

**Applying Axiomatic Design Methodology to Enable Adaptation of  
Clinical Guidelines to Local Contexts**

By

**Yaron Denekamp**

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Technion – Israel Institute of Technology, 1994

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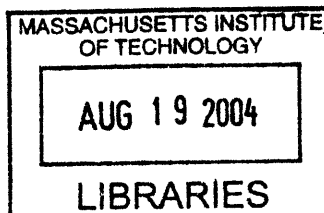
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Signature of Author.....  
Harvard-MIT Division of Health Sciences and Technology  
January 15, 2004

Certified by.....  
Aziz A. Boxwala, MD, PhD  
Assistant Professor, Harvard Medical School  
Adjunct Faculty, Harvard-MIT Division of Health Sciences and Technology  
Thesis Supervisor

Accepted by.....  
Martha L. Gray, Ph.D.  
Edward Hood Taplin Professor of Medical and Electrical Engineering  
Co-Director, Harvard-MIT Division of Health Sciences and Technology



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## Abstract

### Background

Local adaptation of guidelines may increase compliance with guidelines that have been developed at a national level and are often not used in practice because of contextual factors. We have developed a representation scheme known as HieroGLIF, that facilitates a two-step approach to development and implementation of guidelines. In the first step, professional medical societies create a setting-independent guideline. In the second step, the guideline is adapted to local settings. The scheme represents the setting-independent guideline knowledge in a hierarchical structure for which we use axiomatic design theory to guide a top-down design. This representation extends the Guideline Interchange Format (GLIF), a frame-based ontology that has been previously developed for representation of guidelines.

### Methods

We encoded conventional national guidelines in the setting-independent format which were adapted to local clinical settings of their practice by primary care physicians (PCPs). We conducted a qualitative analysis of the type of changes that were made by the local adaptors. For each of the guidelines two patients' scenarios were created for which two sets of guideline recommendations were generated, one from the adapted hierarchical guideline and one from the conventional, non-hierarchical guideline.

We evaluated in a randomized controlled trial the potential impact of the local adaptation methodology on adherence to guidelines. For each recommendation, 70 PCPs responded to a questionnaire that inquired if PCPs would follow the recommendations and their ratings for several relevant attributes. We also analyzed the data to look for attributes of recommendations that are important for their acceptance by PCPs.

### Results

In 8 out of 19 of the recommendations the changes made were significant. The most common types of changes were additions of practical information (6/19) and deletions of unnecessary information (6/19). The PCPs significantly preferred the adapted version for one recommendation in which addition of practical information and deletions of unnecessary information were done. The response for changes in clinical content in another recommendation resulted in rejection of the adapted version. The most important attributes for acceptance of recommendations found were agreement with the clinical content and then in descending order - fitness to the practice environment, availability of practical information and succinctness.

### Conclusions

We conclude that the potential role of local adaptation is mainly for adding relevant practical information and deletions of unnecessary information. This combination of changes led to significant preference of adapted guidelines' version. On the contrary, changes to clinical content led to rejection of an adapted version recommendation and should be done cautiously. In addition, efforts should be made to make clinical recommendations fit the practice environment, contain practical information and be succinct. We consider the real impact of local adaptation in this study lower than expected. We also believe that the study sharpens the issues of the optimal level of adaptation in specific and the real impact of local adaptation in general.

## **Introduction**

One important purpose for creating clinical practice guidelines is to improve quality of care by reducing variations in practice. However, guideline recommendations that are insensitive to the care context, or do not recognize necessary variations, can adversely affect acceptance by care providers. For example, a national guideline for a diagnostic workup might recommend an MRI examination if a screening test is equivocal. However, adherence to this guideline would be difficult if MRI equipment were not available in a particular setting.

Practitioners and patients are less likely to adhere to guidelines that are not seen as applicable to their situation or context<sup>[1]</sup>. The contextual factors that can affect patient care decisions can be setting-related (e.g., urban vs. rural practice, equipment availability), practitioner-related (e.g., medical specialty, levels of expertise), and patient-related (e.g., personal preferences, co-morbidity). Guidelines that are implemented as part of computer-based decision-support systems must be further adapted to fit into the clinical information systems environment. These adaptations are made to automate the triggering of recommendations in response to entry of relevant patient data and to support delivery of recommendations to the care provider. For example, decision criteria are modified to work with the patient data that is available in the electronic medical record and the format and vocabulary in which the data are recorded [2]. It is important that guidelines be sensitive to the context in which they will be implemented. In doing so, guidelines must balance the goals of achieving standardization of care based on scientific evidence and of maintaining consistency with local practice [3].

Thus, compliance with nationally developed guidelines may be higher if adapted locally during their implementation. Contextually adapted guidelines may enhance acceptance of evidence-based guidelines by making the guidelines more consistent with local practice and population variations. Guidelines adapted to reflect local practice patterns can be more readily integrated with clinical workflow. Tighter integration with workflow has been demonstrated to improve compliance with guidelines [4]. Further, the process of local adaptation may lead to a feeling of ownership by local practitioners. Ownership and local consensus opinion have been identified as important factors in acceptance of guidelines [5].

We have created a model for representing guidelines with the aim of enhancing their acceptance by (1) improving the consistency of guidelines with local practice and population variations, (2) better integrating guidelines within clinical workflow, (3) incorporating local opinions thus generating feeling of ownership, and (4) including and maintaining the scientific evidence for recommendations. The overall approach, named HieroGlif, is to express setting-independent intentions for the guideline that are then contextualized to the practice setting. We apply axiomatic design theory to guideline modeling, by incorporating it in the Guideline Interchange Format (GLIF) representation [6].

The aim of this study was to evaluate in a randomized controlled trial the potential impact of adaptable guidelines on adherence to guidelines in practice, using our methodology. Specifically, the study compared the acceptance of recommendations contained in guidelines that have been adapted, and recommendations contained in conventional guidelines that have not been adapted.

In addition, we aimed to clarify the incentives for modifications in adapting guidelines to local contexts, and whether the integrity of the setting-independent guideline is maintained.

Lastly, we intended to better understand the attributes of guidelines' recommendations that are more significant in determining whether physicians would accept or reject recommendations.

## **Background**

### **Factors influencing guideline acceptance**

In the current healthcare environment, guidelines are being advocated as a primary means to disseminate research findings, standardize care, improve quality of care, and increase the cost-effectiveness of services that are provided [7, 8]. However, studies have found that compliance with guidelines in practice has not been satisfactory [9-11].

For a guideline to be successfully used, the provider must have knowledge of the guideline, must accept the guideline, and the environment must not prevent the use of the guideline. Thus, factors that affect adherence to guideline have been categorized along the following spectrum [12]:

1. Knowledge of guidelines

- a. Lack of awareness of guidelines
- b. Lack of familiarity with guidelines
2. Provider attitude towards guidelines
  - a. Lack of agreement with specific guidelines
  - b. Lack of agreement with guidelines in general
  - c. Lack of expectancy of desired outcomes
  - d. Lack of self-efficacy, i.e., the belief that one cannot render the recommended care because of lack of skills, experience, or training.
  - e. Inertia of previous practice
3. Factors affecting practitioner behavior
  - a. Patient-related factors such as the inability to reconcile patient preferences with recommendations
  - b. Guideline-related factors such as the presence of contradictory guidelines, convenience of use, and ambiguities in decision criteria and recommendations
  - c. Environmental factors such as lack of resources, lack of time, reimbursement issues, and perceived malpractice liability
  - d. Workflow-related issues such as incorporation of guidelines into clinical activities and non-availability of a reminder system

### **Approaches to increase adherence to guidelines**

Several solutions to the problem of poor guideline acceptance have been investigated.

These approaches correspond, in general, to the classes of problem identified above.

In order to improve knowledge of guidelines, techniques for dissemination and provider education methods have been explored. These techniques include academic detailing, use of opinion leaders, and retrospective feedback on performance [13-15].

In order to integrate guidelines into the clinical workflow, thereby making them more convenient to use, attempts are being made to provide guideline-based decision- and workflow-support in health care information systems [16-19]. Several studies have demonstrated the positive impact of computer-based integration of guidelines on adherence [16, 17].

Representation schemes for guidelines are being developed that address issues about guideline-related factors such as ambiguities and vagueness in recommendations, branching logic, and eligibility criteria [20-25].

Not much attention has been devoted to addressing issues of provider attitudes such as lack of agreement with specific guideline recommendations, environmental factors such as non-availability of resources, and patient-specific factors such as existing co-morbidities, and the consideration of patients' preferences. Practitioners and patients are less likely to accept guidelines that are not seen as applicable to their situation or context [1].

The contextual factors that can affect patient care decisions can be considered as setting-specific, practitioner-specific, and patient-specific. The setting-specific factors include organization type (e.g., hospital vs. office), location (e.g., urban vs. rural), availability of equipment and medications, variations in the patient population (e.g., prevalence of the disease, population demographics), institutional policies, and workflow patterns.

Practitioner-specific issues include levels of training and experience and preferences for different management options. Patient-specific factors include the patient's preferences for different management options and existence of co-morbidities. Preferences for management options are influenced by socio-economic factors including concerns about reimbursement for care.

It is important, then, that guidelines be sensitive to the context in which they will be implemented. Several approaches to creating context-sensitive guidelines can be considered:

1. One approach is that a single guideline document addresses all of the variations that may occur in practice. The obvious problem with this approach is that the large number of permutations required to represent all variations will make the task of developing guidelines intractable. In addition, the guideline document will be large and complex to navigate or comprehend.
2. A possible solution to the above problems is to create guidelines that are specified at a coarse level (such as a recommendation for administering a "cholesterol-lowering drug for high risk patients"). Specific interpretations of the high-level recommendations can be made at the point of care. The advantage of this approach is

that not all the possible variations need to be considered at the time of guideline development. However, guidelines specified at a coarse level can also be difficult to follow for various reasons. Often, in specific clinical situations, it may not be clear how and when to apply a recommendation (which patient is “high risk”?).

