EVIDENCE-BASED MEDICINE BREAKING THE BORDERS-
THE EUROPEAN UNION AS A PARADIGM

By

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Die Grenzen meiner Sprache sind die Grenzen meiner Welt.
Ludwig Wittgenstein

For Dawn –

for endless editing, creative criticism,
and for extending the boundaries of my language.
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Abstract

Evidence-based medicine has instigated a shift in medical paradigms over the last decade. Systematic reviews and meta-analyses in particular have a strong impact on the way we practice medicine today. Although evidence-based medicine focuses on results at an individual patient level, the assumption that an increase in the practicing of evidence-based medicine will lead to health improvements of the general population seems to be a causal chain. The influence of evidence-based medicine is continually extending beyond clinical decision-making to act as a foundation for health policy decisions.

The European Union has realized the potential benefits of evidence-based health care. Under the umbrella of the e-Health initiative, the European Union plans to implement a telematic (telecommunication and informatics) health network by the end of 2004. The objective of this network is to facilitate information exchange and to provide databases of the best evidence available in health care. Health care providers and the general public will be able to access these databases through the internet free of charge. Evaluations of the network will have to focus on the extent and depth health care decision makers accept, use and apply not only the databases but clinical guidelines as well. The only substantial official publication of the EU regarding this program is a report by the European Commission on evidence-based health care. The document mentions three components to improve evidence-based health care in the European Union: (1) Evidence-based medicine; (2) Clinical practice guidelines and; (3) Health technology assessment. However, no official information about the structure of a telematic health network has become available yet. The challenge though is unique – to link 15 different health systems with 11 different languages.

This paper first gives some background information about the practice of evidence-based medicine – a description of the status quo; a review of its development; and a critical appraisal of its usage – including benefits and risks of evidence-based medicine and a detailed look at its influence on health policy in general. Next, the paper provides an overview of the health systems of the European Union and the political and theoretical framework of a telematic health network. Based on these premises, a hypothetical structure of evidence-based databases is proposed. This concept takes the heterogeneity of the European Union into consideration and examines factors that will be crucial for the acceptance of evidence-based databases and clinical practice guidelines by health care decision makers. It discusses lessons that could be learned from existing databases on national and international levels. It also describes the necessity of a parallel evaluation program and outlines methods of evaluation that could be successfully used to assess the impact and effectiveness of the program and provide a base for cybernetic decision-making.
Introduction

For thousands of years, medicine was an empirically based science – an approach with very often amazing results. There was always some kind of a “state of the art” in medicine, strongly influenced by ethical and cultural backgrounds and consequently very different over time. In the Twentieth century the empirical base was gradually replaced by a medicine based on clinical trials, which retrospectively seen, often were methodologically flawed.

Parallel to these developments was the dramatic increase in the amount of new medical knowledge being published every year. About 200,000 biomedical articles are released each year - a figure unprecedented in medical history. For clinical practitioners and health policy decision makers it has become virtually impossible to keep up with this enormous amount of information. A tool is needed to prove the effectiveness of medicine and to condense the amount of medical information to a manageable format.

With the emergence of evidence-based medicine, in the form of systematic reviews, meta-analyses, and guidelines, such a tool has been created. It synthesizes a myriad of medical information from clinical trials and other studies into a manageable amount of the current best knowledge of a medical
topic. The effectiveness of medicine can now be assessed to a certain extent, although this synthesis is not as clear-cut and straightforward as one would imagine.

Controversy still remains about assessment of the quality of studies that have been included or excluded. Differing scales may lead to different results\(^1\). Also the external validity, or generalizability, of the results is mainly a matter of subjective judgement by the reader. The application of results to an individual patient’s care may be problematic. Nevertheless, evidence-based medicine currently remains the best way to unlock the “truth” about medicine and treatments, and therefore it continues to gain acceptance among practitioners and health policymakers alike. Evidence-based medicine is an efficient tool for keeping clinicians and health policy decision makers informed about the state-of-the-art solutions for medical problems.

The need for an efficient tool to assess the effectiveness of medicine has been apparent for quite sometime. In the early 1970’s Archie Cochrane, a British epidemiologist, published his book “Effectiveness and Efficiency – Random Reflections on Health Services”. The principles he stresses sound straightforward and matter-of-fact, but the subsequent evidence shows that they have not been, until recently. Cochrane suggested that medical resources should be used to provide those forms of medical treatment that have been proven to work in objective evaluations, especially Randomized Controlled
Trials. He stressed RCTs as the most effective and reliable source of evaluation for medical treatments.

In 1979 Archie Cochrane wrote, "It is surely a great criticism of our profession that we have not organized a critical summary, by specialty and subspeciality, adapted periodically, of all relevant randomized controlled trials." His propositions were widely acknowledged as very important, but the time was not yet ripe. However during the 1980's an international collaboration was established to develop the Oxford Database of Perinatal Trials, based on his theories.

In the early 1990's, as the world-wide-web increased in importance and accessibility, the exchange of information, especially medical information, reached new dimensions. Efficient information technologies seemed to have been the missing link for a successful international launch of evidence-based medicine. Databases of clinical trials and articles were established and made available online. Literature research switched from the library and the manual search of medical books and journals to the personal computer and an unprecedented availability of medical information online.

In 1992, four years after Archie Cochrane had died, the Cochrane Center in Oxford, UK was founded and one year later the Cochrane Collaboration was established, dedicated to the synthesis of evidence-based medicine.
Ten years later systematic reviews and meta-analyses increasingly meet the needs of practicing physicians. The overwhelming amount of published medical literature and clinical trials is synthesized into evidence-based “best practice” guidelines or provided as systematic reviews or meta-analyses by a variety of institutions. Health policy and political decision makers realize that the expectation of “best practice” should be more than depending on the subjective initiative of clinicians. If best practice is to be a right of every patient, political measures have to be put forth to make that reality. A technological infrastructure has to be established to make evidence-based medicine available in a quick, easy and reliable way for all physicians and health policy decision makers. Evidence-based medical facts offer a great resource for making medicine and health systems more efficient with a better outcome for the patient and lower costs for the health system.

The European Union faces a special challenge. 15 different nations with 15 different health systems and 11 different languages have the potential to be connected to an information network without harmonizing the health systems. Programs have been developed and firsts steps have been taken, but the challenge is unique, because of the heterogeneity of the task.

All European health systems are either national health care systems or are based on widely available health funds that are more or less subsidized by the
governments. The prime objective for the European Union remains an improvement of population health as a result of the use of all valid and relevant information gained through evidence-based medicine and the monitoring of health outcomes. The improvement of the cost effectiveness of the various health systems would be a very welcome side effect, even if not officially outlined as an objective. In 1999 the European Union started a program called e-Europe. This program is considered a political initiative by the European Commission to ensure that the EU and its citizens are prepared for the challenges and changes an emerging information society is bringing. Key objectives of e-Europe are bringing every citizen and institution in the EU online, creating information networks for an efficient exchange of knowledge and information and ensuring that these processes are socially inclusive.

One part of e-Europe is e-health. Under the above-mentioned premises, e-health should improve the quality of health care of European citizens in the future. The challenge is unique: as previously noted, 15 different countries have 15 different health systems that are culturally grown and all reflect some kind of national philosophy towards health care. Article 29 of the European Union Treaty rules out a harmonization of health systems in Europe. One of the main goals is the implementation of a telematic (telecommunication and informatics) health network for all European health professionals and health policy decision makers to provide the infrastructure for evidence-based prevention, diagnosis, and treatment, under the title of evidence-based health
The telematic health network will combine two closely related health care realms: information and communication.

Communication in this case is the exchange of information facilitated by the tools of modern technology such as Internet databases of evidence-based medicine and chip cards of patient medical information. E-health, for example, is currently conducting a program to distribute such patient data cards called "health smart cards." Family physicians issue credit-card sized cards to each of their patients. The cards have microchips that contain the relevant medical history and data for the individual patients. When a patient visits various doctors, hospitals or clinics, he or she simply takes along the health card. Medical personnel can readily access patient data and new information can be added. A doctor can be alerted if a new prescription does not combine with one the patient is already taking. Emergency rooms can see a person’s blood type, medical conditions, medical history, all at a click of the mouse.

The future network will not only make it easier for health care providers to access patient information, it will also ease the access to the newest studies, treatments and clinical practice guidelines. European-wide databases will make data on successful treatments in England available to doctors in Germany. Information on all kinds of diseases and treatments can be readily found in one place. Such information sharing will be faster, easier, less expensive and more up-to-date than the traditional methods of medical journals and texts.
A document reported to the European Commission by Perleth et al. in 1999, developed a theoretical framework for categorizing different parts of health research and information gained through evidence-based medicine. The authors see three components of “best practice” that will create a base for evidence-based health care:

- Health Technology Assessment
- Evidence Based Medicine
- Clinical Practice Guidelines

The report does not deal with how a telematic health network could be established practically. The concepts upon which these databases will be structured, and what the contents will be are rather vague. No official documents are currently available that deal with this topic.

Consideration of this has caused me to examine the possible advantages and limits of evidence-based databases in a European telematic health network. Since no official European documents exist about the form and concepts of this database, the approach will be mainly a hypothetical one, based on literature research and existing paradigms used on national levels.

