic control-flows and advanced branching and synchronization patterns is relevant in our research. As such, our work can be viewed to address adherence measurement for a basic workflow process definition language [32].

In view of the impact adherence might have on the cost and quality of care, our work provides models and algorithms to extend clinical workflow modeling languages with adherence measurement functionality. The models and algorithms enable to measure pathway adherence accurately, taking into account expert opinions on deviations, and relying on a formal pathway definition. The definition supports the core of workflow process definition languages [32] as visualized in process flow charts [26, 27] and supports multidisciplinary process orientation (see e.g. Figures 1 and 2). The model includes precedence relations and partial orders, parallelism, exclusive alternatives, and nested pathways. Exclusive alternatives model the situation where a choice of appropriate exclusive alternatives exists for a certain medical action. In such a case, adherence to the pathway means that one of the alternatives must be selected. The proposed adherence measurement model is more general than models that simply give binary penalties per violation. Instead, it allows to value omissions, substitutes, or additional activities on a continuous scale. In combination with the allowable process flow structures, the thus defined adherence measurement problem is highly nontrivial. We propose polynomial algorithms for pathway adherence measurement that rely on techniques from combinatorial optimization. Remarkably, our dynamic programming approach is akin to sequence alignment algorithms developed in molecular biology in the context of genetic pathways [33]. Since the practical problem at hand relaxes order preservation constraints within the sequences, we embed in the dynamic programming recursion a maximum weight matching algorithm [34].

Methods: Pathway Modeling

We now formalize the concept of pathways and pathway adherence as appropriate with current practice in MUMC. The care a patient receives is defined as a set of activities of various types, ranging from

interventions, to lab tests, to communication. Although we will not explicitly model it, patient need not be present for each of the activities (consider e.g. lab tests). As MUMC database records on provided care activities specify the date, but not the starting and ending times of the activities, we adopt the convention [6, 35] that pathways contain consecutive sets of activities (a set per date). The order in which activities must be performed is not always explicitly specified.

Definition 1. An *activity* is an atomic unit of care delivered to the patient, as meaningful to execute or record the care.

A set of activities must oftentimes be executed in a prescribed order. A simple two activity example is a path in which an echo (activity x) must be taken before its outcomes can be discussed with the patient in a consult (activity y). As customary, we denote such *precedence* relationships by $x \prec y$ and say x *precedes* y, or y *succeeds* x. Before further developing the precedence relationships, we first define sets of activities between which such relationships will not exist:

Definition 2. A set $S = \{s_1,\ldots,s_m\}$ of activities is called a *parallel activity set* iff for all $1 \leq i < j \leq m$, neither $s_i \prec s_j$ nor $s_j \prec s_i$.

Notice that we use a rather loose concept of parallelism. It does not enable to enforce that activities overlap in execution time, or start/end simultaneously, as commonly encountered in formal modeling languages for clinical guidelines [30].

When a patient actually receives care, precedence relationships between the corresponding activities may exist, but not necessarily so. The execution of some of the activities may overlap, or the registration may not be accurate enough (e.g. per day) to specify the order. Consequently, the care received by a patient can be viewed to exist of an ordered set of parallel activity sets:

Definition 3. A *care set* is the set of all parallel activities sets of which the care received by a patient exists.

Trajectories model the real life situation where a prescribed order exists between different parallel activity sets:

Definition 4. A *trajectory T* is a linearly ordered set $(S_1,\ldots,S_m)$ of parallel activity sets. (that is, for every $S_i, S_j, S_k \in T$, either $S_i \prec S_j$ or $S_j \prec S_i$, and $S_i \prec S_j$ and $S_j \prec S_k$ together imply $S_i \prec S_k$). For trajectory T, the *trajectory activity set* $A(T)$ is defined as $A(T) = \cup_{i=1}^{m} S_i$.

The interpretation of the precedence constraints in the definition above is that if a precedence relation exists between two activity sets, i.e. $S \prec S'$, all activities in parallel activity set S must be completed before any of the activities in parallel activity set S' starts. An example trajectory is depicted in Figure 1. In Figure 1, the precedence relationships between the parallel activity sets are depicted using arrows, and hence the activities between which a direct relationship is depicted by a line instead of an arrow are elements of a same parallel activity set.

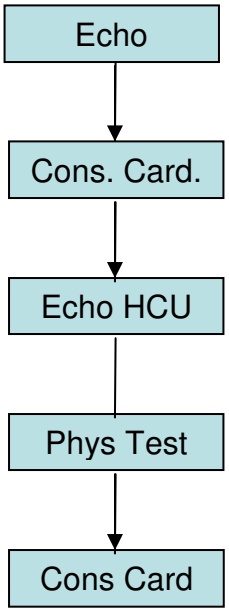

Figure 1: A trajectory (Basic Diagnosis Pathway): ({Echo},{CC}, {EchoHCU,PhysTest},{CC})

Trajectories capture processes as they semantically appear to be described as pathways. As will become clear below however, real life clinical pathways refer to more complex process descriptions, in which

several different routings and sets of activities are feasible. Still, clinical pathways are prescriptions on the trajectories as they may be executed in real life. We now constructively derive a formal pathway definition from the definition of trajectories. Pathways are defined as the union of a set of mutually exclusive trajectories and relations between these trajectories:

Definition 5. Let T_x and T_y be trajectories, let $S_x \in T_x$ be such that $S_a \prec S_x$ for all $S_a \in T_x$, $S_a \neq S_x$, and let $S_y \in T_y$ be such that $S_y \prec S_b$ for all $S_b \in T_y$, $S_b \neq S_y$. (In words, S_x is the last parallel activity set in T_x, and S_y the first activity set in T_y.)We say T_x *precedes* T_y, that is $T_x \prec T_y$, iff $S_x \prec S_y$.

Definition 6. A set $K = \{T_1, T_2, \ldots, T_l\}$ of trajectories is called *unordered* if for each $i,j,\ 1 \leq i,j \leq l$, $T_i \prec T_j$ nor $T_j \prec T_l$.

Definition 7. A *pathway P* is a linearly ordered set $\{K_1, \ldots, K_z\}$ such that

a) each element is either a trajectory,

b) an unordered set $K = \{k_1, \ldots, k_l\}$ of (one or more) pathways, where a set of pathways is unordered *i*ff any two trajectories, which are elements of two different pathways in *K* form an unordered set of trajectories,

a) $A(S) \cap A(T) = \varnothing$, for each two trajectories *S* and *T* which are elements of (elements of) *P*.

The unordered sets in the pathway definition model exclusive choice between alternative sub pathways of care. When providing care, exactly one of the sub pathways must be selected:

Definition 8. A *feasible realization R(P) of Pathway P* is a pathway, that is a linearly ordered set $\{r_1, \ldots, r_y\}$, such that *R(P)* contains exactly one element of each unordered set of *P*. For a given pathway *P*, we define $\rho(P)$ as the *set of all feasible realizations* of *P*.