Furthermore, such guidelines are subject to misinterpretation, thus unintentionally reducing adherence. Coarsely specified recommendations are not straightforward to operate in the routine workflow of a clinical practice and difficult to encode for implementation in a decision support system.

3. Another approach to creating setting-sensitive guidelines is to create separate guidelines for each local context. However, creating guidelines at a setting-specific level requires tremendous effort and skill, not only for initial development but also for update and maintenance. Another problem with such an effort is that it may result in guidelines that do not have an evidence base [26]. Furthermore, locally developed guidelines may perpetuate practice variations among institutions or regions, negating one of the primary reasons for developing guidelines.

#### **Increasing guideline acceptance by adapting it to the care context**

Guidelines must balance the goals of achieving standardization of care (based on scientific evidence) and of maintaining consistency with institutional or local practices [3].

This approach involves first authoring a high-level setting-independent guideline and then adapting it to local context [5]. The setting-independent guideline is expressed at an intentional level, in terms of objectives to be achieved. The guideline can be adapted by customizing recommendations and decision criteria. That is, the setting-independent guideline is elaborated on, by embedding details of locally acceptable actions and decisions that aim to achieve the objectives of the guideline.

Contextually adapted guidelines may enhance acceptance of evidence-based guidelines by making the guidelines more consistent with local practice and population variations. Locally adapted guidelines, which by definition reflect local practice patterns, can be more readily integrated with clinical workflow. Tighter integration with workflow has been demonstrated to improve compliance with guidelines [4]. The integration of guidelines into workflow has often taken the form of computer-generated patient-specific



reminders to clinicians during an encounter with a patient [16-18]. In computer-based clinical information systems, even stronger integration of locally adapted guidelines can be achieved, for example, by integrating guideline recommendations with an institutional order entry system. Further, the process of local adaptation may lead to a feeling of ownership by local practitioners. Ownership and local consensus opinion have also been identified as important factors in acceptance of guidelines [5, 27, 28]. In a letter to the editors of the British Medical Journal, Williams explains "... *nationally produced guidelines still require local adaptation to suit local circumstances and to achieve a sense of ownership by local clinicians, which is a major factor in uptake and use*" [29]. In addition to the advantages outlined above, there are indications that site-specific guidelines can potentially impact health care expenditure [30]. For example, economic benefits may be realized if the recommendations for screening tests are in concordance with local prevalence of the disease under consideration.

The setting-independent guidelines can consider commonly occurring variations in patients and can provide recommendations (at the intentional level) for these variations. The adapted guideline can further specify variations that are specific to local practices and the recommendations that are based on these variations.

Further, guidelines can include different management options for a clinical situation. Factors such as scientific evidence basis, contraindications, costs, and side effects that influence the selection of each option in the care of patients can be described for each of the variations. The physician and the patient can then make the decision about the management strategy for a specific patient by considering all the important factors including the preferences of the patient.

A potential issue with the approach to guideline development described in this section is that the recommendations in an adapted guideline may deviate from the intent of the setting-independent guideline. In addition, during the care of a particular patient, the management options chosen may not be the most strongly supported by scientific evidence or may not be the most cost-effective. In the next section, we discuss the effect of these deviations of the adapted guideline on adherence to the guideline.

### **Maintaining guideline integrity when adapting guidelines to context**

One of the important goals in developing guidelines is to standardize patient care for the problem with which the guideline deals. Thus, by adapting guidelines differently for different settings, the approach described in the previous section appears to be in conflict with the goal of standardizing care.

However, it may be argued that standardized care does not necessarily mean to pursue the exact same care path for each patient. Rather, it means that care decisions for all patients are made using the same considerations. Thus, when variations occur among patients or when they exist in practice settings, the optimal decision for that situation is made based on evidence, patient preferences, available treatment options, etc.

Therefore, by addressing the barriers to contextual applicability of guidelines, adapting guidelines to local settings may, in fact, enhance the acceptance of guidelines. Guidelines have been viewed by practitioners to reduce their autonomy, to be impractical, and representing “cookbook medicine” [31, 32]. The approach of adapting guidelines explicitly recognizes the variations that occur in clinical practice and provides a means to account for these variations when using guidelines.

Another problem that may be encountered in adapting guidelines is that the contextual interpretation may not follow the intent of the setting-independent guideline. For example, if the intent of the setting-independent guideline is to evaluate morphological aspects of a mass, a functional imaging study may not be an appropriate adaptation. Thus, a formal method for adapting guidelines is required that reduces deviation from the intent of the setting-independent guidelines.

### **Need for a formal methodology to create adaptable guidelines**

While several significant advantages could result from having contextually adapted guidelines, there are problems associated with the process of adaptation. First, as mentioned above, in the process of adapting a guideline, the integrity of the setting-independent guideline from which it was derived may not be maintained. That is, in adapting the guideline to local contexts, the intent of the recommendations and decision criteria in the setting-independent guideline may not have been preserved. Second, creating such guideline adaptations from prevalent verbose guideline publication formats may require much effort and be subject to interpretation errors. Moreover, when revisions

of the guidelines are published, the local adaptation effort would have to be repeated to a large extent.

These problems suggest that a formal methodology is desirable for developing setting-independent guidelines and for adapting these to local contexts. Such a methodology would maintain the integrity of the setting-independent guidelines during adaptation, i.e., preserve the *intentional* objectives. This methodology should incorporate revision control techniques to assist in adaptation and revision. In such a methodology, the guidelines would be represented in a structured form. In the structured form, a guideline can be described as a sequence of steps in a flowchart. Within each step, the intentions of the recommendations and decision criteria must be explicitly stated. The structured format would allow constraints to be specified in the setting-independent guideline that define how each step may be modified by the adapted guideline. In the following section, we review efforts by various investigators to model guidelines that can be adapted.

#### **Efforts in adaptable guideline representation**

Asbru is an intention-based language for representing skeletal plans [22]. Plans (or guidelines) in Asbru are represented hierarchically with deeper levels providing more details. Plans can be expressed at various levels of detail, thereby describing the intention of the plan while allowing for interpretation and flexibility in executing the plan. The latter attribute makes this approach vulnerable to some of the limitations described earlier for incompletely specified guidelines. Additionally, the Asbru language does not provide specifications for constraints and for operations that may be applied to plan components in order to adapt a guideline to different clinical contexts.

Fridsma et al have developed a program known as CAMINO for adapting “generic” guidelines for local use [33]. The CAMINO program provides a series of operators (e.g., addition, deletion, and substitution) that are applied to a guideline step to adapt it for local use. The program maintains the links between the corresponding steps of the generic guideline and the locally adapted guideline. However, the authors have not described a formal method to create generic guidelines that are easily adaptable. Further, this approach does not provide mechanisms that enforce maintenance of the integrity of the generic guideline.

Miller et al have described an approach for successfully maintaining multiple versions of a childhood immunization guideline [34]. They utilize an approach that disassociates decision rules from parameters of the rules (e.g., the parameter *age* at which the DPT vaccine is due). The authors recognize that their technique may have narrow applicability, i.e., primarily for use in childhood immunization guidelines.

The next chapter reviews our efforts to create structured representations of guidelines.

### **HieroGLIF: our approach to representing adaptable guidelines**

We have created a model for representing guidelines with the aim of enhancing their acceptance by (1) improving the consistency of guidelines with local practice and population variations, (2) better integrating guidelines within clinical workflow, (3) incorporating local opinions thus generating feeling of ownership, and (4) including and maintaining the scientific evidence for recommendations. The overall approach is to express setting-independent intentions for the guideline that are then contextualized to the practice setting. We apply axiomatic design theory to guideline modeling, by incorporating it in the Guideline Interchange Format (GLIF) representation [6].

### **Axiomatic design of guidelines**

Our approach utilizes the strengths of the above methods. Setting-independent guidelines are created in a hierarchical manner with the outer level of the guideline specifying high-level objectives. The deeper levels of the guideline contain detailed specifications of the recommended actions and decision criteria. Authors can specify constraints that affect how particular steps can be modified during local adaptation. Authors may also provide thresholds for decision criteria, which can be modified locally. During local adaptation, changes to one step of a guideline should ideally have no impact on other steps in the guideline at the same level of the hierarchy. This is analogous to modular development of software, wherein internal changes to the implementation of a module do not usually impact other modules.

However, with respect to steps of a guideline, such modular design is often not easy or not possible. A goal for authors of setting-independent guidelines is to design steps such that changes made to it for local adaptation will have no impact on other steps. If that is not possible, the authors should identify those steps that will be impacted by a change to another step. Preferably, a procedure should be provided that the authors could follow for

adapting a guideline. Axiomatic design theory was developed in the field of mechanical engineering as a principled approach to product design [35]. The use of a set of axioms results in product designs that are flexible and can be easily modified. This theory can be applied to the design of guidelines that are easily modified in local practice settings.

### **Design**

The process of axiomatic design involves mapping design elements among four domains. The customer domain consists of the customer's needs (CN) for the product being designed. An example of a customer need is that of reducing risk of cardiovascular disease (CHD) in patients with elevated LDL. In the functional domain, the customer needs are translated by the designers into a set of functional requirements (FRs). In the above example, an FR would be to reduce LDL cholesterol level. In the physical domain, the FRs are satisfied using certain solutions called design parameters (DPs). A DP in this case may be a CHD-risk-proportionate treatment plan. Finally, in the process domain, a process characterized by process variables (PVs) is created for producing the product. For treatment of high blood LDL cholesterol guideline, a PV may be a workflow for implementing the treatment plan.