In this master paper, I will first draw a brief overview of the status quo of evidence-based medicine and how it is developed. Evidence-based medicine
has led to a shift in what is viewed as best practice in the past decade and changed paradigms in medicine in almost an unprecedented way. I will outline the formation of evidence-based medicine and critically appraise the pros and cons of evidence-based practice and its influence on health policy.

In the second part of my paper, I will give an overview of the European health systems, their differences, and the legislative background of the European Union treaties regarding health systems. I will outline how an evidence-based information database could be implemented and how this could affect an improvement in the efficiencies of health systems and health outcomes.

Possible obstacles, like technological, political, economic, and legal limitations will be considered as well. Clinical practice guidelines will definitely play a key role in this health network. I will have a close look at practice guidelines and factors that increase their acceptance among health decision-makers, particularly in the European Union.

Finally I will outline a concept for an evaluation program that can support and guide the successful implementation of a European telematic health network. I will look at different forms of evaluation and how they could be used considering the heterogeneity of the European health systems, the political varieties, and multinational backgrounds of EU members.
Evidence-based medicine breaking the borders

Throughout history physicians have always based their medical practices on some type of evidence. Such evidence could have been grounded on narratives, expert opinions, experience, or religious revelations, and, in the 20 Century, clinical trials. Medicine is an art, changing with time and knowledge. Physicians are expected to practice lege artis - meaning in accordance with the current best evidence and the consensus of medical society. This is true, even though that which may be considered the best treatment today may not be so tomorrow or may even vary from one country to another.5

Evidence-based medicine evaluates whether or not treatments are effective and to what extent. In particular, systematic reviews and meta-analyses have brought a new level to quality of care into many fields of clinical medicine. An example of such success has been the changes induced in the usage of corticosteroids and premature babies.6 In 1972 the first randomized controlled trial showed an improved outcome for premature babies by administering corticosteroids to mothers about to go into premature labor. A decade later 6 additional studies showed similar results. However, most obstetricians did not become aware of this fact until 1989, 17 years after the first study, when a systematic review was published. This review reported how the odds of dying from complications of immaturity were reduced by 30 to 50% for a premature baby whose mother was administered an inexpensive course of corticosteroids.
As a result of this systematic review, the administration of corticosteroids for women at risk to having premature births has become a gold-standard-treatment worldwide.

Tens of thousands more babies could have survived had a systematic review been conducted 10 years earlier. Today the logo of the Cochrane Collaboration illustrates the results of a hypothetical systematic review done with the first 7 studies that were conducted on corticosteroid use and premature babies. These results would have shown a clear benefit of the treatment had a systematic review been conducted years earlier.

Evidence-based medicine probably would not have progressed to such a great extent in clinical medicine without the global expansion of Internet use during the last decade. Evidence-based medicine is taking advantage of the speed and ease of the Internet to spread and share medical information in a manner that truly is breaking borders. The databases of the Cochrane library are an impressive example. Physicians and scientists from around the world develop evidence-based reviews on pertinent clinical topics. The results can be viewed from any personal computer with Internet access. Internet access, however, remains a critical factor. E-Europe and its programs are striving to promote Internet use. Once the adoption of the Internet in the health care sector reaches a critical mass, progress will rapidly advance. This phenomenon has already
taken place years ago in other technological fields such as the telephone, the CD and the computer.\textsuperscript{7}

In one decade evidence-based medicine has changed the way clinical medicine is practiced. Systematic reviews not only influence clinical decisions but increasingly health policy. Following the initial enthusiasm, the discussion about the use of scientific evidence has become more stratified and the boundaries of evidence-based medicine are more evident today. Still, many questions remain and the differences between the chances and limits are often a matter of a subjective viewpoint.

\textit{The boundaries of evidence-based medicine- the chances}

When evidence-based medicine evolved in the early 1990’s, it initiated a paradigm shift in clinical decision-making\textsuperscript{8}. Until then the majority of physicians depended mainly on opinion-based information for best practice. Medical best practice was more or less authoritatively defined and distributed by leading clinical members of the medical society and experts in their fields. Their opinions were generally supported by clinical trials and experience. Evidence-based medicine started to question ostensibly high quality evidence. The methodologies and generalizabilities of clinical trials were critically appraised, and a hierarchy of the strengths of research-based evidence was developed. The importance of beneficial changes in morbidity and mortality
outcomes versus pathophysiologic changes was emphasized. By and large, evidence-based medicine stated that intuition, unsystematic clinical approach and personal opinion are insufficient grounds for clinical decision-making, and therefore it places a lower value on authority than the traditional medical paradigm.9

Evidence-based medicine focuses explicitly on the application of valid research concerning clinical treatment of individual patients. Its rationale is strictly quantitative, this can be a strength but also a weakness. The strength lies in an approach to see evidence-based medicine as only one factor in the complex process of clinical decision-making at the individual level.

Experience, psychosocial conditions, and patient values are all additional and at least equally important factors that contribute to the decision process in which the best evidence is applied. However they should not be the sole determinants either. Evidence-based medicine can provide the quantitative, scientific framework. Human decision-making is a complex process in daily life as well as in clinical settings. What Schulkin calls decision-sciences identify the underlying value of a decision determined by the analysis of consequences and the probability that a particular decision is correct or incorrect.10 In addition various kinds of inherent biases are crucial factors that influence such decisions. For example Schulkin also states that” omission bias is the tendency not to do something that could cause harm, and naturalistic
bias is the view that natural things do less harm than man-made things."\textsuperscript{11}

Evidence-based medicine can help to minimize the influence of some biases and help evaluate the consequences of decisions. In a health care world of limited resources, it is important to determine which interventions work best. This helps health care decision-makers to focus on effective interventions. Any discrepancy between what is emphasized and what works best will compromise health outcomes.\textsuperscript{12}

Evidence-based medicine in the forms of systematic reviews or guidelines, offers a time saving tool to clinical decision-makers, who can not possibly keep up with and critically appraise the tremendous amount of new medical information. This so-called preprocessed evidence meets the needs for information about current scientific evidence in an efficient way.

\textit{The boundaries of evidence-based medicine- the limits}

One limiting factor that can be an advantage of evidence-based medicine has already been mentioned herein. The rationale is a strictly quantitative one. Critics say that this will lead to the emergence of a new utilitarian orthodoxy.\textsuperscript{13}

The danger certainly exists, but it is worth mentioning that lack of evidence does not necessarily equate to lack of effectiveness. Immeasurable or unmeasured factors such as empathy and psychosocial aspects might be crucial for the success of an evidence-based therapy. In a world where psychosomatic
diseases increase, a holistic approach seems to become increasingly important. Too much emphasis on evidence-based medicine neglects the complex, interpersonal matter of clinical care. Therefore evidence-based medicine should remain just a tool in clinical decision making, it’s not a reflection of the truth. Research can only provide best current evidence but never absolute certainty. Karl Popper, one of the most influential philosophers of the last century wrote, "Science is the search for truth; and it is very possible that some of our theories are indeed true. But even if they are true we can never know that for certain."\(^{14}\)

Another point of critique is what is considered the highest quality of evidence. Randomized controlled trials are the gold standard in many hierarchies of evidence. RCTs try to minimize bias through strict methodological criteria and a clearly defined outcome of interest. Yet a high internal validity does not necessarily mean a high external validity. The strictly selected study populations might be very different from the heterogeneous, co-morbid population of daily clinical practice. Criteria that guarantee high internal validity often conflict with those for external validity. Older patients and women are often underrepresented and patients with co-morbidities are frequently excluded from the study population. Therefore, generalizability can be problematic, and the external validity of study results must be evaluated for each single patient by the treating physician.
Some authors demand that for externally valid evidence we need “medicine-based” studies that include, not ignore, medical reality. Although RCTs are an ideal design for interventional studies, results rarely reflect the magnitude of possible harms. Observational studies on the other can provide us with information that RCTs do not reflect. Observational studies are a better tool to assess harms and prognosis, but still they are ranked lower in the hierarchy of evidence because they are more prone for bias. Nevertheless reducing scientific evidence to RCTs alone could cause us to overlook very important aspects of medicine and health care.

Moreover, critical appraisal is especially important in a field where the results of a single trial can trigger enormous financial gains or losses for pharmaceutical companies. Monetary interests underlie most trials, so the importance of monetary benefits may supercede health care priorities. Yet, critical appraisal relies on the knowledge and consensus on high quality of scientific evidence – what it is and what it is not. Even this basic question is still a matter of debate.

The hierarchy of the evidence

The core of evidence-based medicine consists of clinical studies and trials. In the search for the “best evidence”, however, quality criteria are commonly applied. The pursuit of quality criteria is founded in the belief that the manner in which studies and trials are designed and conducted correlates to the
likelihood that the results reflect the “truth”. As systematic reviews and meta-analyses become increasingly important in evidence-based medicine, the issue of quality assessment gains significance. Systematic reviews use a comprehensive review of literature, focusing on a clinical question as their base. Health analysts must first critically appraise the quality and applicability of scientific evidence retrieved during literature reviews.