Since a realization enforces a choice between the elements of an unordered set, and trajectories are the linearly ordered elements of the sub pathways at the bottom of the recursion of the pathway definition,

any feasible realization of a pathway forms a linearly ordered set of trajectories, and is therefore itself a trajectory.

Let us illustrate these principles using the example of Figure 2. The pathway depicted in Figure 2 is an ordered set that consists of the next three elements:

1. the trajectory *{ECG, Cons Spec. Nurse, Lab tests, Echo, Check diameter},*
2. a set of two parallel pathways
    a. a pathway consisting of the simple trajectory ∅ (the empty set).
    b. a pathway consisting of
        i. Trajectory *{CT Scan, TAAA}*,
        ii. A set of two unordered pathways, each of which is a trajectory:
            1. *{{Echo:HCU,Exercise},*
            2. *{ Echo(spec), {Exerc Test, LF: Antrup}}*. Notice that the second element of this trajectory forms a parallel activity set.
3. the trajectory *{Consult}*.

The interpretation of this diagnosis pathway is as follows. In any feasible realization, the patient should first receive the diagnososstic steps *{ECG, Cons Spec. Nurse, Lab tests, Echo, Check diameter}*. Then there is a choice between alternatives. If the diameter of the Aorta does not exceed 5.5 cm, there is no further diagnosis. If it does exceed this diameter, there is a choice between two further diagnosis pathways, in the second of which there is no precedence relation between the activities *Exerc Test* and *LF: Antrup.*. Each feasible trajectory must be concluded by a *Consult*.

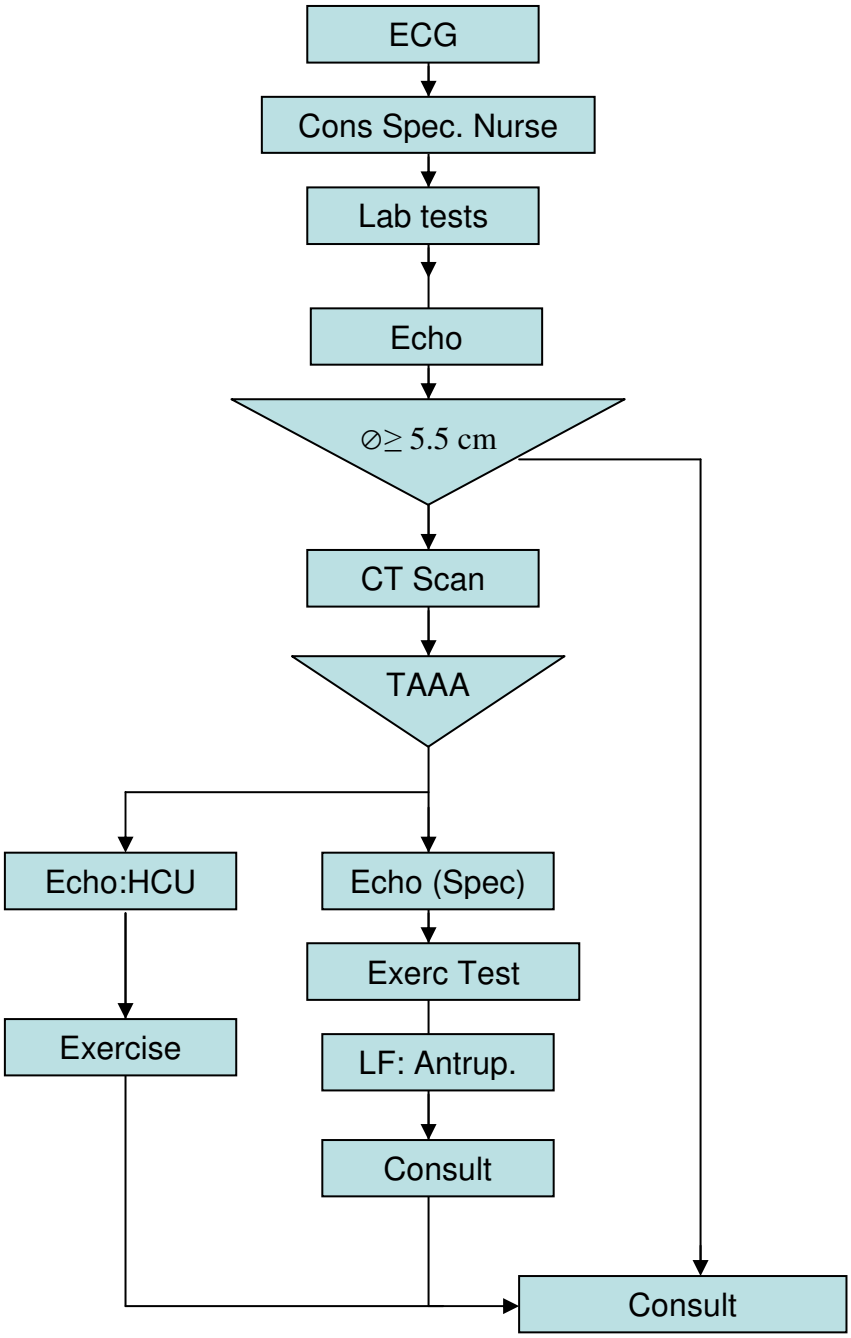

Figure 2: Pathway for Aneurysm Diagnosis

Using unordered sets of trajectories, the pathways defined above allow modeling any variety of feasible realizations by explicitly specifying them (inefficiently) as elements of an unordered set. On the other hand, when defining a pathway that consists of a sequence of *n* unordered sets of *2* pathways each of

which consists of a single activity trajectory, one obtains a pathway that has 2^n feasible realizations. In general, the number of feasible realizations can therefore be exponential in the input size. In all practical applications known to the authors however, the number of feasible realizations is bounded from above by a small constant.

Methods: Adherence Modeling

Using the definitions above, we might speak of pathway adherence if the trajectory that a patient follows is a feasible realization of the pathway, or equivalently if the care a patient has received is exactly according to one of the allowable prescriptions. For all practical purposes however, this strict binary model - as often encountered in the literature - is an oversimplification of reality. Deviations for good reasons are common in practice, and do not necessarily incur a quality or efficiency loss. For instance, if an echo or CT scan has been made recently, perhaps in another referring hospital, its outcome might suffice for the diagnosis, and hence the corresponding activity can be skipped. This would mean an efficiency gain, rather than an omission. In addition, if a certain device is out of order or has a long waiting list, finding a substitute for an activity might be preferable over waiting. Moreover, the diagnosis trajectories of inpatients often interfere with other activities as they are taking place by other medical disciplines in parallel. New insights obtained during the diagnosis may lead to changing the planned trajectory. Patients themselves might interrupt their process for medical reasons, et cetera.

