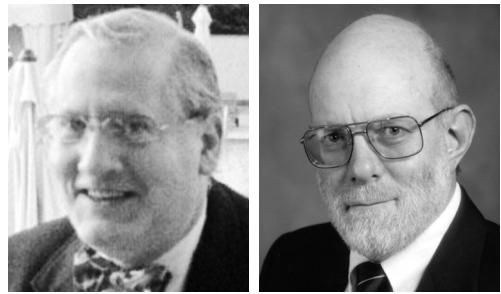


# Patient Questionnaires for Clinical Research and Improved Standard Patient Care: Is It Better to Have 80% of the Information in 100% of Patients or 100% of the Information in 5% of Patients?



A series of reports by Strand and colleagues<sup>1-4</sup> provides a model for analysis of clinical trial data beyond the initial primary outcomes, adding substantial value at a fraction of the costs of collecting these data. Extensive analyses of 3 clinical trials, US301<sup>5</sup>, MN301<sup>6</sup>, and MN302/304<sup>7</sup>, have contributed much new information to the rheumatology community, particularly concerning the effectiveness of patient questionnaires to assess and monitor patients with rheumatoid arthritis (RA)<sup>1-5,8</sup>. [Disclosure: The present authors have participated in two efforts involving further analyses of US301<sup>8,9</sup>.] Many large clinical trial data sets could be analyzed beyond whether statistically significant differences exist between active and placebo treatment, to improve management of RA and other diseases.

In this issue of *The Journal*, Dr. Strand and colleagues<sup>10</sup> analyze differences between active versus placebo treatments in patients with RA according to the problem elicitation technique (PET) questionnaire<sup>11</sup> and the physical component scale of the Medical Outcome Study Short-Form 36 (SF-36), a generic questionnaire to assess health related quality of life<sup>12</sup>. The findings indicate similar levels of superior efficacy of leflunomide and methotrexate to placebo to those seen according to the primary outcome measures, the Health Assessment Questionnaire (HAQ)<sup>13</sup> and its modified version (MHAQ)<sup>14</sup>. These observations add to the authors' previous reports that patient questionnaire measures have a higher relative efficiency and are less likely to improve with placebo than joint counts<sup>1,2</sup>. Further, patient questionnaire scores are as sensitive as joint counts, American College of Rheumatology (ACR) 20 improvement criteria, or disease activity scores in the capacity to recognize differences between active and placebo treatment in patients with RA<sup>8,9</sup>.

Why is this important? Patient questionnaires were initially regarded by most clinicians, including ourselves, as research tools or a "poor man's" surrogate in clinical care, to be used when time or resources were lacking for a tradition-

al joint count, quantitative radiographic score, or laboratory measure. Many rheumatologists continue to believe that patient questionnaires are weak "subjective" measures compared to stronger "objective" measures assessed by health professionals.

Our viewpoint changed dramatically when patient questionnaire scores were found in 1984 to predict mortality in patients with RA more effectively than previously documented for any traditional measure<sup>15</sup> (and have consistently been confirmed since then<sup>16</sup>). These findings suggested that questionnaires should be incorporated into standard patient care, similar to routine monitoring of important predictors of premature mortality such as blood pressure or cholesterol in cardiovascular and other diseases. The practice of assessing a clinical measure is based on epidemiologic research concerning longterm prognosis, but is applied in standard care to improve outcomes in individual patients. Improvement in indicators of poor prognosis is associated with increased well-being and survival, although that cannot necessarily be determined in individual patients in standard care.

Incorporation of patient questionnaires into standard clinical care requires different strategies from those used in clinical research, just as the degree of stringency in assessment of blood pressure and serum lipids differs in clinical care compared to clinical research (Table 1). Research questionnaires generally are elaborate, increase the length of a visit, add significantly to staff and physician time, and require special tools or programs to analyze, as well as expertise to interpret. These questionnaires necessarily include much information that may be superfluous to patient assessment in standard care. The SF-36 may have many uses, such as cost-benefit analyses<sup>17</sup> and comparison of quality of life in patients with RA compared to other diseases. Questionnaires used in our own clinical research may include extensive queries about work history, hospitaliza-

*See Physical function and health related quality of life: Analysis of 2-year data from RCT..., page 590*

Table 1. Patient questionnaires in clinical research and clinical care.

Feature	Clinical Research	Clinical Care
Design considerations	Complete, long	Patient-friendly, < 10 min
Effect on patient visit	Adds time, interferes with flow	Saves time for MD and patient
Scoring	Complex, requires computer	Simple, may "eyeball" results
Goal of data	Add to research database	Add to clinical care
Focus of analysis	Groups of patients in clinical trials or observational databases	Individual patients cared for by individual physicians
Data management	Send to data center	Review for patient care
Major criteria for use	Validity, reliability; assess minimum clinically important significant difference	Document status, medical and medicolegal rationale for aggressive therapies
Disposition of questionnaire	Enter into computer	Enter into flow sheet in medical record

tions, etc., and additional instruments such as the SF-36 to develop improved measures, such as assessment of complex activities in a multidimensional HAQ (MDHAQ)<sup>18</sup> and more evenly spaced scoring in a HAQII<sup>19</sup>.