How “quality” is defined in studies and clinical trials is still a matter of debate. Numerous quality-rating scales have been published with more than 60 grading scales identified. The approaches vary in how they weigh efficacy versus effectiveness. Well-known institutions working on these tasks include the Canadian Task Force on Periodic Health Examination, the Cochrane Collaboration, and the U.S. Preventive Services Task Force (USPSTF). The later has developed a hierarchy of evidence that has been widely adopted internationally for use in systematic reviews:

U.S. Preventive Services Task Force Evidence Codes:

I Evidence obtained from at least one properly designed randomized controlled trial.
II-1 Evidence obtained from well-designed controlled trials without randomization.
II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments
III Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.
The USPSTF evidence codes are based on the rationale that Randomized Control Trials (RCTs) minimize systematic bias and therefore rank at the top. On the other hand, expert opinions, the bases of clinical decisions over decades, rank lowest. Nevertheless, some health analysts argue that a methodological viewpoint alone provides an incomplete description of quality. Woolf et al. have concluded that the strength of the evidence also depends on factors such as consistency of findings across studies and emphasize that RCTs may not always be the “gold standard”. For example, observational studies, like prospective cohort studies, provide more information on effectiveness in terms of health outcomes than RCTs.

Furthermore, meta-analyses and systematic reviews would have to be ranked higher than a single RCT, because they combine the results of single studies. Each of these single studies might have certain systematic or random errors that affect their results. By summarizing and pooling the results, the errors are minimized and weigh less in the combined result.

Two articles in the New England Journal of Medicine have also challenged the common hierarchy of evidence. Benson et al. compared the results of observational studies with those of randomized controlled trials. In seventeen of nineteen analyses of combined treatment effects, estimates of the magnitude of results of observational studies were within the 95% confidence interval of the combined magnitude of results of randomized controlled trials. These
findings foster a common criticism that well-designed observational studies are underrated in the USPSTF evidence codes. Concato, et al. arrived at a similar conclusion by comparing the results of observational studies with the 95% confidence intervals of meta-analyses of randomized clinical trials. The authors summarize that the results of well-conducted observational studies do not systematically overestimate the magnitude of the effects of treatments.

To increase a reader's understanding of the results of randomized controlled trials, the design and methods used in the trials must be transparent. The CONSORT (Consolidated Standards of Reporting Trials) statement strives to improve the reporting standards of RCTs. This statement outlines how trials should be reported in publications and provides a checklist and flow diagram to accomplish this goal. Clear specifications on methods, results, and discussions of trial conclusions in articles should ease the critical appraisal process of trials. The QUORUM (Quality of Reporting of Meta-analyses) has a similar rationale regarding publication standards of meta-analyses.

As mentioned, high quality methodology in designing and conducting studies is crucial in avoiding both systematic and unsystematic bias. On the other hand, the relevance of assessments apart from the methodology of a study, though harder to define, is also essential. Such assessments reveal whether or not a study is clinically significant or policy relevant. The applicability of
results on a larger population is ultimately one of the most important factors in systematic reviews.

Finally, assessing the quality of studies is a subjective process. Even when quality criteria are uniformly accepted they may be inconsistently applied. A report on pharmacological agents in alcohol dependence showed that the reviewer’s background affected the quality ratings. Ratings given by clinician tended to be higher than those given by methods experts. Therefore, if a systematic review has more than one analyst, all analysts must review all the articles to avoid differential bias. An interesting research question would also be if a “nationality bias” exists in rating the quality of studies. For example are results of German reviewers different from results of their English counterparts?

The issue of grading articles as inputs into evidence-based medicine is complex. Future research will be necessary to make grading systems themselves more evidence-based. Grading literature must become reliable and reproducible. The applicability of the results must be valid and useful. Such standards will combine to increase the quality of evidence-based medicine.

The floating borders between chances and limits of evidence-based medicine and the intense discussion about the hierarchy and quality of scientific
Evidence show that clinical practice guidelines and evidence-based databases are at the status of a constant “work in progress”. A fact a telematic health network will have to take into consideration.

As mentioned above, e-health was founded as a political initiative with the objective to improve health care in the European Union. One effect that an increased emphasis on evidence-based medicine will have in the European Union in addition to this objective is an increased influence of evidence-based facts on health policy.

Evidence-based medicine and health policy

Because evidence-based medicine used in clinical decision-making focuses on the health problems of individual patients its impact on health outcomes remains rather small compared to the potential impact of policy changes. Life expectancy, morbidity, mortality, DALYs (disability adjusted life years) and QUALYs (quality adjusted life years) on a population level can be best improved by policy decisions that affect clinical decisions very broadly or improve public health measures for sizable populations. This can be through direct implementation of programs, like primary or secondary preventive measures, or through the erection of an infrastructure that fosters improved clinical practice. An example would be the fostering of evidence-based practice through the provision of evidence-based databases, clinical practice
guidelines, and a functioning infrastructure enabling widespread access by practicing clinicians.

Noting the increasing success of evidence-based medicine in clinical practice, some health care professionals demand the incorporation of evidence-based knowledge into health policy decision-making and public health. Information gained from evidence-based medicine is already used by health insurance coverage decisions. Although it is not clear such an approach helps to reduce costs, it can help to direct medical resources towards more effective health care. Besides health insurance, it is unclear to what extent evidence-based medicine influence health policy decisions. Some health analysts suspect that the influence over media might be indirect since findings in systematic reviews have higher media coverage than single studies.

Others see a demand that goes beyond the use of data already available. Heller, a British epidemiologist, suggests the development of a counterpart to evidence-based medicine called “Evidence for Population Health.” He states that evidence-based medicine lacks population perspective and demands the creation of methodologies that have special relevance to public health.

On the other hand, some experts argue that systematic reviews could already be the ideal tool for policy makers and consumers as adjuncts to decision-making. Although systematic reviews usually do not focus on health
outcomes on population levels, they reflect the intermediate outcomes on an
individual level. Information gained through systematic reviews could be
utilized to address two of the main concerns of health policy:

- Costs
- Quality of health care

For both topics, results from systematic reviews and meta-analyses as
intermediate findings could probably extrapolate on the population level in
many cases. In particular meta-analyses can reflect the effectiveness of
intervention on broader scale.

Costs

Financial health care resources are limited and must be allocated in a way that
achieves the maximum benefit for the population. Health care systems are
confronted with increasing costs throughout the Western world. People
accountable for managing these health care systems must decide what types of
services will be covered - not only diagnostic, interventional, and therapeutic
procedures, but also primary and secondary preventive measures. As a recently
published article in Lancet illustrates, even a well established preventive
measure like screening for breast cancer with mammography suddenly lacks
scientific evidence after the underlying clinical studies show strong
methodological flaws.\textsuperscript{33} In fact, the risks associated with mammographies may
even outweigh potential benefits in certain age groups. Consequently, health
care officials in Switzerland are reconsidering patient reimbursement for mammographies.

Clinical preventive services (screening, counseling, immunizations, and chemoprevention) can be an enormous waste of financial resources, if not evidence based, since they represent major investments in the future health of large populations.\(^3\) Cost-effectiveness analysis compares expected benefits, risks and costs of alternative strategies and is a valuable tool to bring economic aspects into consideration.

**Quality of care**

Lohr defines quality of care as “the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.”\(^5\) Ultimately, “quality of care” means the outcome that patients experience and this is often, in turn, related to cost. This relationship stems from factors that strongly influence the quality of care: overuse, under-use, and misuse of health care.\(^6\) Overuse occurs when inappropriate and unnecessary care is administered, under-use is the lack of appropriate and needed care, and misuse stems from poor technical or personal performance of health care professionals. All three ultimately increase costs. High quality of care also takes factors such as patient values and preferences into consideration. Evidence-based medicine, per se, does not consider such aspects. The use of decision analysis based on findings
of evidence-based medicine, could increase the consideration of patient preferences and values, which should be a significant factor in long-term health policy planning.\textsuperscript{37}

Although evidence-based medicine can offer a lot to policymakers, it should not be the sole base for decision-making. Values and societal expectations must be considered as well. Greater reliance on scientific evidence and a systematic approach in decision making could lead to improved health policies. Health care participants must learn to use evidence-based medicine and must be able to distinguish between narrative and systematic reviews. Woolf proposes a bibliographic evidence collection center with simulation modeling programs.\textsuperscript{38} The models import evidence-based data from databases and incorporate complex patient data to conduct sensitivity analyses from different perspectives (e.g. deaths, cost-effectiveness ratio, quality adjusted life expectancy). Such analysis would have great value for clinicians and policymakers and could be used for a more rational resource allocation. Woolf uses the example that evidence-based primary preventions such as exercising, not-smoking, lowering cholesterol and controlling blood pressure can prevent more deaths per year than evidence-based treatments for cardiovascular diseases. Thus, he detects a mismatch in priorities since most of the US expenditures in health are geared towards treatments.
Using scientific evidence under these premises could open new perspectives for health policy and health care. Systematic reviews can summarize large amounts of data and highlight gaps in scientific evidence.