We conclude that (parts of) the potentially long trajectories that patients undergo over a period can deviate from the clinical pathways, where some of the deviations are more significant than others. We now introduce a model, which is based on input of medical experts, in which deviations of trajectories from clinical pathways are measured on a numerical scale, allowing for a richer and more meaningful discussion on the observed deviations.

The resulting measurement of deviations of trajectories representing the actual care received by patients is a non-trivial task because of the potentially complicated structure of clinical pathways themselves. We continue our formal modeling approach to enable measuring deviations. In the remainder, T refers to the

trajectory defining the care a patient has actually received, whereas trajectory *R* models a feasible realization of a clinical pathway *P*.

Definition 9. Let *T* and *R* be trajectories. A *match M is* a pair of mappings M_T:$A(T) \rightarrow \{A(R) \cup \{-\}\}$ and M_R: $A(R) \rightarrow \{A(T) \cup \{-\}\}$ such that:

a) For each $t \in A(T)$, $r \in A(R)$, $M_T(t) = r \Leftrightarrow M_R(r) = t$. That is, the restriction of M_T to *R* is an injection, as is the restriction of M_R to *T*. However, several $t \in A(T)$, $(r \in A(R))$ may have $M_T(t) = - (M_R(r) = -)$.

b) For $t, t' \in A(T)$ $t \prec t'$, and $r, r' \in A(R)$, such that $M_T(t) = r$ (or equivalently) $M_R(r) = t$) and $M_T(t') = r'$ (or equivalently) $M_R(r') = t'$) it must hold that $r \prec r'$.

Moreover, we define $\mu(T,R)$ as the s*et of all possible matches M(T,R).*

Definition 10. For a given match *M(T,R)*, the *deviation cost d(M(T,R))* or simply *d(M)*, is defined as the sum over all the deviation costs of the mappings of the elements, which are calculated using the following three types of deviation cost:

a) For each $t \in A(T)$ there is a set I_t of substitutes, $- \notin I_t$, and for each substitute $g \in I_t$, the nonnegative substitution costs are denoted by $c(t,g)$, where $c(t,t)=0$.
b) For each element $t \in A(T)$, the deviation cost $c(t,-) = c_T$, that is the cost of mapping to a void is not dependent on *t*.
c) For each element $r \in A(R)$, the deviation cost $c(-,r) = c(r)$, that is the cost of mapping depends on the clinical pathway activity *r* that remains unmatched.

Notice that b and c are in fact symmetrical deviations, incurring a cost for leaving an element unmatched. As is clear from the discussion above, assigning costs to substitution or not matching (matching to a void) is not an exact science. Our practical experiments lead us to the conclusion that medical professionals typically reach consensus on costs from the categories a and c. We consider category b costs to be less relevant and analyze them parametrically below. Let it be noted however, that

the computational complexity of the algorithms introduced below is not affected when the deviation costs $c(t,-)$ are not constant.

With this model at hand, we now proceed to define the problem formally:

Definition 11. Given a pathway P and a trajectory T, the *adherence* $A(T,P)$ of trajectory T to pathway P is defined as:

$$\min_{R \in \rho(P)} \min_{M \in \mu(T,R)} d(M(T,R)).$$

This definition consists of two parts. Let us first examine the inner part, which minimizes for a given R, the deviation costs over all feasible matches. Now noting that R is a feasible realization of pathway P, the adherence problem is to determine the realization R with lowest possible deviation costs. As there may be multiple feasible realizations of a pathway and the deviation costs of a match are not easy to calculate, adherence measurement is a highly non-trivial problem.

For an example, consider again the pathway depicted in Figure 2. The trajectory *{ECG, Cons Spec. Nurse, Lab tests, Echo, Check diameter, Consult}* forms a feasible realization of the pathway, where the empty set is chosen as the alternative for the second pathway. The trajectory *{ECG, Cons Spec. Nurse, Lab tests, Echo, Check diameter, CT Scan, TAAA, Echo:HCU, Exercise, Consult}* forms a feasible realization when the other pathway alternative is selected. The trajectory *{ECG, Cons Spec. Nurse, Lab tests, Echo, Check diameter, CT Scan, Echo:HCU, Exerc Test, Consult}* is an infeasible realization of the pathway. In comparison to the first pathway, it has redundant activities *{CT Scan, Echo:HCU, Exerc Test}*. In comparison to the second alternative, activity *TAAA* is missing. Moreover, the activity *ECHO:HCU* should be followed by activity *Exercise*, or activity *Exerc Test*, should be preceded by *Echo(spec)* and preceded or succeeded by *LF: Antrup}}*. Thus depending on the chosen realization, the deviation is differently defined, and so are the deviation cost. The adherence measurement problem is to find the realization that minimizes the deviation cost. In fact the deviation measurement is already non-trivial when there are no unordered subpathways, which is the case considered in the algorithms below.

Methods: Adherence Measurement Algorithms

We now proceed in steps to derive two algorithms to measure the adherence of a trajectory *T* representing the care received by a patient to a clinical pathway *P*. We restrict ourselves to the case where *P* is a trajectory, and therefore does not contain unordered sets of sub pathways. This is an oversimplification of reality as discussed in the case study. We have however not been able to provide an exact algorithm for the general case, and therefore enumerate over all feasible choices of exclusive alternatives implied by the unordered sets of sub pathways. The number of such feasible choices never exceeds 10 in the case study at hand.

Thus we refrain ourselves to studying the problem of calculating the adherence of a trajectory to a trajectory. We start by considering the special case where all sets of parallel activities *P* and *T* have cardinality one. In this special case, any realization *R* of *P,* as well as *T* are linearly ordered sets of activities. This case corresponds to the alignment problems discussed in relation to DNA sequences [33,36,37,38].

Let $T= t_1t_2\ldots t_m$ and $R = r_1r_2\ldots r_n$ be the two corresponding trajectories (where the linear order increases with the indices). We intend to find a match M^* such that

$$M^* = \underset{M \in \mu(T,R)}{\arg\min} \; d(M).$$

We define $T_i= t_1t_2\ldots t_i$ and $R_j = r_1r_2\ldots r_j$, for $i = 1\ldots m, j =1\ldots n$, and let

$$d(i,j) = \min_{M \in \mu(T_i,R_j) \wedge M_T(t_i)=r_j.} d(M).$$

Defining $d(0,0)=0,$ and taking the linear order into account, we subsequently observe that

$$d(M^*) = \min_{0\le i\le m,\ 0\le j\le n} d(i,j) + (m-i)\times c_T + (n-j)\times c_{R,}.$$

We now establish a dynamic programming recursion for $d(i,j)$.