### **Axioms of design**

The framework provides two axioms or principles to guide the design process [36]. The first axiom, known as the Independence Axiom, states that the independence of functional requirements must be maintained in the design. The second axiom, known as the Information Axiom, states that the design must contain the least information. FRs comprise a minimum set of independent requirements that the design must satisfy. According to the Independence Axiom, when there is more than one FR, the design must be such that each of the FRs can be satisfied without affecting other FRs. Therefore, the DP for a FR must be chosen or designed such that it satisfies the requirement of its corresponding FR without affecting other FRs. The Information Axiom aids in selecting among alternative design solutions. The axiom provides a measure of the "goodness" of a design: the design with the least information content is the best. Shannon's information theory can be used to measure a design's information content [37].

## The design matrix

The relationship among the FRs and the corresponding DPs is specified by the design equation,

$$\{\text{FR}\} = [\text{A}] \{\text{DP}\}$$

where  $\{\text{FR}\}$  is the vector of functional requirements,  $\{\text{DP}\}$  is the corresponding vector of design parameters, and  $[\text{A}]$  is the design matrix. The design matrix is a square matrix, the elements of which signify the mapping of a DP to an FR, and is of the form

$$[\text{A}] = \begin{bmatrix} A_{11} & A_{12} & A_{13} \\ A_{21} & A_{22} & A_{23} \\ A_{31} & A_{32} & A_{33} \end{bmatrix}$$

for a design consisting of three FRs (rows) and three DPs (columns). In order to satisfy the Independence Axiom, the design matrix must be a diagonal matrix (all elements not on the diagonal are zero) or a lower triangular matrix (all elements above but not including the diagonal are zero). A zero value of a matrix cell indicates no effect of a DP on an FR. When the design matrix is diagonal, the design is called uncoupled because each FR is satisfied independently by a single DP. When the design matrix is lower triangular, the design is decoupled. In such a case, the independence of FRs is only possible if the DPs are determined in a specific order (from top to bottom of the DP vector). In other forms of the matrix, the design is coupled. A coupled design is not desirable since DPs must be changed iteratively until a solution is reached. Consider the following design for the management of metabolic syndrome:

FR1 = Diagnose metabolic syndrome

DP1 = Metabolic syndrome diagnostic criteria

FR2 = Treat metabolic syndrome

DP2 = Weight and lipid control algorithm

In this case, the design matrix is given by

$$[\text{A}] = \begin{bmatrix} X & 0 \\ 0 & X \end{bmatrix}$$

This matrix indicates that DP1 has an effect on FR1 only and DP2 has an effect on FR2. In other words, if the diagnostic criteria for metabolic syndrome change, the treatment algorithm does not have to be modified. The reverse is also true.

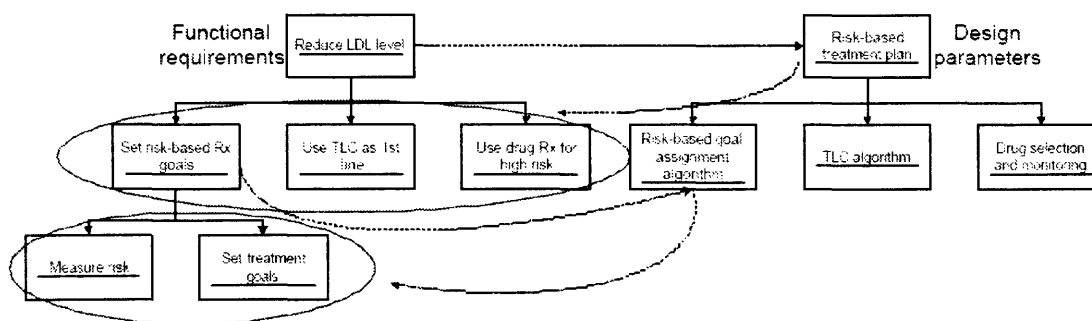
### **Design by zigzagging**

A design starts by specifying CNs, FRs, DPs, and PVs at a very high level. Design then proceeds in a hierarchical manner to more detailed levels for each of these elements. Lower level elements can only be determined once their corresponding higher level element is specified. In fact, the design proceeds in a zigzag manner. That is, once the highest level FR is selected, a DP must be selected or formulated as a solution. The set of FRs at the next level is then determined based on the DP at the level above. In the preceding example, for the DP, Risk-based treatment plan, the next level FRs would be to Measure risk, Use therapeutic life-style changes as first line treatment and Use drug therapy for high-risk cases (Figure 1). The corresponding DPs would then be selected. In this manner, design proceeds top-down, adding more detailed levels of FRs and DPs until an implementable solution is reached.

### **Modeling guidelines using axiomatic design**

Modeling setting-independent guidelines using the axiomatic design approach involves (1) specifying the setting-independent top-level objectives or intentions of the guideline; (2) partially refining the guideline through decomposition and zigzagging. For each intention identified in step 1, a DP consisting of a flowchart, a decision criterion or an atomic task is specified. For each step of the flowchart, the intentions are specified as in step 1; and (3) minimizing interactions among steps by following the Independence Axiom. This may involve restructuring of flowcharts such as splitting an algorithm into two. During local adaptation of the setting-independent guideline, the following procedure is followed: (1) any refinements necessary to steps of the guideline are carried out by adding more levels to the FR and DP trees; (2) changes such as addition, deletion, or modification of steps (i.e., recommendations) are made; and (3) if the changes made above have an impact on other steps in the guideline, these steps must be inspected and adjusted appropriately.

**Figure 1 – Axiomatic design principles**



The FR tree (left) and the DP tree (right) for a guideline for management of elevated cholesterol illustrating the zigzagging process during guideline design. The trees show the hierarchy of the FRs and DPs respectively. The dashed arrows indicate the order of creation of FRs and DPs.

Hierarchical design facilitates local adaptation by supporting (1) selective implementation of the guideline recommendations. Those branches of the hierarchy which may not be essential or possible to implement locally can be deleted; (2) inclusion of more details for a coarsely-specified setting-independent guideline by adding more depth to a branch of a tree; and (3) modification of a recommendation by replacing a branch of the tree with a new sub-tree. Due to the top-down design, typically these changes will be made at the lower levels of the tree, thus minimizing changes to the broader intent of the setting independent guidelines. Further, explicit specification of the FRs can assist in making local modifications that are consistent with the intent of the guideline. The axiomatic approach is used to design a hierarchically specified guideline such that the resulting specification can be easily modified. The steps of a flowchart produced following the first axiom are uncoupled or decoupled. The steps can thus be adapted to local settings with minimal impact on other steps. The refinement process is guided by the change order process map derived from the design matrix. This map suggests the order in which the modifications must be made based on the impact of change to a step on other steps.

### **HieroGLIF**

The Guideline Interchange Format (GLIF) is a language for structured algorithmic representation of guidelines [6]. HieroGLIF is an extension of GLIF to support the representation of hierarchical modular guidelines [38]. HieroGLIF extends the GLIF



ontology by explicitly supporting representation of intentions (FRs). An intention is associated with a guideline step object, which represent the DPs. The Algorithm class in GLIF was extended to include the representation for the FR-DP mapping described above. A design matrix class was also created and a slot added to Algorithm for containing the matrix.

The design tree in GLIF is constructed by the use of subguidelines. That is, a step which is the DP is decomposed into its lower level DPs by adding a subguideline to that step. The steps in the subguideline are the lower level DPs.

A software tool known as SIGTool was developed to support authoring of guidelines in HieroGLIF. The software tool was implemented in Java by extending libraries developed for the GLIF project [39]. In addition to the flowchart view supported by GLIF, SIGTool provides hierarchical (tree) views of the guideline structure. A component for constructing the design matrix is also included. The tool functions in two modes, one for creating new guidelines and the other for modifying an existing guideline. During guideline creation the tool facilitates creation of the hierarchical structure and allows the user to specify the design matrix. In the guideline modification mode, when a guideline step is changed, the tool uses the design matrix to identify other steps needing to be inspected by the author and considered for change.

## **Materials and Methods**

We evaluated our methodology of creating adaptable guidelines with respect to the degree of acceptance of the guidelines' recommendations by physicians in a randomized controlled study. For this study, we encoded guidelines for two medical problems that are commonly encountered in primary care practices. Two versions of each guideline were created: a conventional (i.e., non-adapted) and an adapted guideline. Recommendations for patients were generated from the guidelines, and were provided to physician subjects to assess acceptance of the guideline recommendations.

### **Study site**

The study was conducted from November 2003 to December 2003 among primary care physicians (PCPs) affiliated with Brigham & Women Hospital (BWH) and Massachusetts General Hospital (MGH). Both these institutions belong to Partners Healthcare System, an integrated delivery network in the Boston area.

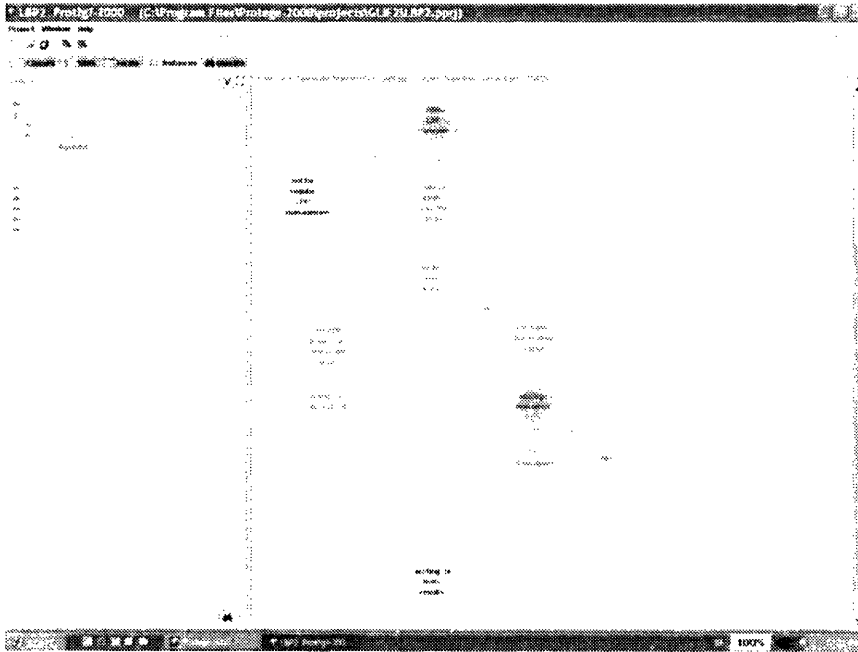
### **Study design**

Selected recommendations from two guidelines, created by national organizations, were encoded in this trial. One guideline was for the treatment of high blood cholesterol in adults [5, 40] and the other for the management of low back pain or sciatica in the primary care setting [41]. These problems are among the commonly occurring ones and have significant variation in how they are managed in different practice settings.