Patient questionnaires for standard clinical care should be pragmatic, short enough to be completed in less than 10 minutes, reviewed (eyeballed) by a clinician in less than 10 seconds, and scored by the clinician or designated associate in less than 30 seconds without a computer or calculator. This type of questionnaire facilitates and improves clinical encounters. The findings of Strand, *et al*, if confirmed in other data sets, indicate that omission of the SF-36 and PET will not result in loss of important information to assess and monitor patients in standard care.

The HAQ<sup>13</sup>, Clinical HAQ (CLINHAQ)<sup>20</sup>, MHAQ<sup>14</sup>, MDHAQ<sup>18</sup>, or HAQII<sup>19</sup> are as informative as all additional questionnaires to assess patient responses to therapies. These questionnaires are useful in all rheumatic diseases, including RA, osteoarthritis, fibromyalgia, systemic lupus erythematosus, scleroderma, ankylosing spondylitis, etc.<sup>16</sup>. Only a few simple measures on a short questionnaire are needed to assess a patient fully: a measure of function, pain, global severity, fatigue, and psychological distress.

The physical function scales of the HAQ and derivatives are as effective as any questionnaire (or even any other clinical measure including joint count, radiograph, or laboratory test) to predict most important longterm outcomes in patients with RA, such as functional and work disability, costs, joint replacement surgery, and premature mortality<sup>16,20</sup>. A visual analog scale to assess pain is as effective as a 2-page Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index to distinguish active from placebo treatment in osteoarthritis<sup>21</sup>. A visual analog scale to assess fatigue is as effective as a 2-page fatigue questionnaire to detect changes over time<sup>22</sup>.

In many situations, we do not need questionnaires to inform clinical decisions — just as we often do not need joint counts, erythrocyte sedimentation rate (ESR), or C-reactive protein at many visits. But in some instances patient

questionnaire scores illuminate in a few seconds degrees of functional loss, pain or psychological issues, or improvement or worsening, which are not apparent in the simple clinical interview, particularly when accompanied by a flow sheet of serial scores. A patient's level of pain, physical function, and global status at a given time, or as these problems may change over time, cannot be documented quantitatively from a careful history, physical examination, laboratory test, or radiograph, but only from a patient questionnaire.

Predicting which patient will provide important unexpected patient questionnaire information in standard rheumatology care is not possible. Patients almost always have 5–10 minutes to complete a questionnaire while waiting to see the physician, but are (appropriately) anxious to leave the clinical setting when the visit is complete. Therefore, asking each patient to complete a simple questionnaire at each visit, similar to checking weight or blood pressure in each patient at each visit, provides the most thorough care and is logically the most feasible procedure.

Progress in medical care requires quantitative measurement to assess clinical status and document improvements over time in conditions ranging from hypertension to hypercholesterolemia. Initially, complex measurements are developed in clinical research settings, which are then simplified for pragmatic use in clinical care. All rheumatologists recognize differences between ultracentrifugation and mass spectroscopy in a research laboratory to assess autoantibodies and inflammation versus a rheumatoid factor kit or simple ESR for standard care. However, many rheumatologists do not recognize substantial differences between patient questionnaires for clinical research versus those for clinical care. Therefore, most quantitative rheumatology assessment in the medical literature involves thorough measurement in a small fraction of patients who are enrolled in clinical trials, rather than pragmatic measurement in the vast majority of patients seen in standard clinical care. This situation is consistent neither with medicine as a quantitative "scientific" endeavor nor with optimal patient assessment and care.

In standard care, simple patient questionnaires are more than adequate and provide permanent medical and medicolegal documentation of patient status at a given time. If such a questionnaire is not included in a visit, an irreplaceable opportunity is lost for the patient and the rheumatologist. Even if small amounts of incremental data might be missed in use of pragmatic office questionnaires rather than extensive research questionnaires, we answer our question in the title by suggesting that it is better to have 80% of the information in 100% of patients than 100% of the information in 5% of the patients. Simple clinical patient questionnaires save time and make us better physicians.

### THEODORE PINCUS, MD,

Division of Rheumatology and Immunology,  
Vanderbilt University School of Medicine,  
203 Oxford House, Box 5,

Nashville, Tennessee 37232-4500;

### FREDERICK WOLFE, MD,

National Data Bank for Rheumatic Diseases,  
Wichita, Kansas, USA.