Theorem 1. For $i=1\ldots m$, $j=1\ldots n$,

$$d(i,j) = \min_{0\leq i'<i, 0\leq j'<j} d(i',j') + (i-i')\times c_T + (j-j')\times c_{R,} + c(t_i,r_j)$$

Proof. Let M_{ij} be a minimum deviation match of T_i and R_j, that is

$$M_{ij} = \underset{M \in \mu(T_i,R)) \wedge M_T(t_i)=rj.}{\arg\min} d(M).$$

By definition $M_T(t_i) = r_j$. Let i', $1\leq i'< i$, be the maximum index for which $M_T(t_{i'}) \neq$ -, and hence $M_T(t_{i'}) = r_{j'}$, for some j', $1 \leq j'< j$ (we let $i'=j'=0$ if such i' does not exist). By definition of i' and because of the linear order, all i'', $i' \leq i''< i$, and all j'', $j' \leq j''<j$, must have $M_T(t_{i''})$= -, resp. $M_R(r_{j''})$= -. Hence we conclude that $d(M_{ij}) = c(t_i,r_j) + (i-i')\times c_T + (j-j')\times c_{R,} + X$, where X refers to the cost of the restriction of the match M to $T_{i'}$ and $R_{j'}$. Now, since $d(M_{ij})$ is minimum over all matches for T_i and R_j, we derive that X must be the minimum cost of a match for $T_{i'}$ and $R_{j'}$, such that $M_T(i')=j'$, meaning that $X = d(i',j')$, and indeed $X = 0 = d(0,0)$ if $i'= j'=0$. Now, by definition of i' and j' we have that

$$d(i',j') + (i-i')\times c_T + (j-j')\times c_{R,} + c(t_i,r_j) \leq d(i\tilde{},j\tilde{}) + (i-i\tilde{})\times c_T + (j-j\tilde{})\times c_{R,} + c(t_i,r_j)$$

for all $i\tilde{}$, $0 \leq i\tilde{}< i$, and all $j\tilde{}$, $0 \leq j\tilde{}<j$, establishing the correctness of the theorem. ■

This result (re)establishes the correctness of the approach by Needleman and Wunsch [36] for alignment of linear ordered sets. The method proposed by Smith and Waterman [37] delivers, for given T and R, two sub trajectories $T_s = t_{i'},\ldots,t_i$, $1\leq i'\leq i \leq m$ and $R_s = T_s = r_{j'},\ldots,r_j$, $1\leq i'\leq i\leq$ m such that $d(M(T_s,R_s))$ is minimum over all possible choices of T_s and R_s. Improvements on the time and space complexity of these and related algorithms are possible [33,38].

In the medical context under consideration, the care set of a patient, i.e. the set of all activities of which the care received by the patient exists, often spans several departments and pathways. Hence, in order to

measure adherence for a specific clinical pathway, one has to restrict the deviation to a subset of the trajectory of a patient. This can be reasonably modeled by considering the following problem.

Definition 12. Given a pathway P and a trajectory T, the *restricted adherence RA(T,R)* of trajectory T to pathway P is defined as:

$$RA(T,R) = \min_{R \in \rho(P)} \min_{1 \le i' \le i \le m} \min_{M \in \mu(t_{i'} \ldots t_i, R)} d(M).$$

The special case of the restricted adherence problem where all activity sets have cardinality one, can be solved by straightforward extensions of the dynamic programming formulation of Theorem 1.

We now turn our attention to the more general case where R is restricted to have parallel activity sets of cardinality one, but T is not. In other words, the actual care received by a patient forms a trajectory, which may contain activities whose execution has been performed in parallel. This situation naturally arises when care is registered per date, rather than in hours and minutes, or when activities run in parallel indeed.

Let $T = A_1 A_2 \ldots A_l$ and $R = r_1 r_2 \ldots r_n$ be the two corresponding trajectories, where the A_k, $k=1 \ldots l$ represent the parallel activity sets of T, and in both trajectories the linear order increases with the indices. We denote $T_i = A_1 A_2 \ldots A_i$ and $R_j = r_1 r_2 \ldots r_j$. As before, we intend to find a feasible match M^* such that

$$M^* = \arg\min_{M \in \mu(T,R)} d(M).$$

Definition 13. For $1 \le k \le l$, $0 \le j' < j \le n$, we define $e(M(A_k, r_{j'+1} \ldots r_j)) = d(M(A_k, r_{j'+1} \ldots r_j))$ subject to $M_R(j) = t$ for some $t \in A_k$.

Lemma 1. For $1 \le k \le l$, $0 \le j' < j \le n$, $e(M(A_k, r_{j'+1} \ldots r_j)$ can be calculated in polynomial time.

Proof. The value $e(M(A_k, r_{j'+1} \ldots r_j))$ equals the minimum cost induced by a match between the unordered elements of A_k and the activities $\{r_{j'+1}, \ldots, r_j\}$, with the additional constraint that $M_R(r_j) \neq -$. Since there is

no order on the elements of A_k, this minimum cost match is the solution to the minimum cost bipartite maximum cardinality matching problem on the following bipartite graph $G(V_1 \cup V_2, E)$. Vertex set V_1 is the union of A_k and a set of $j\text{-}j'$ elements representing voids. Vertex set V_2 is the union of $\{r_{j'+1}, \ldots, r_j\}$ and a set of $|A_k|$ elements representing voids. The arc costs are defined according to definition 10, and the arc costs between two voids are zero. For the vertex r_j in V_2 only arcs connecting to elements of A_k exist which are in the substitute set I_{rj} (and no arcs connecting to voids). If $|V_2| > 1$, vertices $\{r_{j'+1}, \ldots, r_j\text{-}1\}$ of V_2 have arcs connecting to elements of A_k in their respective substitute sets and to all voids in V_1. Moreover each vertex in V_1 (representing an element of A_k) is connected to each of the void vertices in V_2. It is not hard to verify that the cost of a minimum cost maximum cardinality matching in G equals $e(M(A_k, r_{j'+1} \ldots r_j))$. This minimum cost maximum cardinality matching can be found in polynomial time [34]

Enumeration over all $k, j', j, 1 \le k \le l, 1 \le j' < j \le n$, now allows calculating all $e(M(A_k, r_{j'+1} \ldots r)$ in polynomial time. We now present a polynomial time dynamic programming algorithm to compute the minimum cost matching M^*.