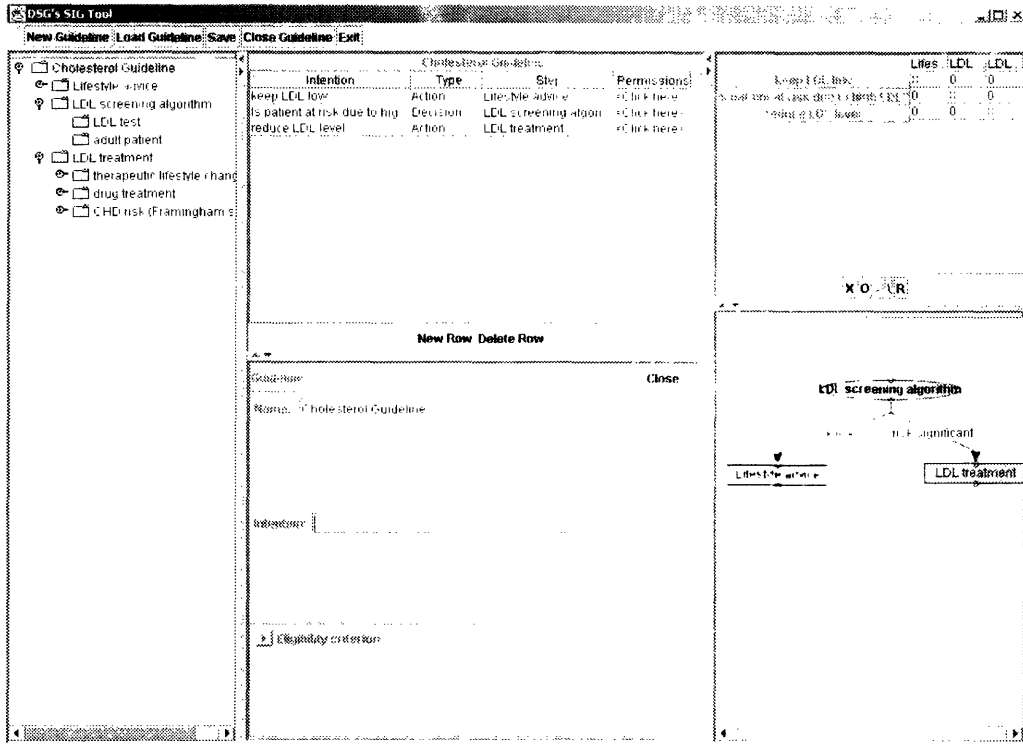
We encoded the national guidelines in HieroGLIF's setting-independent format using SIGTool. Then, the setting-independent guidelines were adapted to the clinical settings by two experienced primary care physicians (PCPs) from the study sites. These PCPs are recognized as leaders among their colleagues. The local adaptors reviewed the guideline documents before we started the local adaptation process. We then had a series of meetings with each one of them to incorporate changes they asked for into the guidelines' recommendations using SIGTool. While this process of local adaptation was conducted with each one of the PCPs independently they agreed by consensus on one final locally adapted version.

In addition to encoding the guidelines in HieroGLIF, we encoded both the guidelines in the Guideline Interchange Format (GLIF) format using Protégé, an ontology editing tool [42]. In encoding the guidelines in GLIF, we attempted to model the recommendations exactly as they were specified in the documents from the national organizations. These guidelines are henceforth referred to as non-adapted guidelines.

**Figure 2 - Screenshot of GLIF modeling using Protégé for the first scenario:  
High blood LDL cholesterol with zero or one risk factors**



**Figure 3 - Screenshot of SIGtool, HieroGLIF setting independent guideline tool for the high blood cholesterol management in adults guideline**



We created four patient’s scenarios to test recommendations from the two guidelines used in this experiment. The two clinical scenarios used for the cholesterol guideline were about patients with zero to one risk factor (one for a patient with newly identified elevated LDL cholesterol and the other for a similar patient who was treated for 12 weeks according to the lifestyle change recommendations). The low back pain guidelines included one scenario for acute of low back pain and one for chronic low back pain. The scenarios were used to create clinical case vignettes. The specific data items for the four clinical vignettes were based on the constraints of the scenarios. The cases were created by an internist who was not involved in any part the study (see appendix pp. 44-50). For each one of the four test cases, two sets of recommendations were generated, one from the corresponding locally-adapted guideline and one from the non-adapted guideline. For one case vignette, more than one recommendation was generated (e.g., referral to dietitian and start exercise). For all four cases combined, a total of 19 recommendations were generated.

Finally, two sets of Microsoft Word™ documents were assembled from the case vignettes and recommendations. One set of documents consisted of the four case vignettes, the corresponding recommendations from the non-adapted guidelines, and the study questionnaire. The other set consisted of the four case vignettes, corresponding recommendations from the locally-adapted guidelines, and the study questionnaire.

### **Qualitative analysis of the changes in the local adaptation process**

We conducted a qualitative analysis of the type of changes that were made by the local adaptors. We created a simple taxonomy of the various types of changes and used it for this analysis. We also used this analysis to look for associations between the type of modifications and the willingness of PCPs to implement recommendations.

### **Assembly of subjects**

This study was performed with institutional review board approval. We recruited the study subject via electronic mail invitation to the attending and resident PCPs at BWH and MGH. The subjects were offered a remuneration of \$100 for participating in the study. Ninety- nine PCPs who were not involved in the authoring process agreed to participate. The PCPs were then randomly assigned to receive the locally-adapted or the non-adapted version of the guidelines' recommendations for all four cases.

Randomization was stratified based on position (resident or an attending) and on institution practice affiliation (BWH or MGH).

### **Exposures**

The PCPs were provided with case vignettes and the generated recommendation for each of the four test cases. A PCP either received the document set with locally-adapted recommendations or the document set with non-adapted recommendations.

The documents were emailed to the PCPs who could complete questionnaire electronically using Microsoft Word and e-mail it back to us. Optionally, the participants could print the document set, complete the questionnaire on paper, and send us the paper copy.

## The study questionnaire

The study questionnaire was designed to analyze relevant attributes of acceptance of guidelines' recommendations. In forming the questionnaire we incorporated attributes for guideline acceptance that were reported in study by Grol et al [1]. We chose to study only those attributes that were related to local adaptation.

For each recommendation, the PCPs responded to six questions. The questionnaire inquired: (1) their rating for five attributes on a five-point scale (1=best and 5=worst), and (2) their response for one binary question. We also allowed an optional free text response for each question. The following is the questionnaire:

---

1) To what extent is the recommendation clear about how to manage this specific patient?

Completely clear

1

2

3

4

Completely unclear

5

If unclear – what is unclear?

---

2) To what extent does the recommendation fit your practice environment?

(Are the required resources (time, staff, etc.) easily available? Is there a need for modification of policies or procedures?)

Perfect fit

1

2

3

4

Does not fit at all

5

If not - what does not fit?

---

3) To what extent does the recommendation contain the practical information needed to manage the patient today in your practice?

Contains all  
practical  
information

1

2

3

4

Contains no  
practical  
information

5

If it does not - what type of information would have helped you in implementing the recommendation?

---

4) To what extent do you agree with the clinical content of the recommendation?

Completely agree

1

2

3

4

Completely  
disagree

5

Comments:

---

5) To what extent is the amount of information in the recommendation appropriately succinct?  
(balances between the amount of information required and readability)

Just right					much too much or much too little
1	2	3	4	5	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments:

---

6) Will you implement the recommendation as is?      Yes      No  
     

If your answer is no, why will you not implement it?

---

### Outcomes

For each recommendation, the PCPs were asked to respond to all 6 questions. We compared the frequencies of acceptance of recommendations from locally adapted guidelines with those from conventional guidelines.

### Statistical methods

Statistical methods included summary statistics, Student's t-test, Chi-square test based on contingency tables, z-test of normality, transformation, Wilcoxon rank-sum test, non-parametric Spearman's rank correlation analysis and logistic regression analysis.

First, a one sided two sample Student's t-test of the mean difference was used to evaluate whether PCPs accepted a greater proportion of recommendations from the adapted guidelines than from the non-adapted guidelines. We used t-tests for all the six questions per recommendation for all 19 recommendations. In order to look for potential differences between the responses of attendings and residents, and between BWH and MGH affiliated PCPs, we also used t-test by stratifying based on position (resident or an attending) and on institution (BWH or MGH).

Second, we conducted the Chi-square and Wilcoxon rank sum tests to analyze the relationships between the five attributes used for each recommendation and the 6<sup>th</sup> question. The latter question inquired whether a PCP would implement the recommendation using a yes/no binary response.

Third, non-parametric correlation analysis using Spearman's rank correlation coefficient ( $r$ ) was performed to assess if there was a correlation between each of the 5 attributes used.