*Address reprint requests to Dr. Pincus, E-mail: t.pincus@vanderbilt.edu*

### REFERENCES

- Strand V, Tugwell P, Bombardier C, et al. Function and health-related quality of life: Results from a randomized controlled trial of leflunomide versus methotrexate or placebo in patients with active rheumatoid arthritis. *Arthritis Rheum* 1999;42:1870-8.
- Tugwell P, Wells G, Strand V, et al. Clinical improvement as reflected in measures of function and health-related quality of life following treatment with leflunomide compared with methotrexate in patients with rheumatoid arthritis: Sensitivity and relative efficiency to detect a treatment effect in a twelve-month, placebo-controlled trial. *Leflunomide Rheumatoid Arthritis Investigators Group. Arthritis Rheum* 2000;43:506-14.
- Cohen S, Cannon GW, Schiff M, et al. Two-year, blinded, randomized, controlled trial of treatment of active rheumatoid arthritis with leflunomide compared with methotrexate. Utilization of leflunomide in the Treatment of Rheumatoid Arthritis Trial Investigators Group. *Arthritis Rheum* 2001;44:1984-92.
- Strand V, Cohen S, Crawford B, Smolen JS, Scott DL. Patient-reported outcomes better discriminate active treatment from placebo in randomized controlled trials in rheumatoid arthritis. *Rheumatology Oxford* 2004;43:640-7.
- Strand V, Cohen S, Schiff M, et al. Treatment of active rheumatoid arthritis with leflunomide compared with placebo and methotrexate. *Arch Intern Med* 1999;159:2542-50.
- Smolen JS, Kalden JR, Scott DL, et al. Efficacy and safety of leflunomide compared with placebo and sulphasalazine in active rheumatoid arthritis: A double-blind, randomised, multicentre trial. *Lancet* 1999;353:259-66.
- Emery P, Breedveld FC, Lemmel EM, et al. A comparison of the efficacy and safety of leflunomide and methotrexate for the treatment of rheumatoid arthritis. *Rheumatology Oxford* 2000;39:655-65.
- Pincus T, Strand V, Koch G, et al. An index of the three core data set patient questionnaire measures distinguishes efficacy of active treatment from that of placebo as effectively as the American College of Rheumatology 20% response criteria or the disease activity score in a rheumatoid arthritis clinical trial. *Arthritis Rheum* 2003;48:625-30.
- Pincus T, Amara I, Koch GG. Continuous indices of core data set measures in rheumatoid arthritis clinical trials: lower responses to placebo than seen with categorical American College of Rheumatology 20% responses (ACR 20). *Arthritis Rheum* 2005; (In press).
- Strand V, Scott DL, Emery P, et al. Physical function and health related quality of life: Analysis of 2-year data from randomized controlled studies of leflunomide, sulfasalazine, or methotrexate in patients with active rheumatoid arthritis. *J Rheumatol* 2005; 32:590-601.
- Buchbinder R, Bombardier C, Yeung M, Tugwell P. Which outcome measures should be used in rheumatoid arthritis clinical trials?: clinical and quality-of-life measures' responsiveness to treatment in a randomized controlled trial. *Arthritis Rheum* 1995;38:1568-80.
- Ware JE Jr. SF-36 health survey manual and interpretation guide. Lincoln, RI: QualityMetric, Inc.; 2000.
- Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137-45.
- Pincus T, Summey JA, Soraci SA Jr, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. *Arthritis Rheum* 1983;26:1346-53.
- Pincus T, Callahan LF, Sale WG, Brooks AL, Payne LE, Vaughn WK. Severe functional declines, work disability, and increased mortality in seventy-five rheumatoid arthritis patients studied over nine years. *Arthritis Rheum* 1984;27:864-72.
- 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.
- Wolfe F, Michaud K, Choi HK, Williams R. Annual and lifetime productivity costs and income losses in persons with rheumatoid arthritis [abstract]. *Arthritis Rheum* 2003;48 Suppl:S243.
- Pincus T, Swearingen C, Wolfe F. Toward a Multidimensional Health Assessment Questionnaire (MDHAQ): Assessment of advanced activities of daily living and psychological status in the patient friendly Health Assessment Questionnaire format. *Arthritis Rheum* 1999;42:2220-30.
- Wolfe F, Michaud K, Pincus T. Development and validation of the Health Assessment Questionnaire II: a revised version of the Health Assessment Questionnaire. *Arthritis Rheum* 2004;50:3296-305.
- Wolfe F, Pincus T. Listening to the patient: A practical guide to self-report questionnaires in clinical care. *Arthritis Rheum* 1999;42:1797-808.
- Pincus T, Koch G, Lei H. Patient preference for placebo, acetaminophen or celecoxib efficacy studies (PACES): two randomized placebo-controlled cross-over clinical trials in patients with osteoarthritis of the knee or hip. *Ann Rheum Dis* 2004; 63:931-9.
- Wolfe F, Michaud K, Pincus T. Fatigue, rheumatoid arthritis, and anti-tumor necrosis factor therapy: an investigation in 24,831 patients. *J Rheumatol* 2004;31:2115-20.