Information for policy makers in the form of evidence-based medicine could provide a strong base. Cultural, philosophical, and ideological factors play other key roles in decision-making, but vary from nation to nation. The European Union with its heterogeneous cultures and differing health care systems are a paradigm.
The European Health Systems

The European Union does not have a universal health care system. Each of the 15 EU member states' health care systems is unique and nationally grown. Specific political, historical and cultural traditions have influenced the development. As a result, the health care systems of the member states differ considerably. There are three predominant types of health care finance in the European Union. The first is publicly financed by general taxation (e.g. Italy, Sweden, United Kingdom). The second is based on a compulsory social insurance operating with social insurance funds. These funds may be independent from the government but are usually subsidized by the government in years of deficit (e.g. Austria, France, Germany). The third is privately financed in the form of additional health insurances on a voluntary, supplemental base. These private insurance policies pay for single rooms in hospitals; treatments that are usually not covered by compulsory insurances like acupuncture or homeopathy, and provide additional fees for the treating physicians.

The European Parliament has provided for a comparative study of the European health systems.

In essence, the fifteen health care systems in the EU reflect a variety of different philosophies and approaches and retain their own peculiarities.... Each system has its own strengths and weaknesses and none of the systems provide a wholly
successful solution. Hence, each has to learn from the experience of the other fourteen.\textsuperscript{39}

Health policy mainly remains a national matter and is guided by the subsidiary principle. Article 29 of the European Union Treaty specifically excludes the harmonization of national health laws.

Nevertheless a "silent" harmonization of the European health systems is taking place. The 1991 Maastricht Treaty has not only eased travel within the European Union through the elimination of border controls but has also created more competencies for the European Union in public health. The European Commission has started to develop specific policies in public health fields with high priorities, such as AIDS, tobacco and alcohol abuse, and environmental causes of illness. In relation to these public health issues, the member states believe that the European Union can introduce legislation to coordinate the problem approach more efficiently and more effectively. The 1997 Treaty of Amsterdam provides an even stronger legal basis for public health legislation.\textsuperscript{40} Besides the legal aspects, the approval of new drugs has been an agenda of the European Union for a couple years, entirely replacing national drug approvals.

A report of the Center for Tobacco Control Research and Education of the University of California, San Francisco illustrates that a common legislation, however, can also have its down sides.\textsuperscript{41} In 1998, the European Union adopted
a directive restricting, and later ending, tobacco advertising and sponsorships in the European Union. In 2001, however, Germany fought the directive before the European Court of Justice and successfully had it annulled. Once secret tobacco documents reveal how the tobacco industry lobbied German and Dutch politicians to defeat the directive and subsequently influence tobacco policy in all of the 15 member states.

A single European market, unified legislation, and an increase in migration in a Europe without borders, bring forth new challenges in the field of public health. Two rulings of the European Court of Justice in 1998 imply that health care goes beyond national borders and is subject to European laws on the free movement of people and services according to the Maastricht Treaty.

Therefore, national insurance agencies are generally required to cover the costs for the fees of all health care services rendered within a country of the European Union to a European Union citizen. What is convenient for sick travelers can also lead to political tensions in other fields. An example of this can be found in the different abortion laws in Portugal and Spain. Abortion is illegal in Portugal. A Portuguese woman who wants to have the procedure can, however, travel to Spain to have it done. She can then file a claim to have her Portuguese health insurance cover the costs as long as she is able to prove that the abortion was due to medical reasons. Conservative groups in Portugal are active against these circumventions of Portuguese law.
Although all major health policy decisions will still be handled on a national level, a convergence of policies and new routes of exchange in medical knowledge, medical technologies and health service know-how will be the focus and challenges of the new century. In April 2001 the European Parliament voted for a renewed attempt to extend the European Union’s influence over national health policies. The Parliament seeks to establish a European Health Coordination and Monitoring Center over the next 5 years. Especially with the emergence of the Internet and other information technologies, new opportunities for improvements in effective and efficient use of medical knowledge and information are apparent.

The European Union started a program called “e-Europe” in December 1999. It is a political initiative aimed at accelerating Europe’s transformation into an information society. E-Europe uses the World Wide Web as a new medium to create an information and interaction base for European citizens with the European government and EU institutions. Furthermore, e-Europe promotes Internet access for all European citizens and the creation of an information network - especially in the fields of health and business.

E-Europe consists of various initiatives such as e-Commerce, e-Education and among others, e-Health. In front of a special European Council meeting in Lisbon in March 2000, the European Commission published a statement on the
future concepts and visions of e-Europe. The chapter on e-Health takes a closer look at the status quo of the relationships between health care systems, costs and the use of new communication technologies.

Digital technologies can improve the productivity and scope of health care. This potential is not being fully exploited – only 1% of total health spending is used on information technology. In summary, secure services have to be developed linking hospitals, pharmacies, primary care centers and homes of people. Fragmented health markets in the EU also hamper innovation and the spread of best practice.

The Commission explicitly mentions that the goal is not a harmonization of health care systems at a European level that would conflict with Article 29 of the European Union Treaty. The Commission instead lists some innovative targets for the future. Two of them are particularly interesting and closely relate to the use of evidence-based medical knowledge and information technology. The targets by the end of 2004 include:

All health professionals and managers should be linked to a telematic health infrastructure for prevention, diagnosis and treatment. The priorities agreed for a number of key pan-European medical libraries-on-line and health care expertise centers to be operational by the end of 2004.

The WHO defines three intrinsic goals of health systems: improving health, increasing responsiveness to legitimate demands of the population, and fair distribution of financial burdens. The WHO measured the performance of individual countries in view of resources available. In overall performance of health systems, the WHO ranks 13 of the 15 European Union member states in
the top 25 systems worldwide. But plenty of room still remains for improvements and innovations. Currently, these initiatives of the e-Health program such as an effort to furnish all European citizens with chip-cards (Health-Smart Card) for insurance and health data are being implemented. Other targets, like the telematic health network, seem more distant.

“Healthcare best practices in networking” was mentioned as one of the goals for the end of the year 2000. A look at the e-health website under “best practice” reveals a collection of scientific programs, databases and technologies that are definitely highly innovative but not up to par with the kind of data usually expected under the heading “best practice” in medicine. Such expectations may include evidence-based guidelines for clinical practice for physicians and a similar database for patient use. The programs presented have been selected by IST, the Information, Society and Technology program of the EU. Even though they are all medicine related, the term “best practice” is somewhat misleading since none of them primarily deals with clinical aspects.
A framework for evidence-based health care in the European Union

The European Commission released a statement on the development of public health policy in the European Community in April 1998 with references made to evidence-based medicine and best practice.

A major emphasis within the information strand covering both health status and health systems would be placed on best practice in health care, i.e. the current best evidence as regards the safety, efficacy, effectiveness, and cost-effectiveness of different approaches to health promotion, prevention, diagnosis, and treatment; for instance the cost-effectiveness of screening programmes, health education programmes, emergency services and new pharmaceutical products. The work would aim to promote and bring together activities in the Member States in the fields of evidence based medicine, quality assurance, and improvement, appropriateness of interventions and health technology assessment. Co-ordination of work in these fields would be supported and set on a formal footing in order to pool the expertise of the centres in the Member States, to gather and exchange information, stimulate international studies and improve the dissemination of findings.46

The European Union has begun to outline strategies to address the increasing demand for quality health care in the European Union. Demographic changes have led to an “over-aging” of the population that is unprecedented in history. Age related diseases will increase costs and further strain the already limited health care resources. Applicant countries of the former Eastern Bloc will soon join the European Union. These countries have even fewer resources and more substantial health problems than the existing member states. Thus,
improvements in the effectiveness and efficiency of the health systems will become increasingly important.

According to the 1998 statement cited herein, “best practice” leads to an overall improvement of health systems. Such an assumption seems logical, but to my knowledge, has not been proven through any type of studies. Evidence-based medicine examines clinical outcomes. Such outcomes must be viewed as intermediate outcomes in relation to the entire health system. The inference that the advancement of many intermediate outcomes will lead to an improvement in the overall performance and outcomes (measured in morbidity, mortality, DALYs...) of a health system appears to be based on a causal chain but without proof, remains a hypothesis.

How can “best practice” be defined? Originally, this term was used in the industrial sectors. There, “best practice” has been used as a process oriented concept for achieving improvements in quality, effectiveness, cost-effectiveness and productive output. "Best practice” in health care is also an emerging concept and mainly associated with evidence-based medicine. In a report to the European Commission about “best practice” and European health systems, the authors (Perleth et al.) take a more comprehensive approach to the definition of “best practice”, extending beyond quality issues.