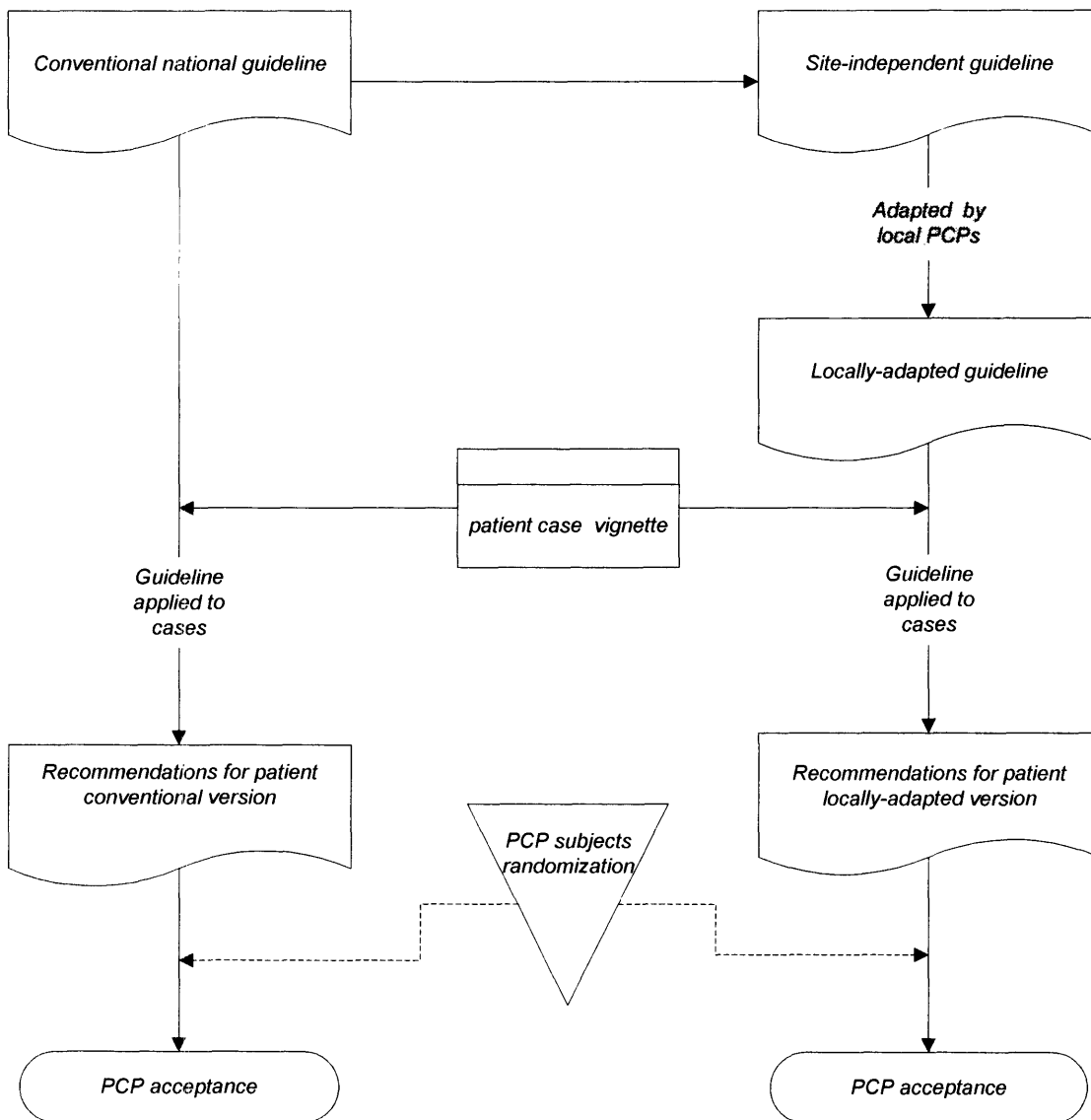
Finally, we used a multiple logistic regression analysis to find predictors for the outcome if a PCP would follow a recommendation and to assess the relative importance of the predictors. These predictors are the five attributes mentioned above.

The Student's  $t$ -tests were conducted using Microsoft-Excel all other analyses were performed using S-Plus 6.0 (<http://www.insightful.com>).



**Figure 4 - A flow scheme of the study.**

*A national guideline in the conventional format was converted to a setting-independent guideline. The setting-independent guideline was adapted to the primary care practice by PCPs from the practice. Synthetic case vignettes were produced and recommendations for the cases were generated for the conventional guideline and for the locally adapted guideline. The cases and the recommendations were provided to PCPs to measure their acceptance of the recommendations.*



## Results

A total of 70 out of the 99 PCPs (70%) who agreed to participate in the study completed and returned the questionnaires. Among the responders 49/70 (70%) filled out the electronic forms and returned it by e-mail and 21/70 (30%) returned printed completed questionnaires by regular mail.

Thus, the study population included 34 attending PCPs and 36 residents. Thirty six PCPs were exposed to the adapted version of the guideline's recommendations and 34 to the non-adapted version.

Table 1 - Study population by affiliation, position and guideline version

		BWH	MGH
Attendings	Adapted	8	7
	non-Adapted	10	9
Residents	Adapted	6	15
	non-Adapted	4	11
<b>Total</b>		<b>28</b>	<b>42</b>

Table 2 - Counts of the study's questionnaire

	Case 1	Case 2	Case 3	Case 4		
Number of recommendations per case	4	3	9	3	19	total

Number of recommendations for all PCPs	1330		
Number of questions per recommendatios	6	5	scale (1=>5)
		1	binary
Number of questions per PCP	114		
Number of questions per for all PCPs	7980		
<b>Missing data</b>			
Number of missing data questions	83		
Percentage of missing data questions in proportion to all questions	0.0104		

\* when 2 options were marked in sequence in using a 5-point rating scale we considered the average of these 2 numbers. This happened in 0.32 % of the questions' rating.

### **Qualitative analysis of the changes that were made to the recommendations in the local adaptation process**

In order to qualitatively classify the changes that were made in the local adaptation process we defined 5 attributes to categorize the modifications:

- 1) 'No change' – when the local adaptors fully agreed with the original conventional guidelines' recommendations and made no changes.
- 2) 'Minimal change' – for minor style changes like rephrasing.
- 3) 'Clinical content' – modifications that deviated from the original guideline's clinical intentions like changes in time intervals, decision thresholds or dosages.
- 4) 'Addition of practical information' – addition of practical information (site-specific but non-medical) to improve the execution of the guideline like phone numbers for referrals, local available handouts etc.
- 5) 'Deletion' – deletion of unnecessary information to obtain more succinct recommendation.

More than one such attribute can be used for categorizing a recommendation.

Table 3 - Summary of the qualitative analysis of the modifications made for all 19 recommendations.

<i>Scenario no.</i>	<i>Reco. no.</i>	<i>no change</i>	<i>minimal change</i>	<i>clinical content</i>	<i>addition of practical information</i>	<i>deletion</i>
<i>Scenario 1</i>	1				Y	Y
	2		Y			
	3		Y			
	4			Y	Y	
<i>Scenario 2</i>	1				Y	
	2	Y				
	3		Y		Y	
<i>Scenario 3</i>	1		Y			
	2		Y			
	3		Y			Y
	4			Y		Y
	5					Y
	6					Y
	7					Y
	8			Y		
	9			Y		
<i>Scenario 4</i>	1		Y			
	2				Y	
	3		Y			
<i>Total</i>	<i>19</i>	<i>1</i>	<i>10</i>	<i>2</i>	<i>5</i>	<i>6</i>

This qualitative analysis shows that in 11 recommendations the changes that the local adaptors made were not significant and that changes to clinical content were made in 2 recommendations. The most common types of changes were addition of practical information (6/19) and deletions of unnecessary information (6/19).

**Results of the t-test analysis for the difference in recommendations' acceptance between the adapted and non-adapted versions.**

We conducted 114 t-tests for the 6 questions per recommendation for all 19 recommendations.

We found significant p-values in the 6<sup>th</sup> outcome binary question in two out of the 19 recommendations and for some of the related attributes in these recommendations.

Table 4 – P-values t-test analysis results for the two recommendations with significant difference in acceptance

\* Bolded numbers – p-value < 0.05 (significant)

\* Questions 1 to 5 refer to the 1=>5 scaled questions and question 6 is the binary outcome question.

	<i>Question 1 clarity</i>	<i>Question 2 fitness</i>	<i>Question 3 practicality</i>	<i>Question 4 content</i>	<i>Question 5 amount</i>	<i>Question 6 implement outcome</i>	<i>direction</i>
<i>Case 1 rec 1</i>	<b>0.002</b>	<b>&lt;0.001</b>	0.07	<b>0.04</b>	<b>&lt;0.001</b>	0.003	<i>adapted</i>
<i>Case 3 rec 4</i>	<b>0.03</b>	0.27	<b>0.03</b>	0.053	0.01	<b>0.003</b>	<i>non adapted</i>

\* See the two versions for these recommendations in appendix pp 51-53.

*Clarity* – refers to the first question – “To what extent is the recommendation clear about how to manage this specific patient?”

*Fitness* – refers to the second question – “To what extent does the recommendation fit your practice environment?”