For $1 \le k \le l, 1 \le j \le n$, we define

$$e(k,j) = \min_{(M \in \mu(T_k,R_j) \wedge (\exists t \in A_k \text{ such that } M_R(j) = t)} d(M)$$

and $e(0,j) = 0 + j \times c_R, j = 0, \ldots, n.$

Now let us first notice that $d(M^*) = \min_{1 \le k \le l,\, 0 \le j \le n} e(k,j) + (n-j) \times c_R + (\sum_{i=k+1}^{l} |A_i|) \times c_T$. Hence the following recursion on $e(k,j)$ suffices to find $d(M^*)$:

Theorem 2. For $k = 1 \ldots l, j = 1 \ldots n$,

$$e(k,j) = \min_{0 \le k^* < k,\, 0 \le j^* < j} \{ e(k^*, j^*) + (\sum_{i=k^*+1}^{k-1} |A_i|) \times c_T + e(M(A_k, r_{j^*+1} \ldots r_j)) \}.$$

Proof. Since $e(k,j) = \min_{(M \in \mu(T_k,R_j) \wedge (\exists t \in A_{k'},\, k' \le k \text{ such that } M_R(j) = t))} d(M)$

and the match implied by combining the match for A_k, to $r_{j^*+1}\ldots r_j$ having value $e(M(A_k,r_{j^*+1}\ldots r_j))$ and the match for T_{k-1} and R_{j^*} of value $min_{0\le k^*< k,0\le j^*<j}\, e(k^*,j^*) + (\sum_{i=k^*+1}^{k-1} |A_i|) \times c_T$ giving value $e(k^*,j^*) + (\sum_{i=k^*+1}^{k-1} |A_i|) \times c_T$ is a feasible solution for each choice of k, j, j^*, we have

$$e(k,j) \le min_{0\le k^*< k,0\le j^*< j} \{ e(k^*,j^*) + (\sum_{i=k^*+1}^{k-1} |A_i|) \times c_T \} + e(M(A_k,r_{j^*+1}\ldots r_j)) \}.$$

Let $\hat{M}$ be a minimum deviation match of T_k and R_j, where at least one element of A_k is not matched to a blank. Thus $d(\hat{M}) = e(k,j)$. Let $\hat{j}<j$ be the largest index such that for all $t\in A_k$, $\hat{M}_T(t) \in \{r_{\hat{j}+1},\ldots,r_j\} \cup \{-\}$, where $\hat{j}=0$ if $M_T(t)=r_1$ for some $t\in A_k$. Since $\hat{M}_R(j) =t$ for some $t\in A_k$, the precedence constraints imply that the elements of A_{k+1}, A_{k+2}, etc., cannot be mapped to elements $r_1\ldots r_j$ in any feasible match. By definition of $\hat{j}$, the precedence constraints imply also that elements of $t\in A_{k-1}$, A_{k-2} etc., cannot be mapped to elements $r_{\hat{j}+1}\ldots r_n$ in any feasible match. Thus only elements of A_k can be mapped to $r_{\hat{j}+1}\ldots r_j$, and only elements of T_{k-1} can be mapped to $r_1\ldots r_{\hat{j}}$. Let $j'' = \arg\max_{\{0\le o\le \hat{j}\}} M_R(o) \neq -$, where $j''=0$ if such o does not exist. Let $\hat{t}$ be defined as the match of j'', i.e. $M_R(j'') = \hat{t}$, and let $\hat{k}$ be the unique parallel activity set such that $\hat{t}\in A_{\hat{k}}$. Then, we have

$$e(k,j) = \min_{(M\in\mu(T_k,R_j) \wedge (\exists t\in A_k \text{ such that } M_R(j)=t))} d(M)$$

$$= \min_{(\hat{M}\in\mu(T_{\hat{k}},R_{\hat{j}}))} d(\hat{M}) + (\sum_{i=\hat{k}+1}^{k-1} |A_i|) \times c_T + e(M(A_k,r_{\hat{j}+1}\ldots r_j)).$$

$$= e(\hat{k},\hat{j}) + (\sum_{i=\hat{k}+1}^{k-1} |A_i|) \times c_T + e(M(A_k,r_{\hat{j}+1}\ldots r_j))$$

$$\ge min_{0\le k^*< k,0\le j^*\le j} \{ e(k^*,j^*) + (\sum_{i=k^*+1}^{k-1} |A_i|) \times c_T \} + e(M(A_k,r_{j^*+1}\ldots r_j)) \}.$$

Corollary 1. Given a pathway P with parallel activity sets of cardinality one, and trajectory T, the (restricted) pathway adherence problem can be solved in polynomial time.

Case Study Results

The second and novel adherence measurement algorithm developed in the previous section enables to analyze data from the Cardiovascular Center of MUMC. MUMC serves as an academic hospital but also as the general hospital for the city of Maastricht and vicinity. The academic function entails a considerable inflow of non standard patients for whose treatment strict adherence to pathways is not considered to be of prime importance. On the other hand, MUMC also has an inflow of patients for whom standardized pathways may provide optimal care. This situation has the potential risk of providing non standard care to patients for whom standardized care is appropriate and vice versa. Hence, the Cardiovascular Centre agreed on a procedure where standardized diagnostic pathways are defined for distinguishable patient groups. In doing so, the complex patients are separated from standard cases, which are in turn classified in various groups. The 'triage' process is the procedure by which patients are classified and which determines which diagnostic pathway is appropriate, if any. Early 2001, the Cardiovascular Centre established the set of standardized diagnostic pathways whose structure is presented in Figure 3. The four pathways for which adherence is measured in this research are visualized at the activity level in Figure 4. The pathway definitions have not changed over the years 2001-2005. As medical insights regarding the four diagnosis processes may have advanced over this time period, one must be careful when interpreting deviations from the pathways designed in 2001 measured towards the end of the of the measurement period 2001-2005.

IT is often behind in pathway introductions [15], and so has it been for MUMC's cardiovascular centre. In particular, there is no systematic electronic record keeping on the outcomes of the triage processes. We have used data from the financial information system, which records all activities and the date at which they have taken place. The data appears to be accurate and complete. As it is irrelevant for financial purposes, the exact start and end time of the activities is not recorded. The patient trajectories therefore often contain parallel activity sets. Since the outcomes of the triage processes are not recorded, there is no information on which pathway a patient is supposed to have followed. We have reconstructed this triage outcome and pathway selection decision, by assigning patients in retrospect to the pathways for which deviation is minimum. Per pathway p per year y, $n(p,y)$ is the estimate of medical experts of the number of patients (derived as a fraction of the total patient population) which should have followed pathway p in year y.

Cardiac patients typically engage in a long term relationship with the hospital, and many of them have co morbid conditions. Hence patient data over a longer time interval, such as the five year period 2001-2005 typically consists of hundreds of activities, by various departments (not only the cardiovascular center), and are stretched out over various years. Therefore they sharply contrast the diagnosis pathways that typically consist of between 4 and 20 activities, which take place during a short period. Hence to determine whether a diagnosis pathway has been followed by a patient, we have chosen to match the diagnostic pathway to sub patterns of trajectories [38] instead of matching them with complete trajectories.

