
Should an order to “monitor long-term vital signs,” including mortality outcomes, be as routine as an order for a laboratory test in patients with rheumatic diseases?

T. Pincus, T. Sokka

Theodore Pincus, Clinical Professor of Medicine, New York University School of Medicine, and Director of Outcomes Research, NYU Hospital for Joint Diseases.

Tuulikki Sokka, Department of Medicine, Jyväskylä Central Hospital, Jyväskylä, and Medcare Oy, Äänekoski, Finland.

Please address correspondence to:
Theodore Pincus, MD,
Division of Rheumatology, NYU Hospital for Joint Diseases, 301 East 17th Street, Room 1608, New York, NY 10003, USA.
E-mail: tedpincus@gmail.com

Received and accepted on September 1, 2008.

Clin Exp Rheumatol 2008; 26 (Suppl. 51): S21-S24.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2008.

Key words: Vital signs, physical function, pain, exercise, questionnaires, mortality.

ABSTRACT

Vital signs alert a health professional to problems which may threaten patient well-being and survival. Clinicians are highly familiar with vital signs for acute disease such as blood pressure, pulse, temperature, but unfamiliar with vital signs for chronic disease, such as physical function, pain, global status, exercise frequency and smoking. Long-term vital signs should be collected at each visit and stored in a computer database, ideally in a flow sheet format, as the memory of clinicians and patients is not reliable over long periods. The structure of the database should be identical from one site to another, so that data may be pooled to analyze large series of patients, particularly those with rare diseases, such as systemic sclerosis, polymyositis, and vasculitis. Of course, appropriate additional information beyond simple “long-term vital signs” from a physical examination, radiograph and laboratory are needed for further accurate assessment of prognosis and outcomes, in both acute and chronic diseases, and optimal information will emerge from specialized research centers. A common long-term vital signs database would be a major advance from current descriptive, non-quantitative monitoring of patients with rheumatic diseases, and would allow any rheumatologist to contribute to improved knowledge and mortality outcomes of rheumatic diseases.

Rheumatologists routinely order laboratory tests in most patients to provide quantitative, “scientific,” protocol-driven information for diagnosis, prognosis, and treatment. Laboratory test results clarify clinical impressions and decisions with quantitative data. Laboratory tests have contributed invaluablely to the conquest of acute diseases, the

primary achievement of 20th century medicine.

The discoveries of rheumatoid factor (1, 2) and anti-nuclear antibody (ANA) (3) in the 1940s led to a hope for pathognomonic tests for diagnosis, prognosis, and monitoring, analogous to hemoglobin for anemia or glucose for diabetes. These serological discoveries established rheumatology as a clinical science and led to major advances in therapies such as development of biological agents. However, laboratory tests remain limited in diagnosis and monitoring of individual patients with rheumatic diseases. A recent meta-analysis indicates that only 69% of people with rheumatoid arthritis (RA) have rheumatoid factor, and only 67% have anti-citrullinated peptide (CCP) antibodies (4). Therefore, one-third of individual patients with RA are negative for rheumatoid factor and anti-CCP, but appear at this time to need treatments that are identical to those with positive tests. Only 1 in 100 people with positive ANA has systemic lupus erythematosus (SLE) (5).

Limitations of laboratory tests in rheumatology have led to indices of multiple measures to provide numerical data rather than descriptive impressions to assess and monitor patient status over long periods, such as the systemic lupus erythematosus disease activity index (SLEDAI) (6) or Bath ankylosing spondylitis disease activity index (BASDAI) (7). All rheumatology indices include patient-reported clinical measures which add informative data to laboratory tests. The clinical indices are excellent research tools, but are too complex for busy clinical practice, and used infrequently outside of research settings. Therefore, the long-term course of most patients generally remains depicted descriptively, rather than numerically, severely limiting

Competing interests: none declared.

accuracy. Without quantitative data, information concerning predictors of mortality outcomes in rheumatic diseases and improvements in these outcomes remains limited – much of the world's literature is presented in this Supplement.

Chronic diseases have displaced acute diseases as the primary concern of contemporary medical care in Western countries. Outcomes in chronic diseases are not apparent for years and sometimes decades, in contrast to outcomes of acute diseases, which usually are known within days, sometimes hours. When a chronic disease is characterized by a single “gold standard” measure, as in hypertension and hypercholesterolemia, it is possible to recognize whether correction of unfavorable values improves mortality outcomes. When no single “gold standard” is available, as in chronic rheumatic diseases, and indices are too complex for usual care, new strategies appear needed to improve the quality of knowledge concerning outcomes and results of interventions.