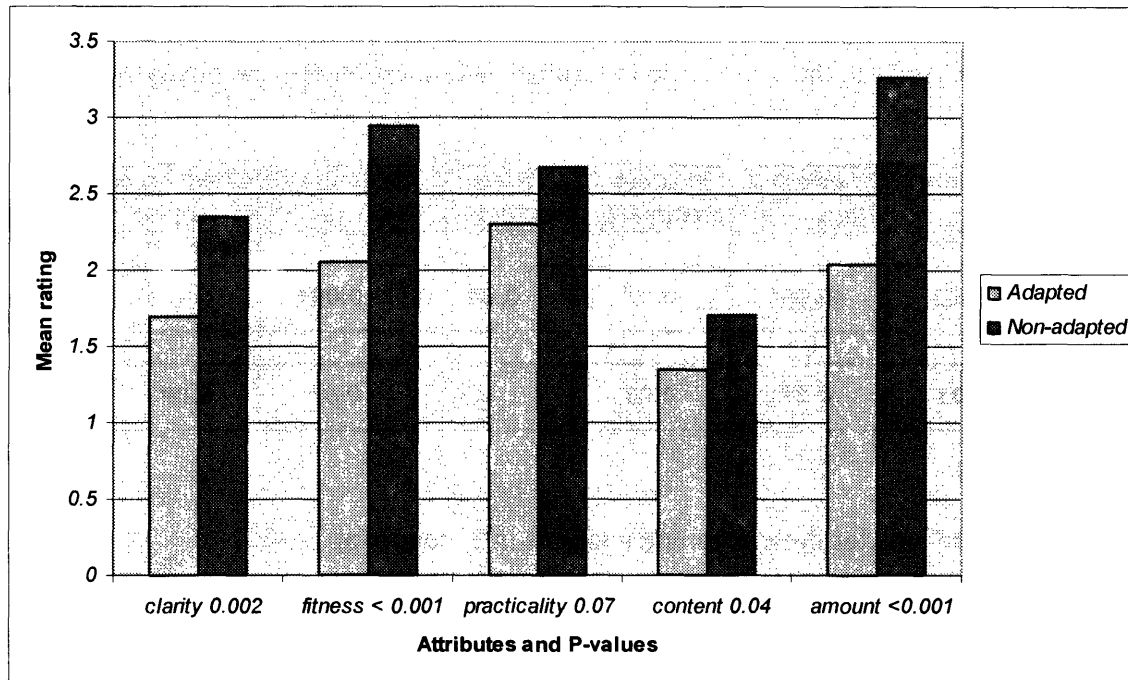
*Practicality* – refers to the 3<sup>rd</sup> question – “To what extent does the recommendation contain the practical information needed to manage the patient today in your practice?”

*Content* – refers to the 4<sup>th</sup> question in the questionnaire – “To what extent do you agree with the clinical content of the recommendation?”

*Amount* - refers to the 5<sup>th</sup> question – “To what extent is the amount of information in the recommendation appropriately succinct? (balances between the amount of information required and readability)”

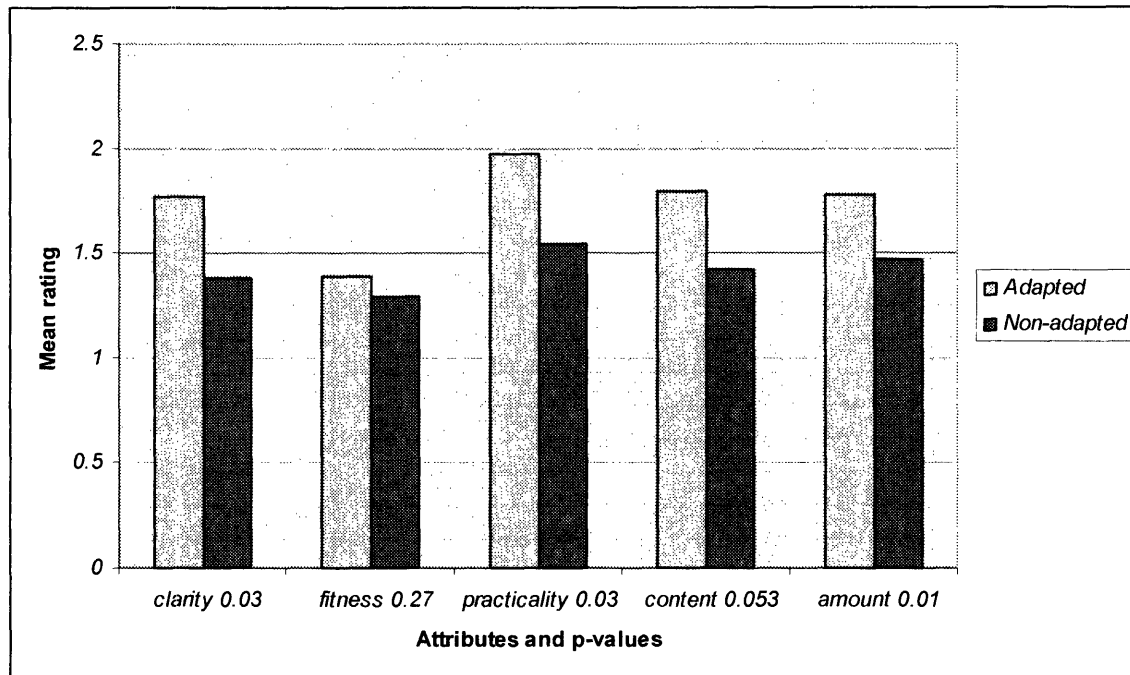
The outcome variable is the binary 6<sup>th</sup> question – “Will you implement the recommendation as is?”

Figure 4 - Mean rating between the adapted and non-adapted versions for case 1 recommendation 1



This chart reveals that the PCPs accepted all the attributes for the adapted version of this recommendation more than the non-adapted version. They considered the adapted recommendation much more succinct, clear, fits their practice environment and contains practical information.

Figure 5 - mean rating between the adapted and non-adapted versions for case 3 recommendation 4



The chart indicates that the PCPs accepted all the attributes for the non-adapted version of this recommendation more than the adapted version. The PCPs thought that the adapted version of this recommendation was not clear and practical and they did not agree with its clinical content.

**Sub-category stratified analysis of responses between positions**

**(attending vs. residents)**

We found no significant changes in the responses of attending and residents in employing the t-tests analysis for attending PCPs and residents separately.

**Sub-category stratified analysis of responses between institutions**

**(BWH vs. MGH affiliated PCPs)**

We found no significant changes in the responses of BWH and MGH affiliated PCPs in employing the t-tests analysis.

Table 5 - Correlated responses to the types of modifications

Case no.	Reco. no.	no change	minimal change	clinical content	addition of practical information	deletion	direction of response
Case 1	1				Y	Y	adapted
	2		Y				no change
	3		Y				no change
	4			Y	Y		no change
Case 2	1				Y		no change
	2	Y					no change
	3		Y		Y		no change
Case 3	1		Y				no change
	2		Y				no change
	3		Y			Y	no change
	4			Y		Y	non-adapted
	5					Y	no change
	6					Y	no change
	7					Y	no change
	8			Y			no change
	9			Y			no change
Case 4	1		Y				no change
	2				Y		no change
	3		Y				no change

The data in this table reveals that PCPs significantly preferred the adapted version of case 1 recommendation 1 in which addition of practical information and deletion of unnecessary information were done. The response for the changes to the clinical content and deletion changes in case 3 recommendation 4 resulted in rejection of the adapted version for this recommendation.

\* All the following results are based on analysis of the recommendation as the unit of analysis. Since every PCP out of the 70 that participated in the study responded to 19 recommendations we could investigate 1330 recommendations.

**Chi-square, t-test and Wilcoxon tests to analyze the relationships between the attributes used and the acceptance of recommendation**

We examined the following attributes about the PCPs in this analysis in addition to the attributes describing the recommendation:

*Institution* – BWH or MGH



*Position* – resident or attending

*Clinical experience* – the number of clinical experience years since graduation from medical school. We used the log of the number of years for this attribute.

Table 6 – P-values for the attributes' correlation to the outcome:

	<i>Institution</i>	<i>position</i>	<i>clinical experience</i>	<i>clarity</i>	<i>practicality</i>	<i>fitness</i>	<i>content</i>	<i>amount</i>
<i>Chi-square</i>	..	0.69		0	0	0	0	0
<i>Wilcoxon</i>			0.41	0		0	0	0
<i>t-test</i>			0.18	0		0	0	0

Chi-square test based on contingency tables with Yates' continuity correction

Wilcoxon - Wilcoxon rank-sum test

The results showed that the attributes clarity, practicality, fitness, content and amount were significantly associated with the willingness of PCPs to implement guidelines' recommendations.

The results also disclose that the indicators of clinical experience (clinical experience years and position) are not associated with acceptance of recommendations among the PCPs that were studied.

We also conducted a sub-category stratified analysis for the adapted vs. the non-adapted recommendations for all the attributes mentioned in this table. All p-values did not change when we used the same tests.

### **Spearman's rank correlation analysis**

All pairwise non-parametric correlation analysis using Spearman's rank correlation coefficient (r) was performed to look for correlations among the attributes used.

Table 7 – Results of spearman's rank correlation analysis

	<i>clarity</i>	<i>fitness</i>	<i>practicality</i>	<i>clin cont</i>	<i>amount</i>
<i>clarity</i>	x	0.56	0.67	0.49	0.66
<i>fitness</i>	0.56	x	0.58	0.49	0.56
<i>practicality</i>	0.67	0.58	x	0.48	0.72
<i>clin cont</i>	0.49	0.49	0.48	x	0.48
<i>amount</i>	0.66	0.56	0.72	0.48	x

The correlation analysis based on Spearman's rank correlation coefficient (r) showed that all 4 attributes are moderately to highly correlated.

**Logistic regression analysis**

We conducted a first order logistic regression analysis with all predictors for the binary outcome to assess the relative importance of the attributes in acceptance of a recommendation by PCPs.

For the purpose of building the logistic regression model we excluded the recommendations for which we had missing data. This reduced the number of recommendations from 1330 to 1254.

The final model of all the variables without interactions consists of the following attributes -

Table 8 – Significance of the attributes in the logistic regression model (fitness is spelt incorrectly)

	<i>Intercept</i>	<i>fitness</i>	<i>practicality</i>	<i>content</i>	<i>amount</i>	<i>non-significant</i> <i>clarity</i> <i>institution</i> <i>position</i> <i>clinical experience years</i>
<i>Beta coefficient</i>	7.63	-0.53	-0.4	-1.54	-0.38	
<i>p-value</i>	<0.001	<0.001	<0.001	<0.001	<0.001	

The logistic regression analysis reveals that the institution (BWH or MGH), position (resident or attending), clinical experience years and clarity were not significant in predicting the acceptance of recommendations by PCPs. However, the attributes fitness, practicality, content and amount were all statistically significant in predicting whether a PCP would implement a recommendation. The model suggests that disagreeing with the clinical content of a recommendation is the most important attribute in predicting implementation and then fitness, practicality and the amount of information.