Ideally, a diagnostic pathway P matches perfectly to a sub pattern of a trajectory T. In our experiments we give to this ideal match a value of 0. For a given pathway P and trajectory T, let S^* be a sub pattern for which a match M^* exists which minimizes the value $d(M^*)$ over all possible matches M for sub patterns S of T. Then S^* and M^* can be found using the algorithms presented in the previous section, and the value $d(M^*)$ deviates from zero for a combination of the following reasons (see also Definition 10):

a) Activity a of P is mapped to a non identical activity of S yielding a deviation value from substitution between 0 and 10. These deviation values have been specified by medical doctors of the cardiovascular center.
b) An activity of S is mapped to a blank '-' and not to an activity of P. For this case we report two scenarios, one in which the deviation is valued 0, and one in which it is valued 1. For various reasons, among which is co morbidity, unmapped activities of S need not be undesirable deviations from P. Hence a value of 0 might be appropriate. On the other hand, if a diagnostic pathway is executed swiftly and according to its definition, there is little room for unmapped activities. This motivates the value of 1. Neither of these values is preferable or perfect, and they do not form an exclusive optimal set. We simply report computational results for both these choices, and compare the outcomes.
c) An activity of P is mapped to a blank '-' and not to an activity of S. In this case we assign the maximum deviation value of 10, unless a lower deviation value is suggested by a medical expert of the cardiovascular center.

Using the thus defined deviation values, we determine for each *P,S* pair a maximum possible deviation P_{max}, which results from matching all activities of *P* and *S* to blanks. The computational results present *normalized deviations* $d(M)/P_{max}$, $0 \leq d(M)/P_{max} \leq 1$, for ease of interpretation. Obviously, smaller deviations represent stricter adherence.

In our computational experiments we have cleaned up the data set of originally 12103 patients as follows. Firstly we have eliminated all patients who do not have both a first consult (by specialized nurse or medical doctor) and a final consult (by medical doctor). Second, we consider the data per year, allowing for a comparison over the years. Consequently, we assume that the diagnostic pathways are not spread over multiple years. Thirdly, since the chemical lab and blood tests consists of a set of activities, each diagnostic pathway consists of around twenty activities. Since it is supposed to be followed by a treatment, any patient who has undergone a serious diagnosis process must have more than twenty activities. On the other hand, we judge trajectories of more than 500 activities, of which there is a limited number, as abnormally long. Hence we have only considered trajectories of between 20 and 500 activities. As a result, we obtained 2471 patients for 2001, 6701 for 2002, 7542 for 2003, 7796 for 2004, and 5133 for 2005. (For the first and last year our data covers only part of the year). The sets of patients of different years overlap.