*The best way to identify, collect, evaluate, disseminate and implement information on, and monitor the outcomes of, health sector interventions for patients/population groups and defined indications or conditions. The information needs to reflect the*
best available evidence on: safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values and quality of health sector interventions.48

Remarkably, the authors have placed social and ethical values on the same level as efficacy, effectiveness and cost-effectiveness. This reflects a patient-oriented policy and meets the frequently expressed critique that evidence-based medicine and “best practice” give rise to a new form of utilitarian orthodoxy.49

In the same report to the European Commission,50 the authors foresee three best practice activities that will create the basis for evidence-based health care:

- Health Technology Assessment (HTA)
- Evidence-Based Medicine (EBM)
- Clinical Practice Guidelines (CPG)

Health Technology Assessment is a systematical approach for examining the technical performance, safety, clinical efficacy and effectiveness, cost, cost-effectiveness, social consequences, legal and ethical aspects of the application of a health technology.51 Health Technology Assessment is not seen as a defined set of methods, but as an intention to examine health technologies.52 Health Technology Assessment is a crucial part of evidence-based health care, but this paper will focus on the other two components: Evidence-Based Medicine and Clinical Practice Guidelines.
Evidence-based medicine

As previously mentioned, evidence-based medicine promotes the use of scientific evidence to answer clinical questions about the effectiveness of clinical interventions and treatments. The feasibility of evidence-based medicine for everyday clinical use is limited by various factors. Some of the factors occur on a personal and individual level. These include issues such as amounts of motivation, interpretation skills, ability to critically appraise evidence and simply personal time. Others, like accessibility to databases, take place on an infrastructural level.

How could evidence-based medical databases in a European telematic health network look? The most rational approach for the European Union would be to learn from experience – on both national and international levels. Existing databases can be stratified into 3 levels of evidence-based medicine:

- primary databases containing bibliographic listings of clinical trials or studies, reviews, and editorials;

- secondary databases containing “synthetic studies” like systematic reviews, meta-analyses, or cost-effectiveness analyses, that are products of extensive and systematic literature reviews of primary databases; and

- tertiary databases, condensing primary and secondary evidence-based data to make the information more comprehensible for readers.
Examples of primary databases include general databases such as MEDLINE, and EMBASE, and specific databases such as AIDSLINE, and PsycLIT. All of these databases are bibliographic, medical literature databases. Since problems arise from the method of indexing used by some of these databases – an indexing that can limit search results, even with extensive search strategies – users must be aware of retrieval bias. To minimize retrieval bias, the Cochrane Collaboration created the Cochrane Controlled Trials Register. This bibliographic database with improved indexing also contains additional hand-searched studies from medical journals around the world. This approach increases the availability of non-English studies. Furthermore, it reduces publication bias because studies showing no statistically significant results, and initially published in languages other than English are rarely translated and published in English-language journals.

At the outset, the European telematic health network would not focus on primary databases. Complex search strategies and the enormous amount of scientific information associated with primary databases are often too time-consuming for the individual health care decision-maker. In addition, once the Cochrane Controlled Trial register has been completed, an excellent primary database will be available that also includes studies concerning the European population. In my opinion, the European telematic health network should concentrate on the creation and linkage of secondary and tertiary databases tools the average physician is most likely to consult.
Examples of secondary databases include NICE (National Institute for Clinical Excellence) in the UK and the Cochrane Collaboration. These organizations mainly feature systematic reviews and meta-analyses - cost-effectiveness analyses to a lesser extent. The Cochrane Collaboration enjoys a high reputation in the medical community due to its strict methodologies and its global network of contributing scientists and physicians. The Cochrane Collaboration has been particularly effective in minimizing conflicts of interest on a national level. NICE, on the other hand, has frequently been accused of being used by national committees to promote their own interests.\(^{53}\)

An example of a tertiary database is *Bandolier*. *Bandolier* is a print and Internet journal based at the University of Oxford, UK. It is considered the prime source of evidence-based information for general practitioners in the UK. The impetus behind Bandolier is to provide information about the effectiveness (or the lack of it) of treatments for healthcare professionals and consumers.\(^{54}\) Topics are presented in a clear and user-friendly manner although they lack the methodological background information that secondary databases like the Cochrane Database of Systematic Reviews offer.
A Hypothetical Structure of evidence-based databases.

As previously mentioned, secondary and tertiary databases probably offer the most effective tool to reach the average European health decision maker. To insure proper consideration of national priorities in medicine and public health, each country could create an Evidence-based Practice Center (EPC) similar to those founded by the AHRQ (Agency for Health Care Research and Quality) in 1997 in the US. The US centers issue authoritative evidence-reports on high priority clinical topics and technologies.55

Additionally, the European EPCs would pursue national databases in the native languages. Information gained from systematic reviews would have to be exchanged and translated by the EPCs. Promoting national health issues could be another important tasks of the national EPCs. For example, evidence-based reports on immunization programs to control Central European Encephalitis, a tick-borne disease, are of high public health priority in the southern part of Central Europe but of no concern in Scandinavia.

Primarily, topics should cover the effectiveness of treatments and preventive clinical services and health technology assessment. Later the scope could be extended to cost-effectiveness. All these databases must be free of charge and
readily available to health care decision-makers and consumers via the Internet.

NICE is an example of a free database for patients and physicians. One explicitly stated additional function of NICE is clinical audit. NICE is supposed to develop tools to monitor the use of particular interventions or the care received by patients within the National Health System (NHS) of the UK. The necessity of program evaluation is definitely crucial, although I do not think that this should be a task of the EPCs. I believe this for two reasons in particular. First, it is questionable if an institution that develops and implements a program should evaluate itself and the effectiveness of the program, thus creating a conflict of interest. Second, I think that the acceptance of evidence-based databases is higher if health care decision makers don’t have the feeling that the adherence to findings is supervised and controlled.

Numerous activities in health technology assessments, systematic reviews, and guideline developments are reported on federal levels within the European Union. Germany, the Netherlands, and the UK are the avant-garde in these fields. Existing federal activities could be incorporated in national EPC development.

A potential, efficient partner for a working-coalition could be the Cochrane Collaboration. Founded in 1993, the Cochrane Collaboration is a non-profit
worldwide network made up of scientists, physicians, and methodologists working for the organization on a volunteer basis. Of the fourteen Cochrane Centers worldwide coordinating and organizing reviews, seven are located in the European Union. Review groups are responsible for specific topics. Once an author has adopted a topic, he/she will continue to monitor new publications on the topic to keep the reviews up-to-date. All systematic reviews are peer-reviewed before they are published. The Cochrane Library consists of 4 databases:

- *The Cochrane Database of Systematic Reviews*
- *The Cochrane Controlled Trials Register*
- *The Databases of Abstracts of Reviews of Effectiveness*
- *The Cochrane Methodology Database*

The Cochrane Library can be seen as the most important database of systematic reviews worldwide. In the nine years of its existence, the Cochrane Collaboration has completed 1377 systematic reviews (as of 5/2002). In comparison, during the three years of the NICE’s existence, 5 systematic reviews have been completed.

Federal organizations in Europe are highly susceptible to being inefficient due to bureaucracy, attempted influence of interest groups and under-funding. In my opinion, this poses the main threat to the efficiency of EPCs on national levels. A working coalition with the Cochrane Collaboration could create more dynamic. The EPCs should be established as private entities operating on federal and private funds. Bandolier offers a positive precedent. While the base
of the Bandolier's financing comes from the NHS (National Health System) in the UK, sponsors provide additional resources. Industrial sponsorship is only accepted though, if the sponsor signs a contract that rules out any control and influence over Bandolier’s publications.

Obstacles

With 11 different official languages, the European Union must overcome the challenge of establishing evidence-based databases and guidelines that can reach health care decision makers of different languages. Where a physician decides to search for medical information is often based on the language the database uses. Most physicians prefer to use databases in their native tongues. Even when physicians are aware of the existence of evidence-based databases, medical English can challenge and limit physicians who do not speak English as a native language. Most of the institutions that provide evidence-based medicine online in forms of “best practice” databases are currently in English. Although most European physicians are fluent in English as a second language, medical English with its distinct vocabulary and semantics can be a very time consuming obstacle for the non-native speaker. Therefore, the acceptance of these resources is rather low. A recent survey under German physicians shows that 70 % think that medical English is a barrier to their further education.
However many more possible limiting factors have to be considered. One will definitely be the user friendliness of the database. Most health decision makers work under time pressure and have some assertive skepticism towards new technologies that could consume time. Therefore, the efficiency of an evidence-based database will be a crucial factor. Initially, it will be very important that implementation is not a static process but a matter of cybernetic decision making based on feedback from the target group. Improvements must be derived from needs and must be continually administered to guarantee the efficiency of the database and its subsequent acceptance.

McColl et al. conducted a survey among general practitioners in the UK to examine attitudes towards evidence-based medicine\(^6\). The respondents mainly welcomed evidence-based medicine and agreed that its practice improves patient care. But the major perceived barrier in practicing evidence-based medicine was a lack of personal time. These results again demonstrate how important it is for evidence-based information to be accessible over an efficient, user-friendly database to allow users to view the time spent on information-research as a valuable investment in patient care.
Practice Guidelines

Practice guidelines can help clinicians make informed decisions that are evidence-based and provide effective clinical practice while considering the unique situation of the individual patient. Field and Lohr define guidelines as being

systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances

On one hand, guidelines assist clinicians in evaluating and reflecting upon their own patient management strategies. On the other hand, guidelines can be seen as state-of-the-art suggestions to meet information needs and face medical problems. In addition, the demand by patients to receive evidence-based treatment is steadily increasing.