One approach to meeting the need for quantitative data in chronic diseases is to include recording of “long-term vital signs” prognostic of poor outcomes and mortality in chronic diseases – physical function, pain, global status, exercise frequency and smoking – as a routine procedure in usual care (8). All these data can be obtained from a simple self-report patient questionnaire, and obtaining quantitative data is no different in concept from ordering a laboratory test. When a physician orders a laboratory test, several workers are mobilized, to draw the blood, transport it to a laboratory, perform the test, record the results, and transmit the results to the physician. Why not order mobilization of workers to monitor long-term outcomes, to record data, enter into a computer, manage a database, add periodic data, and record deaths?

Patient care activities generally are regarded as reflecting the “practice” or “art,” rather than the “science” of medicine, although many advances in patient care depend on laboratory science. Certain clinical activities are “scientific,” *i.e.*, conducted according to a standard protocol to collect quantitative data for

each patient seen. Every person seen in an emergency room has acute “vital signs” of pulse, temperature and blood pressure measured to alert health professionals to a possible need for immediate attention. Every newborn has an APGAR score recorded, based on five 0-2 scales, which directs whether the neonate is sent to a regular or neonatal intensive care nursery (9, 10). Clinical trials introduce a “scientific” approach into clinical activities, mimicking a laboratory experiment by isolating a single variable, the test therapy (11), although clinical trials have many limitations based on inclusion and exclusion criteria and a short time frame of 2 or fewer years, and many others (12, 13).

“Vital signs” for chronic diseases which predict severe long-term outcomes such as work disability, costs and premature mortality, should be available to every physician caring for any patient with any chronic disease. Collection of these data on a standard patient questionnaire (8) and recording in a standard database platform could allow pooling of data from many sources to advance knowledge of the natural history, responses to therapy, and prediction of mortality in chronic diseases.

Many registries of patients with rheumatic diseases have been established in many settings in recent years, reflecting the concept of “a standardized database in rheumatic diseases,” introduced by Fries and colleagues in the 1970s (14-18). These pioneers recognized that similar information is collected in all patients in usual care, but not standardized to provide a common “scientific” database. Furthermore, large administrative databases from insurance companies and pharmaceutical sources have contributed to advances in knowledge concerning rheumatic diseases.

Rheumatic disease registries and databases have provided substantial knowledge concerning mortality in rheumatic diseases, as described in many chapters in this Supplement. However, data in contemporary databases are standardized only within each database, although many include much similar information. Different database formats and architectures limit greatly pooling of data for robust analyses. Furthermore, most

registries are limited to patients with specific diagnoses or therapies, such as biological therapies in patients with RA, and do not include patients with other rheumatic diseases.

The concept of a “consecutive patient database” was introduced by Moses (19) to overcome issues of selection in registries, clinical trials, and other databases, by including every patient seen in a given setting in an outcomes database. A consecutive patient database in an identical format to monitor “long-term vital signs” in all patients of many participating rheumatologists could introduce a “scientific” protocol to clinical activities. Such a database could advance greatly knowledge of long-term rheumatology outcomes, including mortality outcomes.

Several advances over the last two decades render a goal of a large simple database for rheumatic diseases a realistic possibility at this time:

- 1) The most valuable long-term vital signs, including function, pain, global status, exercise status, smoking and other variables, are provided by the patient (8, 20). Of course, data from a physical examination, radiograph or laboratory test add valuable and sometimes critical information, to be incorporated into any rheumatic disease database. However, the basic data for a long-term database can be obtained from patients in busy clinical settings, more reliably in a cost-effective manner than information from health professionals and other sources.
- 2) The personal computer and software programs allow recording of this information in a cost-effective, simple manner.

A proposed protocol to monitor long-term outcomes in rheumatic diseases is not complex:

- 1) Standard baseline “vital signs” data are collected from each patient on a simple patient self-report questionnaire, completed by each patient with any diagnosis while waiting to see the rheumatologist, at the first visit and each subsequent visit. Demographic data include date of birth, sex, education level, race, occupation, and

work status. Clinical long-term vital signs from the patient include physical function, pain, and global status – the three patient-reported Core Data Set measures for RA – as well as exercise frequency and smoking. Of course, each local site is free to add data from a physician, radiograph or other imaging study, laboratory test, genetic test, index or any other data for appropriate patients. However, minimum standard “common” data in a standard format must be available. Comparisons of patients for whom only basic questionnaire data are available versus patients with more extensive data are possible and informative – the questionnaire data alone generally represent overall clinical status well.