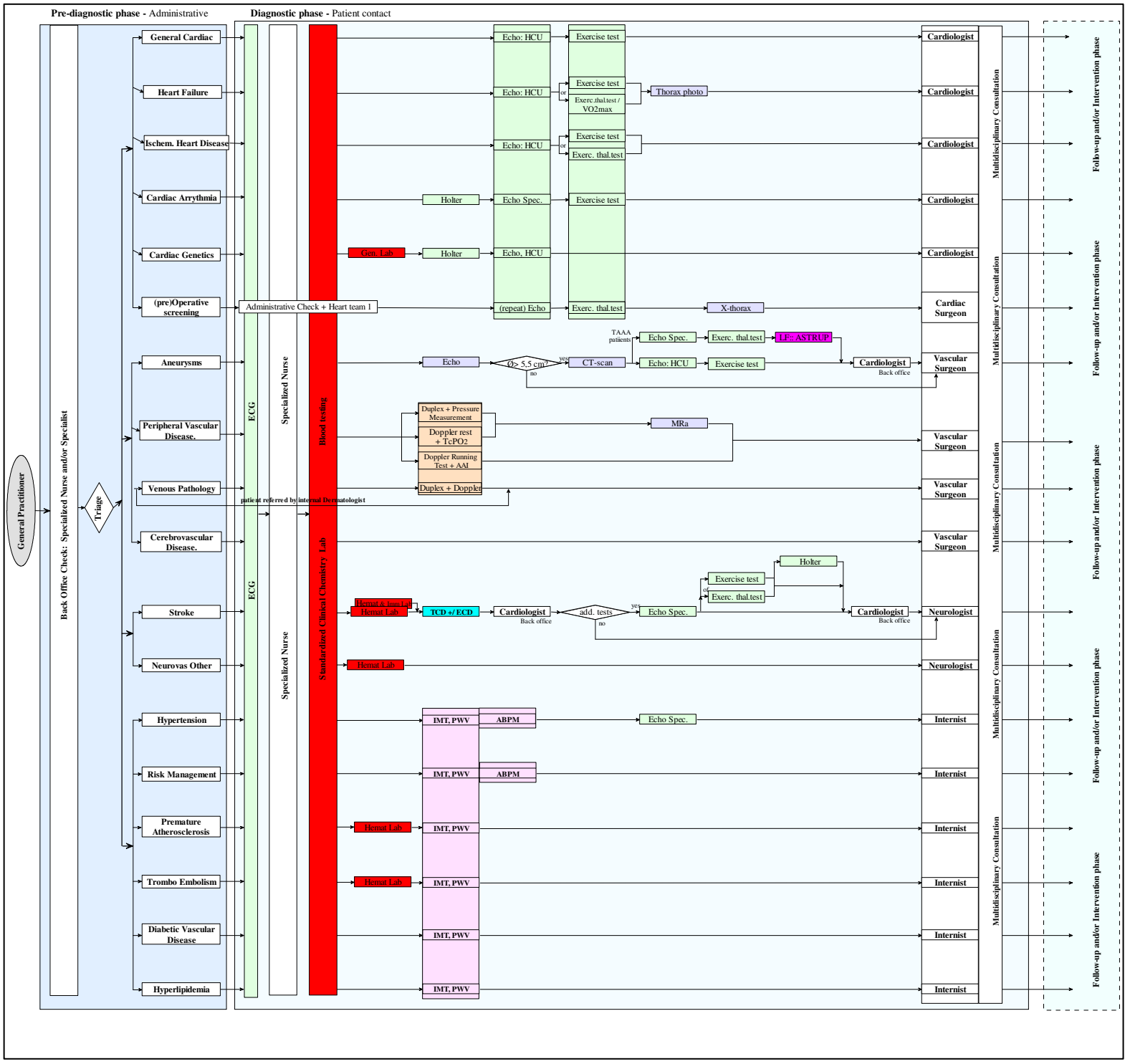

Figure 3: Clinical Pathways at Cardiovascular Center of MUMC

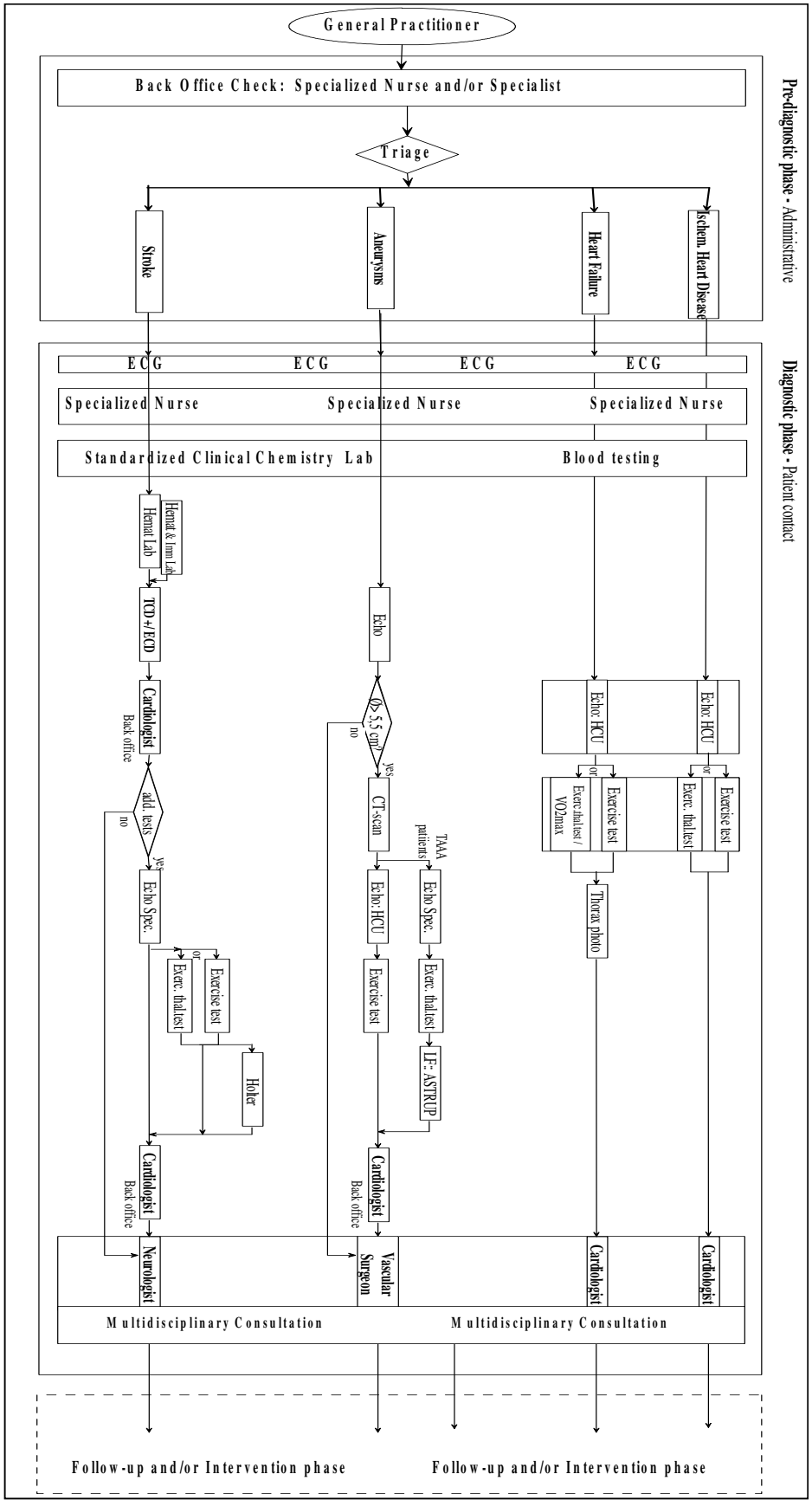

Figure 4: The 4 pathways for which adherence is measured

Table 1 presents the computational results for the base scenario where the cost of leaving activities in the realized trajectory unmatched is zero. There is a sub table for each pathway and each sub tables has a column for each year. Per pathway *p* per year *y*, the *n(p,y)* (or less) patients are sorted in increasing order of deviation cost. For pathway *p,* column *y*, row *i* presents the deviation cost of the patient at position $\lfloor i \times n(p,y)/10 \rfloor$ in the sorted list, i.e. the maximum deviation cost occurring in the i^{th} decile of patients selected to follow pathway *p* in year *y*.

As *0* refers to perfect adherence, and *1* to complete lack of adherence, all table entries are between *0* and *1*. For ease of interpretation we mention here that a normalized deviation of *0.5* corresponds to the case where the average deviation value of elements of the pathway as obtained by mapping to substitutes or blanks is *5* on the *10* point scale. Thus when the deviation cost of received care is *0.5*, it is as much like the prescribed pathway as it is different from it.

In general the computational results reveal that in many cases, the deviation is above *0.5*. Ischemic heart disease appears to be the exception, where especially in the early years 2001, 2002, low deviation cost are observed. When considering how adherence developed over time, one observes that for all pathways and for almost all deciles, the deviation cost went down from 2001 to 2002, but increased since then, often resulting in largest deviations for 2005.

Table 2 provides the same results, but now for the scenario where the deviation cost for unmatched activities from the realized patient trajectories has value *1*. For this case, the minimum deviation penalty is still *0*, but the maximum – non normalized – absolute deviation is higher, as the unmatched activities from the realized patient trajectory each have deviation cost of *1* in addition to the deviation cost of unmatched pathway activities. Nevertheless, we observe that the overall patterns of Table 1 reoccur in Table 2, but that the normalized deviation cost have increased by 0.0 until 0.15 in almost all cases. Thus, we conclude that the trajectories contain activities that do not belong to the clinical pathways.

Pattern							
		Years	**2001**	**2002**	**2003**	**2004**	**2005**
Aneurysm							
	1st decile		0.59	0.52	0.54	0.52	0.55
	2nd decile		0.63	0.56	0.6	0.56	0.61
	3d decile		0.65	0.61	0.63	0.6	0.61
	4th decile		0.67	0.63	0.67	0.63	0.62
	5th decile		0.67	0.64	0.7	0.64	0.64
	6th decile		0.71	0.66	0.72	0.65	0.66
	7th decile		0.72	0.67	0.73	0.68	0.69
	8th decile		0.73	0.69	0.73	0.7	0.71
	9th decile		0.75	0.71	0.74	0.72	0.72
	10th decile		0.75	0.73	0.74	0.73	0.73
Stroke							
	1st decile		0.35	0.31	0.44	0.49	0.53
	2nd decile		0.39	0.35	0.49	0.52	0.56
	3d decile		0.44	0.4	0.5	0.53	0.57
	4th decile		0.47	0.43	0.53	0.56	0.6
	5th decile		0.48	0.46	0.54	0.59	0.6
	6th decile		0.5	0.47	0.56	0.6	0.62
	7th decile		0.53	0.49	0.57	0.62	0.63
	8th decile		0.54	0.51	0.59	0.63	0.65
	9th decile		0.56	0.51	0.6	0.65	0.65
	10th decile		0.56	0.53	0.62	0.65	0.66
Heart Failure							
	1st decile		0.63	0.36	0.44	0.45	0.53
	2nd decile		0.74	0.42	0.45	0.53	0.56
	3d decile			0.45	0.53	0.56	0.56
	4th decile			0.53	0.56	0.56	0.6
	5th decile			0.56	0.57	0.63	0.65
	6th decile			0.59	0.63	0.65	0.67
	7th decile			0.65	0.67	0.7	0.72
	8th decile			0.67	0.76	0.74	0.74
	9th decile			0.74	0.9	0.79	0.78
	10th decile					0.9	0.79
Ischemic Heart Disease							
	1st decile		0.18	0.11	0.24	0.36	0.49
	2nd decile		0.29	0.18	0.31	0.47	0.55
	3d decile		0.36	0.24	0.36	0.53	0.55
	4th decile		0.42	0.27	0.36	0.55	0.55
	5th decile		0.45	0.35	0.42	0.55	0.55
	6th decile		0.49	0.35	0.47	0.55	0.55
	7th decile		0.53	0.4	0.49	0.55	0.6
	8th decile		0.58	0.45	0.53	0.6	0.67
	9th decile		0.64	0.45	0.53	0.62	0.71
	10th decile		0.65	0.47	0.55	0.65	0.71