A study by Gorman found that patients have high expectations of their physicians to know the right answer. Expectations such as these act as an impetus, encouraging physicians to seek further information. Guidelines and evidence-based reviews can efficiently satisfy this demand for information and are far more accessible than research articles as a guide for current best practice.
Guidelines are ideally based on scientific evidence that is extracted from medical databases through systematic searches. Predetermined search criteria and predetermined criteria of effectiveness are ways to reduce bias. Selected trials or meta-analyses are rated by quality criteria and internal and external validity are carefully assessed. The often very heterogeneous evidence must be integrated and expert opinion is used to support these decisions.

The advantage of an evidence-based approach versus an expert-opinion-based approach is that it provides a clear rationale to defend medical patient management and public health policy. Limits of an evidence-based approach include the usual shortage of good data - especially for preventive interventions where the time lag between interventions and outcomes can be very long. Therefore, intermediate outcomes must be used to infer effectiveness, which inevitably involves trade-offs. Short-term physiologic changes can lead to premature conclusions and an overestimation of the effectiveness as long as the overall outcome is not assessed. Therefore accepting intermediate outcomes might introduce type I errors, which means finding a significant result or difference where there actually is none.

All in all, synthesizing practice guidelines is a very complex, labor intense effort. The U.S. Preventive Service Task Force is an example of a national, governmental effort to provide evidence-based guidelines on preventive medicine. Teams work on prioritized topics using so-called “analytical
frameworks" graphically map out specific linkages in the evidence that must be present to be considered effective. For example, direct linkages show a relationship between the intervention and reduced morbidity or mortality. Direct linkages are weighted higher than indirect linkages that show a relationship between an intervention and an intermediate outcome. The topic team’s primarily focus on high-quality evidence if available and may exclude low-quality evidence. The process must be well documented and replicable for outsiders. This minimizes the danger to cite evidence selectively in support of a recommendation. Graded levels of recommendations show where research evidence is less conclusive.

Making recommendations, however, goes beyond reviewing scientific evidence. Issues like cost effectiveness, ethical and legal concerns, or societal expectations must be considered as well. Historically, the Task Force’s main-focus has been on recommendations that reflect the state of the evidence. This leaves room for decision makers to consider additional factors in their process of decision-making.

As mentioned above, clinical practice guidelines should reflect scientific state-of-the-art knowledge. Grant et al. looked at articles cited in clinical guidelines using bibliometric analyses. Their objective was to evaluate the impact of research on health and to characterize the papers cited on clinical guidelines. An interesting aspect of the results was a characteristic coined by the authors
as “knowledge cycle time”. This is the time between the publication of a paper and its citation in a guideline. The median knowledge cycle time for all 15 guidelines was 8 years. In other words, it takes a median of 8 years for scientific evidence to find its way into clinical practice guidelines. This may be a problem in an active area of study, like HIV, where the half-life of knowledge is very short. The majority of articles cited were high in quality and originally published in level 1 (clinical observation) or level 2 (clinical mix) research journals. Nevertheless, 15% of the cited papers did not have a research level.

*Dissemination and Acceptance of Guidelines*

The success of a telematic health network in the European Union will rise and fall with the acceptance of practice guidelines and evidence-based databases by clinicians and health care decision makers.

Pathman D., Konrad T. et al. have developed an “Awareness-to-Adherence Model” to outline the steps of physicians to clinical guideline compliance. The article explores the cognitive and behavioral steps that physicians take when accepting and using clinical guidelines. They postulate that there are four sequential steps that physicians make as they comply with guidelines. (Awareness-Agreement-Adoption-Adherence) First, they must become aware of the guideline, then intellectually agree with it, then decide to adopt it in their clinical practice and then adhere it at appropriate times. At each of the
four steps, progression can stop for various reasons. They also mention that in times when clinical practice is increasingly monitored, agreement as a factor might not always exist when a guideline is still adopted and adhered.

Once a health decision maker consults guidelines, there are still features of the guidelines themselves that will be critically appraised and could be seen as possible obstacles. The most important attributes determining guideline acceptance are scientific validity and credibility. Guidelines must be based on available scientific evidence accepted among respected authorities in the field. Another factor is the degree of generalizability and preciseness of definitions within the recommendations. Theoretical acceptance of guidelines, however, does not necessarily translate into implementation of them in practice. A Dutch observational study looked at attributes of clinical practice guidelines that influence the use of guidelines in clinical practice. Three reasons were cited for the failure to comply with guidelines.

- The recommendation is controversial and not compatible with current values
- The recommendation is vague and not precisely defined
- The recommendation demands change of fixed routines

Generally, recommendations based on evidence were used more frequently than those that were not evidence-based. Also, effects on daily work influenced the use in clinical practice.
Another important aspect is the validity of guidelines. Practice guidelines need to be up-to-date and present current scientific knowledge to be useful for clinical practice. The National Guidelines Clearinghouse only accepts guidelines in their database that have been developed or revised within 3 years. Shekelle et al. evaluated 17 clinical practice guidelines in 2001 published by the US Agency for Healthcare Research and Quality (AHRQ) between 1990 and 1996. The results show that 7 guidelines needed major updates, 6 minor updates and only 3 were still valid. A Kaplan-Meier survival analysis suggested that the estimated time of “survival” for 50% of all guidelines is 5.8 years (95% CI (5.0-6.6)). The point at which 90% of all guidelines were still valid was at 3.8 years. Shekelle concludes that, as a general rule, guidelines should be revised every 3 years.

Examples of institutions that provide clinical practice guidelines include NICE in the UK and the National Guideline Clearinghouse in the US. NICE concludes systematic reviews with clinical practice guidelines. On the other hand, the National Guideline Clearinghouse provides comprehensive databases of evidence-based clinical practice guidelines. The National Guideline Clearinghouse is a public Internet forum sponsored by the AHRQ (Agency for Healthcare Research and Quality), The American Medical Association (AMA) and the American Association of Health Plans (AAHP). Guidelines presented are not only the ones developed by the AHRQ, but also other guidelines.
developed by medical specialty associations (e.g. American Heart Association). All guidelines have to be revised at least every 3 years otherwise they will be dropped from the database.

The National Guideline Clearinghouse is by far the most comprehensive database of clinical practice guidelines that exists. An important utility is the possibility to compare two or more guidelines of the same topic and review abstracts about the guideline development. As mentioned above, guideline development is a complex issue, the comparison of guidelines from different sources could reveal different recommendations and enables the reader to critically assess different aspects.

A “European Guideline Clearinghouse” could be centralized and supplied with inputs from national medical specialty associations. Again, providing guidelines in the different national languages will be a crucial factor to guarantee the acceptance and the success of the Clearinghouse.

Nevertheless, there are justified concerns among practitioners about the use of guidelines that go beyond scientific validity and the change of routines. Some fear hidden motives influencing clinical practice guidelines, like costs. Therefore, cost containment should always be explicit. This is especially true in Europe where bureaucratic interference on political grounds occurs on a daily basis. Therefore, the independence of a panel working on guidelines must
be guaranteed. Punitive measures or liability issues against those who deviate from guidelines are also reasons for concern.

Others criticize the lack of psychosocial aspects of medical practice in guidelines. Evidence-based medicine is clearly focused on quantitative research. Guidelines can only be a part of the clinical decision-making process. Individual psychosocial aspects, empathy and social expectations are equally important variables and must be part of this process. Good medical practice depends on more than scientific evidence.
Outline of an evaluation program

Evaluation is the base for improved decision-making. Organizations can learn from information gained through evaluation and these inputs can foster a process called “cybernetic decision-making” – transforming a program from a static procedure to an ongoing process of improvement. Senge views this from an organizational level and calls it “generative learning.”

*Adaptive learning [survival learning] is important—indeed necessary. But for a learning organization, “adaptive learning” must be joined by “generative learning”, learning that enhances our capacity to create.*

Evaluation assesses if a given program produces the desired impact in an effective and efficient manner. By identifying obstacles, and factors that threaten or reduce the success of a program, evaluation provides the necessary information for optimization. Speaking in terms of the telematic health network and evidence-based databases, evaluations should identify why health care providers are not accepting, using or applying information contained in the health network. Evaluation results can then be used to improve the program and adapt it to the needs of the health care providers and subsequently increases the acceptance. In the long run, evaluations will determine whether or not the telematic health network has been successful in its goal: improved quality of health care.
Levels of evaluation

The effectiveness, efficiency, impact and sustainability of a program will largely depend on whether or not health care providers accept the program. The goal is well defined - an improvement of health care and health outcomes. The question remains, however, how much these factors can be improved by evidence-based medicine. Again, the success or failure will depend on how many practitioners consult an available database, how frequently they do so and how they utilize the information in their decision-making process. Acceptance will also depend on the user-friendliness of the network – if it is quick, easy and convenient and provides up-to-date, accurate information.

To optimize the decisive factors, cybernetic decision-making will be crucial in increasing the acceptance of a telematic health network since cybernetic decision-making is the only way to quickly and efficiently adapt the program to the needs of health care professionals - a group characterized by an assertive skepticism towards any type of new technologies with time consuming potential.