- 2) Consent is requested from the patient for long-term monitoring, to learn what happens to her or him, to improve advice and treatments given to patients in the future. Despite reasonable privacy concerns, most patients recognize that quantitative prognostic information in all chronic diseases is limited – for example, to identify optimal therapies for different patients. Most patients are willing, if not eager, to contribute to a database, particularly if concerns are allayed by appropriate responses. The authors are unaware of any violations of privacy that have resulted from efforts of rheumatologists, or rheumatology research programs, to monitor long-term outcomes – and such efforts unequivocally have helped improve patient outcomes.
- 3) Enrollment should include some type of national patient identifier. This is automatic in Scandinavia and other European countries and requires a Social Security number in the United States, which allows linkage to a national death index, so that this sensitive matter can be known. The Social Security number is an increasingly sensitive topic; again, appropriate explanations [“in case we lose track of you” (not “to record your death”)] are needed.
- 4) The database should also include the name, address, and telephone number of a contact at a different

address, should the data center be unable to reach the patient.

- 5) The procedure for follow-up, including the interval for collection and what other data to collect beyond questionnaire data, will vary according to local conditions, capacity of computer programs, resources, etc. The additional data may be determined locally, to include joint count and other physical examination, radiographic and other imaging data, laboratory, genetic data, indices, as noted above. The protocol should include a method to account for all patients every 6-12 months through a visit, mailed questionnaire, telephone call, or Internet.
- 6) Matched control subjects from the population, according to age, sex, and other variables, may be included.
- 7) Analysis of mortality from identifier numbers may be performed at 2, 5, and 10 years (21-23), with relatively small amounts of work.
- 8) The protocol should include a procedure that is set in motion when the rheumatology setting learns of a patient death. The procedure may include a possible condolence note to the family, a request for a death certificate (more easily obtained than from government agencies), again varying with local customs, ethics boards, and other circumstances.

Of course, limitations remain to a proposed “long-term vital signs” consecutive patient database, as seen in all “scientific” methods, including:

- 1) Many rheumatologists will question whether a basic “vital signs” database can provide sufficient information concerning long-term outcomes of a rheumatic disease. Basic data cannot be as informative as more extensive data, particularly in complex rheumatic diseases, with varying clinical features. Vital signs for chronic diseases are only the beginning, just as vital signs for acute diseases (blood pressure, pulse, temperature) are only the beginning in an emergency room, recovery room or other acute care setting, to alert the clinician to important problems. The optimal information concerning outcomes in

rheumatic diseases will emerge from comprehensive data collected and analyzed at specialized centers, as has always been the case. Nonetheless, it would appear that some basic data in all patients would be substantially better than having no quantitative data other than laboratory tests in 99% of patients, as is the case at this time. A simple vital signs database allows any rheumatologist to contribute to quantitative long-term data regarding patients with rheumatic diseases.

- 2) There are obvious privacy concerns in the development of large databases, which may be addressed with de-identified data for any common data center, encrypted data sent on disks rather than over the internet, and other strategies. Many data available on the internet are probably potentially more private than a medical record, including bank accounts, brokerage accounts, Social Security information, etc.
- 3) The expenses are incremental to those of usual care. The authors have used elements of the proposed protocol over several decades, and suggest that organization of the information often saves time and costs in clinical settings. A review of systems and recent medical history, and flow sheets of patient questionnaire scores, laboratory tests and medication data, developed from a one-page multidimensional health assessment questionnaire (MDHAQ) saves time per visit with superior documentation (8).
- 4) The procedure may appear to create an unacceptable interruption of patient flow. However, completion of a questionnaire by a patient while waiting to see the physician adds no time and no interference with patient flow, and can save time for the patient and clinician at the visit.

Expenses associated with a consecutive patient database are in the range of (or less than) required for laboratory tests. Such support could be sought from insurance companies, government, and other payers – the data are usually more informative than the simplest laboratory tests, for which payment is routinely

supported. In addition, costs might be supported by government agencies, foundations, pharmaceutical companies, rheumatology professional societies, and patient associations. Some current expenditures on extensions of clinical trials and invaluable expertise in specialized registries and might be mobilized and expanded to include patients with all rheumatic diseases.

An order to implement a protocol to monitor patients for long-term outcomes and mortality could be as routine in rheumatology as an order for an ESR or anti-DNA test. Data would then be available for the unusual "rare" diseases such as scleroderma, polymyositis and vasculitis, for which there are few reports. If each of 1,000 rheumatologists has 3 such patients with each diagnosis, data could be available for a "case series" of 3,000 patients.

A "vital signs" database would advance the science of rheumatology, and enhance provision of optimal care to all patients. Improved information concerning long-term outcomes of all rheumatic diseases would appear an intellectual and ethical responsibility of all rheumatologists, now that implementation of this goal is feasible for the rheumatology community.