Table 1: Computational results for $c_T=0$.

Pattern							
		Year	2001	2002	2003	2004	2005
Aneurysm							
	1st decile		0.66	0.62	0.67	0.64	0.61
	2nd decile		0.71	0.67	0.72	0.66	0.65
	3d decile		0.72	0.7	0.74	0.71	0.7
	4th decile		0.72	0.72	0.75	0.73	0.72
	5th decile		0.74	0.72	0.76	0.74	0.73
	6th decile		0.76	0.74	0.77	0.76	0.74
	7th decile		0.76	0.75	0.78	0.76	0.75
	8th decile		0.76	0.76	0.79	0.76	0.76
	9th decile		0.78	0.77	0.82	0.77	0.78
	10th decile		0.8	0.78	0.82	0.79	0.78
Stroke							
	1st decile		0.37	0.37	0.53	0.56	0.57
	2nd decile		0.44	0.43	0.56	0.57	0.6
	3d decile		0.47	0.44	0.59	0.6	0.65
	4th decile		0.5	0.47	0.6	0.62	0.65
	5th decile		0.51	0.51	0.63	0.63	0.66
	6th decile		0.51	0.51	0.63	0.65	0.66
	7th decile		0.54	0.51	0.63	0.66	0.66
	8th decile		0.56	0.53	0.64	0.66	0.66
	9th decile		0.57	0.54	0.65	0.67	0.68
	10th decile		0.59	0.56	0.66	0.68	0.69
Heart Failure							
	1st decile		0.63	0.46	0.55	0.56	0.56
	2nd decile		0.75	0.53	0.56	0.56	0.56
	3d decile			0.56	0.59	0.56	0.56
	4th decile			0.59	0.62	0.63	0.64
	5th decile			0.59	0.64	0.66	0.68
	6th decile			0.64	0.66	0.68	0.72
	7th decile			0.66	0.68	0.71	0.76
	8th decile			0.68	0.72	0.75	0.79
	9th decile			0.72	0.79	0.79	0.79
	10th decile			0.79		0.8	0.79
Ischemic Heart Disease							
	1st decile		0.33	0.23	0.39	0.49	0.56
	2nd decile		0.39	0.32	0.44	0.54	0.56
	3d decile		0.47	0.37	0.49	0.56	0.56
	4th decile		0.49	0.39	0.51	0.56	0.56
	5th decile		0.54	0.44	0.54	0.56	0.56
	6th decile		0.58	0.47	0.54	0.61	0.61
	7th decile		0.63	0.47	0.56	0.63	0.67
	8th decile		0.65	0.51	0.6	0.67	0.72
	9th decile		0.67	0.53	0.61	0.68	0.72
	10th decile		0.72	0.54	0.61	0.72	0.72

Table 1: Computational results for $c_T=1$.

Discussion

Despite scientific evidence that pathway implementations have often failed to deliver efficiency and/or quality improvements, large scale implementations of clinical pathways are worldwide expected to bring improvements in the near future, as requested by society. Scientific literature reveals that adopting clinical pathways in it self will not suffice. Much attention must therefore be paid to the design and improvement of the pathways as well as to the actual, practical, execution of pathways after implementation. If not adhered to, pathway implementation likely fails to bring improvement. We developed pathway adherence measurement methods which cope with the dynamics and flexibility of pathways, and therefore with the deviations common to practice. By developing an integral numerical adherence measure, as opposed to an activity based binary one, the models and methods recognize that deviation is not necessarily bad, yet allow scoring deviations at various severity levels. Because of the potential impact deviations from evidence based best practices may have on the cost and quality of care on the one hand, and the importance of customizing care to specific patients on the other hand, such a balanced approach is needed and will hopefully contribute to pathway acceptance as it has often obstructed implementation.

The models developed in this paper allow capturing the concept of clinical pathways as practiced in MUMC as well as the patient data. The patient data has been recorded for administrative purposes and is therefore not complete regarding the exact order of activities – it is exact with respect to the date – or reasons for deviations from pathways. Nevertheless, the model captures a variety of medically important characteristics, such as partial orderings and substitutes for activities, and provides a balanced adherence measure. A future model improvements are to incorporate more detailed work flow structures to capture parallelism, e.g. using starting and ending times, as commonly encountered in clinical guideline modeling languages [32]. On the other hand, an interesting future mode improvement is to treat the ordering relationships less strictly, and penalizing rather than forbidding violations of pathway activity orders.

Although we have developed polynomial algorithms, time complexity is certainly another area of improvement. Firstly, running times on the practical instances which contain thousands of patients with long medical record are very long (in the order of weeks). This is partly due to the absence of triage

outcomes. On the other hand, we have not been able to propose a polynomial method for the case where the pathway and/or the actual patient trajectory contain parallel activity sets of cardinality more than one, requiring us to enumerate all feasible realizations. We conjecture that this more general problem is NP-Complete, rendering a polynomial method to be unlikely to exist.

As is the case for several other adherence studies, the adherence measured in the case study can be viewed to be quite low. Without further analysis of the pathways and the medical cases at hand, we are unable to make a scientific normative statement about the observed adherence. We urge however to conduct this analysis, as the value of the methods and results is not in the adherence measurement itself, but in the improvements in provided care that result from it. In this respect, it is worth noticing that adherence improved in the first year, but diminished in subsequent years. A similar phenomenon has been observed by Rood et al. [27].

Our methods rely on techniques from combinatorial optimization problem and are akin to algorithms used for sequence alignment in genetic pathway analysis. The models and methods are not limited to health care processes. Business process compliance is an important issue in manufacturing and service industry. Hence advances made in health care, may certainly also benefit other service industries.

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