Ongoing evaluations and cybernetic decision-making will lead to improvements that will subsequently create a telematic health network that is considered “state of the art”. As previously mentioned, the system must include the highest standard of evidence-based medicine data available in all national languages of the European Union. A telematic health network will not
only depend upon the acceptance of the physicians, but also on the availability of vital resources, like reliable Internet connections and phone lines, still a limiting factor in some southern European countries. Both aspects have to be considered in an evaluation process.

*Outlines of evaluation*

The process of evaluation consists of 2 steps—formative and summative evaluation.

Formative evaluation refers to activities associated with the ongoing program and will be crucial to provide the necessary input for cybernetic decision-making. Repeated surveys among the target population and monitoring of the program will be the base for adjustments to raise the acceptance of the program. Formative evaluation, however, will have to use various perspectives, for example, the physician perspective on how easy and convenient the program is to use; the patient perspective on how the patients feel about the treatments when informed that they have stemmed from evidence-based medicine for clinical decisions. Will patients come to expect evidence-based treatments?

Summative evaluation refers to the goals of a program and would entail a long-term project since it will probably take years for European databases and
guidelines to become widely accepted and used as well as adjusted to all needs. Summative evaluation will assess if the impact of the program has attained the explicit objective of improving health care and health outcomes for all European citizens.

An implicit objective not mentioned by the European Commission in writing, is a reduction of health care costs. Health budgets have been strained for years and savings would be welcome. The reason for keeping this objective implicit lies in ideological backgrounds. A large part of the European governments are social-democratic – individual benefits (health, education, quality of life) are valued higher than monetary gains.

Methods of evaluation

Initially, formative evaluation will be the focus of a program to provide a base for cybernetic decision-making during the ongoing implementation process of the network. In my opinion three main methods of evaluation could be useful in evaluating the implementation of evidence-based databases:

- **Surveys** - descriptive surveys providing information about the status quo of the acceptance and the use of evidence-based practice; analytic surveys providing an insight into the perceived obstacles and barriers for the use of EBM.

- **Monitoring** - mainly reflecting the progress of the program and comparing operation and intermediate results with expectations. Monitoring will also play a role in the summative evaluation.
• **Trend analysis** - focusing more on the outcome of the program including the acceptance and use of an evidence-based telematic health network.

Surveys can be used in conjunction with monitoring and trend analysis to provide a more thorough picture of the program.

*Surveys*

Surveys can be a valuable tool for evaluating implementations of a telematic health system in the European Union. Preliminary surveys should be used to gather information before the implementation process. Ideally, a descriptive survey could be used before the implementation to provide a baseline of the extent of the current use of evidence-based practice. A survey could provide information about attitudes and behavioral aspects regarding the use of guidelines in particular and evidence-based medicine in general.

Questionnaires could be conducted via postal mail and the Internet. Questionnaires over the Internet have the advantage of saving valuable time and money by making information available faster and for less money. The limiting factor and a possible risk of selection bias, however, would be that physicians who use email for communication are also more likely to use the internet as a tool to gather medical information – in other words, those who would respond to an internet survey are already using online tools and therefore may have a more positive attitude towards a European-wide telematic
health network. Therefore, if average European physicians are the defined target group, surveys distributed through the postal mail may remain the most reliable method to reach them.

National medical associations could provide a pool of physician addresses. Researchers could then perform a random selection of a cohort from these addresses. However, physicians from all 15 nations must be represented in the survey in order to consider any national differences. Questionnaires have to be written in the respective native languages and all versions must be consistent and uniformly understood\textsuperscript{70}. The preliminary questionnaire must cover a variety of different aspects.

- Tracers must be defined beforehand and assessed at baseline. Tracer Condition Methodology and Trend Analysis can be conducted later on in the evaluation process on common clinical conditions. Such conditions must have enough evidence available about the most effective treatment methods. Such conditions may include hypertension and/or diabetes.

- General attitudes of physicians towards EBM can be explored.

- Perceived obstacles for the use of the evidence-based databases and clinical practice guidelines should be assessed.

- The current use of evidence-based medicine before the actual implementation of the program can be examined. The \textit{Evidence-Based Medicine Working Group} developed a hierarchy of so called "preprocessed evidence"\textsuperscript{71}. The authors have identified four groups of such evidence:

  1) Studies
  2) Systematic Reviews
  3) Synopsis
  4) Systems (e.g. guidelines )
This hierarchy could be used as a framework for preferences in evidence-based medicine. This would also provide a base to see if shifts in preferences occur over time.

After successful implementation of the network, annual surveys could be conducted to reveal changes in attitudes and perceived obstacles. As stated earlier, Tracer Condition Methodology could monitor changes in treatment patterns. Repeated surveys would also supply data for Trend Analysis.

As mentioned before, Pathman, Konrad et al. have developed an Awareness-to-Adherence Model of the steps to Clinical Guideline Compliance.\textsuperscript{72} This model could be very useful when undertaking analytical surveys on why physicians do or do not accept and use guidelines. Their model reflects the behavioral and cognitive steps that physicians take to eventually accept and adhere to guidelines. As previously mentioned the authors outline four principal steps, or significant “A”s, in this process:

- the Awareness of the guideline;
- the intellectual Agreement with this guideline;
- the Adoption of the guideline;
- the Adherence to the guideline at appropriate times;

At each one of these steps, specific factors and influences can prevent further progression to the next step. This means that surveys following
implementation should be more thorough than those before it. They should also specifically address the four points of the *Awareness-to-Adherence Model* (Awareness- Agreement-Adoption-Adherence). This permits barriers and obstacles to be identified and the program to be adjusted accordingly.

While information is gathered on target groups, the evaluation process should also investigate patient perspectives through interviews of randomly selected patients. The cohort should reflect the national heterogeneity of the European Union to reflect the differences in values, mentalities and preferences of people from 15 different nations. Patient interviews should focus on the preferences and expectations of patients when the patients visit a physician. The amount of empathy a physician displays to a patient combined with the length of time of a consultation may conceivably rank higher in importance for patients than the latest scientific treatments. Patient satisfaction is definitely a highly important intermediate outcome. Discrepancies between patients and health care providers on how quality health care is defined can have a detrimental effect on the patient-physician relationship. The good of the patient must remain more important than guideline adherence.

*Monitoring*

Monitoring will mainly focus on operational aspects of the program. This will start if the implementation process is able to follow a given timetable. A review of the fulfillment of the technical requirements will be necessary to
ensure the smooth implementation of the network in all participating countries.

One of the goals of e-Europe is to bring all citizens online. Such a goal can only be reached if national governments and private companies provide the infrastructure necessary in the form of up-to-date reliable telecommunication networks. Technical difficulties can severely undermine the success and acceptance of a European telematic health network. Surveys can be an additional tool to provide valuable information on any technical difficulties facing health care providers.

Knowledge gained from monitoring must be used to change and improve the process. One way to assess acceptance and the extent of implementation would be to monitor the amount of hits on and time spend at the website. In addition, inputs into the program such as personnel resources, finances and information for the target group on the program should also be monitored. Limitations on monitoring are not the only factors possibly influencing the operation of the program. Nevertheless, it is important to initially identify the main factors of limitation so that these can be adjusted during the monitoring process.

Finally, monitoring will play an important role in the summative evaluation of the program. An improvement in the health status of the European citizens can be seen as the expectation for program’s overall outcome. Since health status per se is hard to define and measure, monitoring of proxy measures like
morbidity and mortality will be an appropriate method of assessing health status improvements. Disability adjusted life years (DALYs) for diseases used in the Tracer Condition Methodology could be particularly interesting. A direct relationship between the use of evidence-based medicine and a possible reduction of lost DALYs could be shown on both the societal level and the disease-subpopulation level. However, no long-term studies exist proving evidence-based health care actually improves health outcomes because evidence-based medicine is still a relatively young concept. Changes in health outcomes are best assessed with prospective observational studies that follow a cohort over many years. One method to evaluate this would be through trend analysis.

*Trend Analysis*

Trend analysis is an evaluation tool that focuses on outcomes and evaluates if a program is responsible for changes in outcomes. Defined performance indicators are examined over a period. Data for trend analysis can be retrieved from surveys or monitoring. Possible dependent variables could be treatments for conditions previously defined for Tracer Condition Methodology; hits on the website; length of time spent on the website; attitudes towards evidence-based medicine; perceived barriers and, in the long run, changes in morbidity and mortality.
The task of Trend Analysis is to show that changes of the dependent variable over time are truly due to the implementation of the program. Possible sources of error, like regression to the mean or miscounting and reactiveness must be considered. Miscounting and reactiveness can stem from the data used from surveys. Selection bias in surveys may occur if users of evidence-based databases are a group that is more motivated to return surveys about these databases.