## **Discussion and conclusions**

Several researchers pointed out that local adaptation of clinical guidelines may be an important factor in compliance with guidelines' recommendations by physicians [5, 27, 28].

Yet, there is very little objective information about the real impact of local adaptation and about the strategy of implementing it. In this study we addressed several aspects of this issue by applying a structured methodology for the local adaptation process. We believe that the aspects of local adaptation studied are not specific to this methodology and therefore the findings of this study clarify issues in local adaptation in general.

We selected to locally adapt the high blood cholesterol in adults and low back pain or sciatica in the primary care setting guidelines [40, 41] , since they represent common clinical problems and we assumed that both are prone to local modifications. Thus, although the results could be different for other guidelines, we believe that using these two guidelines enabled us to extract relevant knowledge about local adaptation. Our conclusions are based on analyzing the responses of 70 PCPs who were randomly exposed to a set of 19 recommendations, adapted (34 PCPs) and non-adapted (36 PCPs).

The qualitative analysis we conducted for the modifications made in the local adaptation process revealed interesting data about the required changes and the types of changes. Significant modifications were made to less than 50% of the recommendations (8/19). The typical changes done by the local adaptors were additions of practical information and deletions of unnecessary information, and the local adaptors modified clinical content in only two recommendations. This demonstrates that the local adaptors found most of the clinical content of the recommendations appropriate for their practice. However, the main modifications that were required in their opinion were to make the recommendations more practical by adding contextual information and make them more succinct by deleting unnecessary information. Thus, it seems that the potential role of local adaptation is mainly for adding relevant practical information and deletions of unnecessary information rather than changing clinical content.

We found statistically significant differences in accepting adapted vs. non-adapted recommendations for two recommendations. Since significant changes were made to eight recommendations, it means that for 25% of them the PCPs responded in favoring a

certain version. Interestingly, while the PCPs preferred the adapted version for one recommendation (case 1, recommendation 1), they rejected the adapted version for the other one (case 3, recommendation 4), preferring the original non-adapted version for this recommendation.

The changes made to the preferred adapted recommendation were addition of practical information and deletion of unnecessary information. This recommendation is about the diet component as part of the therapeutic lifestyle changes required for treating high blood LDL-cholesterol patient. The PCPs considered the adapted recommendation much more succinct, clear, fitting their practice environment, and containing practical information. Further, this recommendation is the only one out of the 19 for which the changes included both, 'addition of practical information' and 'deletion'. This suggests that the compliance with guidelines by physicians may increase if practical information would be added in the local adaptation in addition to removing unnecessary information.

The types of modifications made in the adapted recommendation that the PCPs rejected were modification of clinical content and deletion of unnecessary information. The recommendation was for acute low back pain symptom control by medications. The clinical content modification weakened the role of muscle relaxants in treating acute low back pain. Many of the PCPs used the free text space to comment that they would continue to prescribe muscle relaxants to acute low back patients despite the content of the recommendation. The PCPs regarded the non-adapted version for this recommendation more clear and practical than the adapted version.

We consider this result very helpful in understanding pitfalls in the local adaptation of clinical guidelines. In this case the opinion of the local adaptors did not reflect the professional judgment of their colleagues who objected the diminution of the muscle relaxants' role in the clinical context of acute low back pains. Also, this result suggests a role of physician education and other interventions in addition to decision-support when implementing clinical practice guidelines.

We also believe that this result brings up an essential issue in local adaptation which is the optimal level of adaptation. The ideal solution is probably to build a system that will allow every physician to locally adapt the guidelines based on some predefined constraints. However this may be too ambitious to achieve taking into account the many

expected obstacles like the complexity of such a system, the time resources that will be required by many individuals and the lack of control on modifications.

On the other hand local adaptation done at a high (i.e., institutional) level may probably be too far from the real physicians' needs and preferences. We believe that in this study the level was higher than the optimal and therefore masked some of the potential power in having locally adapted guidelines.

The impact of local adaptation on acceptance of guideline recommendations was lower than we expected. The local modifications led to statistically significant increase in acceptance in just one recommendation. It may be that the results could have been better if some parameters of the study were different. However, this still raises questions about the justification in striving for local adaptation of clinical guidelines. The process is demanding in terms of costs and time resources and could be justified by showing real benefits. We believe that more studies aimed to evaluate the real impact of local adaptation should be conducted in order to come to a clear conclusion about this key issue.

In this study we also intended to better understand why physicians would prefer to accept certain recommendations rather than others. Specifically we expected to identify attributes of clinical recommendations that determine if a recommendation would be implemented. Since 70 PCPs in the study responded to 19 recommendations we could analyze physician's responses to 1330 recommendations, 684 of which were adapted and 646 non-adapted. Each recommendation was analyzed as having attributes and a binary outcome of acceptance ("will you implement it as is?").

We found that clarity, availability of local/contextual information, fitness to the clinical environment, agreement with the clinical content and succinctness were significantly associated with the willingness of PCPs to implement guidelines' recommendations.

Not surprisingly, these five attributes were found to be moderately to highly correlated with each other.

One might suspect that the attitudes of attending physicians would differ from those of less experienced residents who may be helped more by locally adapted recommendations. This assumption was not proven to be true as we could not find any

such difference between more experienced and less experienced PCPs in general, and between attending PCPs and residents in specific.

Building a logistic regression model for the attributes as predictors adjusted to each other, and the binary question as outcome enabled to clarify the relative importance of the attributes. The most important attribute was found to be agreement with the clinical content of a recommendation and then in descending order - fitness to the environment, availability of practical information and succinctness. Interestingly, the model did not include the attribute clarity of the recommendation. It seems that the recommendations were clear to the PCPs and this was not a factor in their decision whether to implement a recommendation. Therefore, we conclude that efforts should be made that clinical recommendations would fit the practice environment, contain practical information and be succinct.

### **Limitations**

The study examined acceptance of locally adapted guidelines by a limited range of users (PCPs) in a single type of environment (office practices affiliated with BWH and MGH). We selected these subjects because PCPs are the target users of a large number and broad variety of guidelines. However, several factors may influence adaptation and use of guidelines by specialists and during hospital care.

Another limitation is the result of using case abstracts and not “live” patients. It is more difficult to make conclusions about physician’s decisions by using this method. In addition, patient preferences were not accounted for in the measurement of acceptance of decisions. Inclusion of patient preferences may bias the results against the model.

The costs and logistics of conducting a prospective study in the clinical setting with real patients made it less appropriate at this stage of the research.

### **Summary**

To the best of our knowledge this study is the first to explore qualitatively and quantitatively in a randomized trial issues in local adaptation of clinical guidelines. We found that the potential role of local adaptation is mainly for adding relevant practical information and deletions of unnecessary information rather than changing clinical content. This combination of changes led to significant preference for adapted guidelines.

On the contrary, changes to clinical content led to rejection of an adapted recommendation suggesting that adaptation should be done cautiously.

In addition, we analyzed the data gathered in this study to look for attributes of recommendations that are important for their acceptance. We conclude that efforts should be made to incorporate practical information that will improve fitness to the practice environment.

We believe that this study sharpens the issues of the optimal level of adaptation in specific and the real impact of local adaptation in general. Local adaptation of clinical guidelines should be further explored by conducting studies aimed to better understand its real impact and the optimal strategy of using it.

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## Appendix

### (1) Detection, Evaluation, and Treatment of High Blood Cholesterol

#### 2 Scenarios - Primary Prevention Zero to One Risk Factor, Cases 1-2

##### (1a) Scenario 1

Outpatient clinic, patient without history of I.H.D, high LDL-cholesterol level in routine fasting lipoprotein profile which should be done every 5 years, secondary dyslipidemia ruled out.

Causes of secondary dyslipidemia: Diabetes, Hypothyroidism, Obstructive liver disease, Chronic renal failure, Drugs that increase low-density lipoprotein cholesterol and decrease high-density lipoprotein cholesterol (progestins, anabolic steroids, and corticosteroids).

Goal:

The goal for low-density lipoprotein cholesterol in this risk category is <160 mg/dL.

Tasks:

- Risk factor assessment.
- The next management steps at this stage are therapeutic life style changes (TLC).

Required data items:

##### **Case 1**

Age: 20-65    Gender:

Chief complaint: *High serum LDL-cholesterol on routine screening test*

Past medical history: *Risk factors 0 or 1 - **including age and low HDL!**  
No I.H.D, Diabetes, Hypothyroidism, Obstructive liver disease*

Current medications: *No drugs that increase low-density lipoprotein cholesterol and decrease high-density lipoprotein cholesterol*

Physical exam: *Vital signs, Blood pressure...*

Lab tests: *LDL Cholesterol > 160  
Total cholesterol -    , HDL cholesterol -    ,  
Triglycerides – norm level.*

*Kidney functions – creatinine and urea – norm levels*

### Major Risk Factors

- Cigarette smoking
- Hypertension (blood pressure >140/90 mmHg or on antihypertensive medication)
- Low high-density lipoprotein cholesterol (<40 mg/dL). HDL cholesterol >= 60 mg/dl counts as a “negative” risk factor. Its presence removes one risk factor from the total count.
- Family history of premature coronary heart disease (coronary heart disease in male first degree relative <55 years; coronary heart disease in female first degree relative <65 years)
- Age (men >45 years; women >55 years)

### (1b) Scenario 2

Outpatient clinic, patient without history of I.H.D, high cholesterol level in routine fasting lipoprotein profile which should be done every 5 years, zero or one risk factors, secondary dyslipidemia ruled out, therapeutic life style changes were started in visit 1, follow up was conducted on visit 2 six weeks later. The patient arrives for the 3<sup>rd</sup> visit 12 weeks after visit 1. The latest LDL-cholesterol is 160-190.

#### Goal:

The goal for low-density lipoprotein cholesterol in this risk category is <160 mg/dL.

#### Task:

The next management steps at this stage is to consider drug therapy if LDL cholesterol > 160.