References

1. WAALER E: On the occurrence of a factor in human serum activating the specific agglutination of sheep blood corpuscles. *Acta Path Microbiol Scand* 1940; 17: 172-8.
2. ROSE HM, RAGAN C, PEARCE E, LIPMAN MO: Differential agglutination of normal and sensitized sheep erythrocytes by sera of patients with rheumatoid arthritis. *Proc Soc Exp Biol Med* 1948; 68: 1-6.
3. HARGRAVES MM, RICHMOND H, MORTON R: Presentation of two bone marrow elements: The "tart" cell and "L.E." cell. *Proc Staff Meet Mayo Clin* 1948; 23: 25-8.
4. NISHIMURA K, SUGIYAMA D, KOGATA Y *et al.*: Meta-analysis: Diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis. *Ann Intern Med* 2007; 146: 797-808.
5. PINCUS T: A pragmatic approach to cost-effective use of laboratory tests and imaging procedures in patients with musculoskeletal symptoms. *Prim Care* 1993; 20: 795-814.
6. HAWKER G, GABRIEL S, BOMBARDIER C, GOLDSMITH C, CARON D, GLADMAN D: A reliability study of SLEDAI: a disease activity index for systemic lupus erythematosus. *J Rheumatol* 1993; 20: 657-60.
7. CALIN A, NAKACHE JP, GUEGUEN A, ZEIDLER H, MIELANTS H, DOUGADOS M: Defining disease activity in ankylosing spondylitis: is a combination of variables (Bath Ankylosing Spondylitis Disease Activity Index) an appropriate instrument? *Rheumatology* (Oxford) 1999; 38: 878-82.
8. PINCUS T: Pain, function, and RAPID scores - Vital signs in chronic diseases, analogous to pulse and temperature in acute diseases and blood pressure and cholesterol in long-term health. *Bull NYU Hosp Jt Dis* 2008; 66: 155-65.
9. APGAR V: A proposal for a new method of evaluation of the newborn infant. *Curr Res Anaesthesiol Analg* 1953; 32: 260-7.
10. APGAR V, HOLADAY DA, JAMES LS, WEISBROT IM, BERRIEN C: Evaluation of the newborn infant - second report. *JAMA* 1958; 168: 1985-8.
11. FEINSTEIN AR: An additional basic science for clinical medicine: IV. The development of clinimetrics. *Ann Intern Med* 1983; 99:843-8.
12. FEINSTEIN AR: An additional basic science for clinical medicine: II. The limitations of randomized trials. *Ann Intern Med* 1983; 99: 544-50.
13. PINCUS T, SOKKA T: Clinical trials in rheumatic diseases: designs and limitations. *Rheum Dis Clin N Am* 2004; 30: 701-4.
14. FRIES JF: Time-oriented patient records and a computer databank. *JAMA* 1972; 222: 1536-42.
15. FRIES JF: A data bank for the clinician? (editorial). *N Engl J Med* 1976; 294:1400-2.
16. FRIES JF: The chronic disease data bank: first principles to future directions. *J Med Philos* 1984; 9: 161-80.
17. FRIES JF, MCSHANE DJ: ARAMIS (The American Rheumatism Association Medical Information System): a prototypical national chronic-disease data bank. *West J Med* 1986; 145: 798-804.
18. FRIES JF: The chronic disease data bank model: a conceptual framework for the computer-based medical record. *Comput Biomed Res* 1992; 25: 586-601.
19. MOSES LE: The series of consecutive cases as a device for assessing outcomes of intervention. *N Engl J Med* 1984; 311: 705-10.
20. PINCUS T, SOKKA T: Quantitative measures for assessing rheumatoid arthritis in clinical trials and clinical care. *Best Pract Res Clin Rheumatol* 2003; 17: 753-81.
21. SOKKA T, HAKKINEN A, KRISHNAN E, HANNONEN P: Similar prediction of mortality by the health assessment questionnaire in patients with rheumatoid arthritis and the general population. *Ann Rheum Dis* 2004; 63: 494-7.
22. KAUPPI M, SOKKA T, HANNONEN P: Survey nonresponse is associated with increased mortality in patients with rheumatoid arthritis and in a community population. *J Rheumatol* 2005; 32: 807-10.
23. SOKKA T, KAUTIAINEN H, HANNONEN P, PINCUS T: Changes in health assessment questionnaire disability scores over five years in patients with rheumatoid arthritis compared with the general population. *Arthritis Rheum* 2006; 54: 3113-8.