Other factors that can possibly influence the outcome variable also must be considered. In the case of the telematic health network, factors like the awareness of a database, the access to Internet, the age and the nationality of the physician, and many more can possibly confound the statistical significance of the acceptance as a dependent variable. Multivariate regression can show if there is a statistically significant change while controlling for other explanations for changes than the program itself. For this to work, however, the time span of the observation must extend long enough to overcome the intermediate results of an evidence-based database that may be time lagged. Stratified analysis can provide valuable information about each country. National differences in attitudes, health systems or infrastructures can lead to different outcomes and might require adjustments and improvements to the program tailored to the specific needs of physicians within that particular country.
Sampling

To take the heterogeneity of the European Union into consideration, samples from each nation must be drawn. This stratified sampling will increase the precision of the results. Just as with surveys, national medical associations can provide pools of physician addresses. Random sampling is critical to guarantee the external validity of results and minimize selection bias. The process of administrating surveys must include the weighing of the advantages and disadvantages of repeated random sampling. Using the same cohort for repeated surveys could provide valuable information for trend analysis, especially if combined with analytic surveys about perceived barriers towards evidence based medicine. On the other hand, repeated random sampling would reduce ascertainment bias. Through the preliminary survey, the participating physicians may become aware of the program and its intentions. By retaining the same cohort for repeated surveys, participants may overestimate their amount of evidence-based practice, unconsciously trying to fulfill expectations. Information on patient conditions and treatments submitted by physicians to health insurance companies could provide information on evidence-based health care that is more reliable. However, privacy concerns in this matter remain a justified public issue.

Low Response rates can impose major problems on any surveys. Nonresponse refers to the unwillingness or the inability of people selected for the sample to
cooperate in answering a questionnaire. In their book "Evaluation and Decision Making for Health Services" Veney J. and Kaluzny A. state:

...nonresponse remains a problem because it is not reasonable to assume that those who fail to respond to a questionnaire or interview are essentially no different from those who do respond in regard to the subject of the survey.

People willing to respond usually perceive the program as important. Generally it is crucial to make every possible effort to collect data from a high proportion of the sample. The authors conclude:

Generally, however, it is better to accept a smaller sample with a lower proportion of nonresponse than a larger sample with a larger proportion of nonresponse.

Cost-effectiveness, Cost-benefit, Cost-utility analysis

Eventually the public will also demand results that are less abstract than DALYs and QUALYs. Cost-effectiveness analysis is the classical approach used in evidence-based medicine to give results of trials a cost perspective and is often used as an example for the success of evidence-based medicine. However, in the context of a population, cost-effectiveness of the treatment for a single patient can only be seen as an intermediate outcome. To assess the overall benefit for a population some kind of utility has to be applied. Cost-utility analysis brings changes in defined utilities like DALYs or QUALYs for a whole population or a diseased-subpopulation into play. Cost-benefit analysis would put a Euro amount on a chosen utility. Both analyses discount the present value when a measure of utility is received in the future.
Threats to validity

Cost-utility and cost-benefit analyses will be the decisive results of summative evaluation in determining the success or failure of a European telematic health care system. Threats to validity could mainly stem from attempts of political influence on the results. E-health is based on a political initiative of the European Commission. Politicians are responsible for the program and the output of any evaluation process will become part of the political discussions in Brussels and the EU in general. Considering the political culture in Europe, the attempt of politically influencing the results of a summative evaluation report could be a matter of concern. Financial independence; participation by experts in the field of evaluation; and both public and media scrutiny should guarantee a minimization of this threat.
Summary and Discussion

Although no official details on the telematic health network and evidence-based databases have been released yet, the European Union has outlined the course of its health care - evidence-based medicine. The European Union has recognized the Zeitgeist of modern clinical medicine and is working to facilitate the practice of evidence-based health care by starting political initiatives like e-Health. In acknowledging the boundaries of evidence-based medicine, the European Union has also remained conscious of the philosophical and ideological influences on European programs - most of them culturally based – and important to the implementation of any successful program.

In a report on evidence-based health care, the European Union equated the classic attributes of evidence-based medicine like effectiveness, efficiency, efficacy, and cost-effectiveness to humanistic values like appropriateness, social and ethical aspects, and patient values. The design of this equation is an important step in the union of cultures deeply suspicious of and critical towards any kind of social Darwinism and the rise of a new utilitarian orthodoxy. In Europe, evidence-based health care must be socially inclusive and must guarantee the best available quality of care for every single citizen to be politically successful.
Health care is conceived as a basic right for each citizen equal to the concepts of free education and freedom to vote. An unwritten social contract exists between the generations that forbids leaving the weak and underprivileged without sufficient health care, one of the main differences to the U.S., where many people view health care as a utility, a benefit rather than a basic right, and one that can only be acquired through hard work. This leads to the common causal fallacy that people who don’t have health insurance either don’t want it or don’t work hard enough to deserve it. For Europeans this state of mind is hard to comprehend, too deeply rooted is a general altruistic, social conscious. It is commonly thought in Europe that a society’s greatness is not measured in economic wealth but rather its treatment of its weakest members.

Therefore the emphasis of evidence-based health care must be on the improvement of the quality of care. Costs are generally seen as important but remain secondary. The European Union reflects this sentiment in not mentioning cost-reduction as an explicit objective. That it is an implicit objective can be deducted from the political reality of increasing health care costs.

What benefits could public health gain from evidence-based medicine and evidence-based health care? As mentioned above, evidence-based medicine primarily improves the quality of care on an individual level through optimizing the process of clinical decision-making through the use of
scientific evidence as a base. An extrapolation of these individual benefits will lead to health improvements of the general population. One such example is the use of beta-blockers after myocardial infarction.

A great potential for public health lies in the use of evidence-based medicine in preventive medicine. On the one hand, some screening programs can be very costly but equally beneficial such as the one targeting the reduction of cervical cancer deaths through PAP-smears. On the other hand, other screening programs either lack effectiveness when scientific evidence is systematically assessed or the benefits fail to outweigh the risks. This happened in the screening for adolescent idiopathic scoliosis in schools – widely practiced even mandatory in some states. Current evidence suggests that the screening methods used had low sensitivity and that the natural course of the disease often was not progressing and more harm than good came from the resulting therapies. The United States Preventive Services Task Force has not found sufficient scientific evidence to support school screening for adolescent idiopathic scoliosis and does not recommend school screenings for adolescent idiopathic scoliosis.77

A similar debate about breast cancer screening with mammography was initiated recently by findings of Olsen and Gotzsche, who critically assessed the methodologies of studies supporting breast cancer screening with mammography.78
These are just a few examples of how evidence-based medicine can help to assess the effectiveness of interventions. In a world of limited resources, this information is important to focus on interventions with proven effectiveness. From a public health point of view, an allocation of money following the rationale of evidence-based findings in preventive medicine will lead to maximizing health benefits for larger populations since resources are limited.

The challenge to implement a network that links 15 different health care systems and provides evidence-based medical databases for health care decision makers with different languages and backgrounds is certainly great. Various factors have to be considered to guarantee the acceptance by the target groups (e.g. databases in the native languages). A lot can be learned from already existing databases like the Cochrane Database of Systematic Reviews or the National Guideline Clearinghouse. The UK is certainly the most advanced nation worldwide in regards to evidence-based medicine and could play an important leadership role.

To attain the goals outlined by the European Union e-Health initiative, I propose the creation of Evidence-Based Practice Centers (EPCs) and a European Guideline Clearinghouse to function as the building blocks for an evidence-based network. The EPCs should be represented in each nation to emphasize national public health priorities and to provide databases in the
national languages. These databases would be readily accessible over the internet free of charge. The EPCs must be coordinated to facilitate the exchange of information amongst them. The European Guideline Clearinghouse should serve as a forum for various guidelines of different associations. These guidelines will probably not all be evidence-based. The main task of a European Guideline Clearinghouse will be to offer the opportunity for health care decision makers to compare various guidelines on the same topic.

Crucial to the continued success of such a huge undertaking and running parallel to its implementation is an ongoing evaluation of the program. This will provide the base for cybernetic decision-making, using information gained from the evaluation as feedback to improve the program. Surveys, Tracer Condition Methodology, Monitoring and Trend Analysis are some methods of evaluation that can be utilized to achieve this goal.

Again, the challenge is unique. In hindsight, the mere creation of a political union, a common currency and a European spirit amongst historically feuding nations was a colossal undertaking. The challenge is indeed unique, but in contrast, just another steppingstone.
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Appendix

Methodology


The search was confined to articles published between 1997 and 2002.

Three hundred and forty-five articles were found. Twenty-one of these related to the topic concerned. The main exclusion criteria included subject matter and language:

- orientation of topic was too clinical;
- articles printed in languages other than English or German.

The same keywords were used to search the Cordis library of the European Union. Two additional articles were found. Furthermore, the archives of the European Commission have five documents related to the topic.

An electronic search of the British Medical Journal produced three more articles and one more was found in Health Policy.

I used the official publications of the European Union to draw a framework of the program. I submitted a request for more information about evidence-based
medicine and the implementation of a future telematic health network to the information service of e-health. The reply stated that there are no further documents available at this time and that evidence-based databases in Europe are currently confined to national levels (e.g. NICE in the UK). In addition, a different request to Europe-direct was made. They suggested I consult the website of the Directorate General for Information Society, where I retrieved some general information about e-Europe. Furthermore I contacted two of the authors (Elke Jakubowsky, Matthias Perleth ) cited in the official publication for the European Commission, “Best Practice”: State of the art and perspectives in the EU for improving the effectiveness and efficiency of European health systems.”

All additional articles retrieved were used for background information and mainly identified from references of other articles.