#### Required data items:

### Case 2

<u>Age:</u> 20-65	<u>Gender:</u>	<u>Weight:</u>	<u>Height:</u>
<u>Chief complaint:</u> <i>Therapeutic life style changes were started 3 months ago due to LDL cholesterol 185, follow up was conducted on visit 2 six weeks later. The patient arrives for the 3<sup>rd</sup> visit 12 weeks after visit 1.</i>			
<u>Past medical history:</u> <i>Risk factors 0 or 1 - <b>including age and low HDL!</b> No I.H.D, Diabetes, Hypothyroidism, Obstructive liver disease</i>			
<u>Current medications:</u> <i>No drugs that increase low-density lipoprotein cholesterol and decrease high-density lipoprotein cholesterol</i>			
<u>Physical exam:</u> <i>Vital signs, Blood pressure, Weight - , Height -</i>			
<u>Lab tests:</u> <i>LDL Cholesterol 160 – 189 Total cholesterol - , HDL cholesterol - , Triglycerides – norm level.</i>			

Relevant quotations from the guideline -

If low-density lipoprotein cholesterol is 160-189 mg/dL after an adequate trial of therapeutic lifestyle changes, drug therapy is *optional* depending on clinical judgment. Factors favoring use of drugs include:

- A severe single risk factor (heavy cigarette smoking, poorly controlled hypertension, strong family history of premature coronary heart disease, or very low high-density lipoprotein cholesterol).
- Multiple life-habit risk factors and emerging risk factors (if measured).

(2) Low Back Pain or Sciatica in the Primary Care Setting

2 Scenarios, cases 3-4

(2a) Scenario 1 – Acute Phase

Description of the scenario:

Outpatient clinic, patient with LBP/Sciatica age  $\geq 17$ y.

Criteria for a case

Inclusion criteria: Age  $\geq 17$ , LBP  $< 6$  wks, no “red flags”.

Red flags: (major trauma) (age $>50$ ) (persistent fever) (metabolic disorder) (major muscle weakness) (bladder OR bowel dysfunction) (saddle anesthesia) (decreased sphincter tone) (unrelenting night pain).

Required data items:

**Case 3**

Age: 17-55 Gender:

Chief complaint: *should include – duration  $< 6$  wks*

History: *no red flags elements*

Past history: *no red flags elements*

Current medications:

Physical examination: *Relevant positive and negative physical examination signs*

(2b) Scenario 2 – Chronic phase

Description of the scenario:

Outpatient clinic, patient with LBP  $\geq$  6 weeks, patient had a trial of conservative therapy, screening for other health problems were negative.

Criteria for a case

Inclusion criteria: Age  $\geq$  17, LBP  $\geq$  6 wks, no “red flags”.

Red flags: (major trauma) (age $>$ 50) (persistent fever) (metabolic disorder) (major muscle weakness) (bladder OR bowel dysfunction) (saddle anesthesia) (decreased sphincter tone) (unrelenting night pain).

Required data items:

**Case 4**

Age: 17-55 Gender:

Chief complaint: *should include – duration, patient had a trial of conservative therapy...*

History: *no red flags elements*

Past history: *no red flags elements*

Current medications:

Physical examination: *Relevant positive and negative physical examination signs  
Include radiation of pain past the knee*

(3) The four synthetic case vignettes used in the study

**Case 1**

Age: 40      Gender: Female      Health plan: Tufts

Chief complaint: High serum LDL-cholesterol on routine screening test.

Past medical history: No ischemic heart disease.  
No known risk factors for Ischemic Heart Disease.  
Allergic reactions.

Current medications: Zyrtec 10 mg, Vancenase nasal spray, Entex PSE

Physical exam: Blood pressure 100/60

Lab tests: Total cholesterol - 252, LDL cholesterol - 173, HDL cholesterol - 48,  
Triglycerides – 156.

**Case 2**

Age: 43      Gender: Male      Health plan: Tufts

Chief complaint: Therapeutic life style changes were started 3 months ago due to LDL cholesterol 185, follow up was conducted on 2<sup>nd</sup> visit six weeks later.

Past medical history: No ischemic heart disease  
Hypertension

Current medications: HCTZ 50 mg, Atenolol 25 mg, Viagra 50 mg

Physical exam: Blood pressure - 130/90

Current lab tests: Total cholesterol - 228, LDL cholesterol -164, HDL cholesterol - 42,  
Triglycerides - 109.



### Case 3

Age: 34

Gender: Male

Health plan: Tufts

Chief complaint: Low back pains (LBP) for one week

History: Construction worker who presents after straining his back last week. He recalls the sudden onset of pain in the mid lower back after hearing a "pop" when he tried to lift a heavy bag of sand at work. The pain, which does not radiate, is exacerbated by movement of any kind, and has only partly responded to rest and high doses of Motrin and Tylenol. Although he has trouble finding a comfortable position to sleep, he eventually is able to get at least 5 hours of sleep a night. He denies fever, chills, sweats, weakness, or bladder or bowel difficulties, but he has noticed numbness in the lateral part of his right foot.

Past history: No previous medical history

Current medications: Takes no medicine except the Motrin and Tylenol.

Physical examination:

Sits stiffly and bent to the right side. He positions himself on the stretcher very slowly, and is most comfortable lying flat with his legs bent. Lifting his straightened right leg more than 20 degrees, and his left more than 30, makes the pain worse.

There is no demonstrable weakness or numbness, though the neurologic evaluation is limited by the amount of pain he is suffering.

## Case 4

Age: 50

Gender: Male

Health plan: Tufts

Chief complaint: Gradually worsening back discomfort for the last 4-6 months

History: He describes a constant burning discomfort in the middle of his lower back, with lances of pain that shoot down both legs all the way to his heels. The back pain is worse at the end of the day but the radiating pain, which is below the knee, is unpredictable, with some days worse than others. He has cut back working in his garden because of the pain, and no longer participates in his local ballroom dancing club. He denies any weight loss, fevers, chills, sweats, weakness, or bowel or bladder problems. He has seen a number of doctors for this problem, but has not had effective relief with any of the therapies suggested, including non-steroidals and a brief trial of physical therapy.

Past history: Diabetes, Hypertension.

Current medications: Glyburide, Lisinopril.

Physical examination:

He has positive straight leg raise signs bilaterally after only 15 degrees of elevation, and some decreased pin prick sensation in both feet consistent with early diabetic neuropathy, but no localizing neurologic deficits.

(4) The first recommendation for scenario one – high blood LDL cholesterol management zero or one risk factor

(4a) The conventional version

### **Recommendation 1 - Diet**

- a. Assess if the patient consumes excess calories in the form of LDL-raising nutrients.
- b. Emphasize reduction in saturated fat and cholesterol.
- c. Provide acceptable substitutions for favorite foods contributing to a patient's elevated LDL level.
- d. Consider readiness to change and level of motivation.

#### LDL-raising nutrients

- Saturated fats – should be less than 7% of total calories
- Dietary cholesterol – should be less than 200 mg/day

#### Therapeutic options for LDL lowering -

- Plant stanols/sterols 2 grams per day.
- Increased viscous 10–25 grams per day (soluble) fiber.
- Total calories (energy) - adjust total caloric intake to maintain desirable body weight and prevent weight gain.
- Physical activity - include enough moderate exercise to expend at least 200 kcal per day.

#### Macronutrient recommendations for the TLC diet component

- Polyunsaturated fat up to 10% of total calories.
- Monounsaturated fat up to 20% of total calories.
- Total fat 25–35% of total calories.
- Carbohydrate 50–60% of total calories. Carbohydrate should derive predominantly from foods rich in complex carbohydrates including grains- especially whole grains-fruits, and vegetables.
- Dietary fiber 20–30 grams per day.
- Protein Approximately 15% of total calories.

#### **Referral to a registered dietitian**

Consider referral to a registered dietitian or other qualified nutritionist for medical nutrition therapy.

(4b) The locally adapted version

**Recommendation 1 – Diet**

- a. Offer referral to nutritionist - your dietician's phone number is 617-777-8888.
- b. Give the patient appropriate diet handouts.
- c. Emphasize reduction in saturated fat and cholesterol.  
*(if you would like more information, see table "LDL raising nutrients" on page 10 at the end of this case).*
- d. Provide information on acceptable substitutions for favorite foods contributing to elevated LDL level. *(if you would like more information, see "Macronutrient recommendations for the TLC diet component" on page 10 at the end of this case).*

(5) The fourth recommendation for the third scenario – acute low back pain

(5a) The conventional version

**Recommendation 4 - Symptom control by medications - Analgesia**

*Acetaminophen and NSAIDs:*

- a. Acetaminophen is reasonably safe and is acceptable for treating patients with acute LBP.
- b. Nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin, are acceptable for treating patients with acute LBP.

*Muscle Relaxants:*

- a. Muscle relaxants are an option in the treatment of patients with acute LBP. While probably more effective than placebo, muscle relaxants have not been shown to be more effective than NSAIDs.
- b. No additional benefit is gained by using muscle relaxants in combination with NSAIDs over using NSAIDs alone.

*Opioid Analgesics:*

- a. When used only for a time-limited course, opioid analgesics are an option in managing patients with acute LBP. The decision to use opioids should be guided by their potential for complications.
- b. Opioids appear to be no more effective in relieving low back symptoms than safer analgesics, such as acetaminophen or aspirin or other NSAIDs.

*Oral Steroids:*

Oral steroids are not recommended for the treatment of acute LBP.

(5b) The locally adapted version

**Recommendation 4 - Symptom control by medications - Analgesia**

*Acetaminophen and NSAID*

*Muscle Relaxant*

- c. While probably more effective than placebo, muscle relaxants have not been shown to be more effective than NSAIDs.
- d. No additional benefit is gained by using muscle relaxants in combination with NSAIDs over using NSAIDs alone.

*Opioid Analgesics*

Opioids appear to be no more effective than NSAIDs and Acetaminophens.