The determination and measurement of functional disability in rheumatoid arthritis

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Received: 10 December 2001
Revisions requested: 18 December 2001
Revisions received: 13 February 2002
Accepted: 15 February 2002
Published: 8 April 2002

Arthritis Res 2002, **4 (suppl 2)**:S11-S15

(Print ISSN 1465-9905; Online ISSN 1465-9913)

Abstract

Although functional outcome is frequently discussed and written about, it is often not clear what functional outcome is and how it can be measured. This paper introduces the concept of latent and observed measures of functional disability, and distinguishes between disability as a process measure and disability as an outcome measure. Using the Health Assessment Questionnaire as the main functional outcome measure in rheumatoid arthritis, we propose and discuss several methods for determining disability, and describe the implications of altering the disability course.

Keywords: disability, functional disability, Health Assessment Questionnaire, outcome, rheumatoid arthritis

Outcomes in rheumatoid arthritis (RA) are the result of disease activity operating over time (Table 1). In general, the higher the level of disease activity, the more rapidly the adverse outcomes will occur and, often, the more severe the outcomes will be. All disease-modifying antirheumatic drug therapy has as its goal the reduction or elimination of disease activity and, consequently, the reduction or elimination of adverse outcomes.

Outcomes are discrete or binary events. Work disability is such an event, as is reaching a certain level of Health Assessment Questionnaire (HAQ) [1,2] impairment or having an average HAQ score of 2 for a period of 1 year. Although events are binary (0 or 1), they can be thought of as part of an underlying, unobserved continuum. For example, a patient can be increasingly work impaired until the point when the patient can no longer work and becomes work-disabled. At that point, the outcome changes from 0 to 1.

Outcomes are also events that are associated with and defined by duration of illness. For example, the proportion of patients work-disabled at 10 years is a meaningful description, but the proportion of patients work-disabled without a duration designator is meaningless and cannot be interpreted. In addition to requiring time as part of the definition of outcome, outcome implies a sense of permanency. Outcomes are irreversible (mortality, joint replacement) or are at least very difficult to reverse (work disability). For functional disability to truly be an outcome measure, it must be present for a sustained period at a defined level.

Outcomes can be further separated as to whether they are disease outcomes or patient outcomes. Although these groupings may overlap, patient outcomes refer to those outcomes that have meaning to the patient. For example, the level of functional disability or the ability to work are important patient outcomes, but the number of erosions or the level of interleukin-6 are not.

AUC = area under the curve; HAQ = Health Assessment Questionnaire; RA = rheumatoid arthritis.

Table 1

Functional outcome in rheumatoid arthritis

Is a dichotomous or binary event that can be thought of as representing an underlying continuum
Is defined by a time variable
Is both a patient outcome and a disease outcome
May be defined by an observed or latent variable
Can be identified using area under the curve methods
Can be identified using the sustained level method

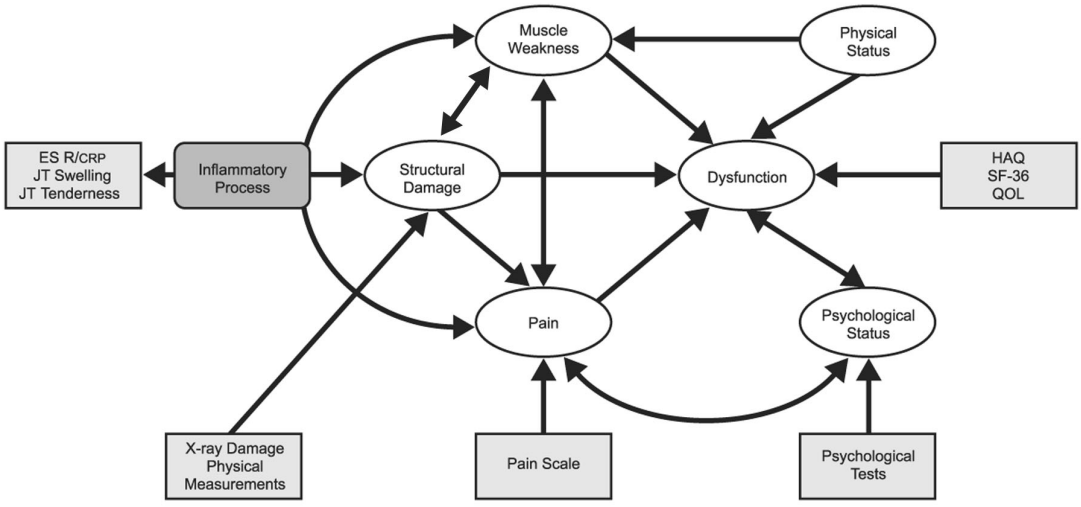
Outcomes, like variables, can be observed or latent. An observed variable can be measured directly, such as age, sex, or HAQ score. An observed outcome refers to events like work disability, death, the number of erosions, or the level of HAQ disability. Variables can also be unobserved or latent, in which case they represent the underlying construct or continuum that was mentioned earlier.

Latent (unobserved) variables cannot be directly measured. An example of a latent variable is happiness. Examples of latent outcomes in rheumatology are structural damage and disablement. Although we can measure aspects of structural damage (e.g. the presence of erosions), we cannot measure the full spectrum of structural damage because it includes abnormalities to tendons, ligaments, and muscles throughout the body. Similarly, disablement or disability refers to the full range of human activities. Latent variables are important because they are what we really want to understand but can only approach approximately with observed variables like erosion scores or HAQ scores. Figure 1, a model of disease activity and outcome, illustrates these issues. Observed variables are enclosed in rectangles, and latent variables in rounded rectangles or ovals. In this illustration, dysfunction stands for the unobserved outcome of functional status.

In many instances in rheumatology, we are forced to accept the variables we can observe rather than the underlying concepts we wish to measure. We do not have good measures for the latent variable functional ability, so we are forced to accept surrogates like HAQ score or functional scores from the Medical Outcomes Study Short Form 36 [3,4] or Arthritis Impact Measurement Scales [5]. When we accept surrogates, we introduce substantial error because these measures are only approximate measures of function or disability. The HAQ, for example, can be quite abnormal in individuals with little apparent functional loss, and can be normal in individuals with substantial and obvious dysfunction [2]. Because of the problems in ascertaining a latent outcome, researchers often preferentially measure observed outcomes such as work disability [6–10], joint replacement surgery [11], income [12], or death [13–16]. Yet these outcomes also have their problems because they often take too long to occur, because they may not apply to all patients, and because they do not touch on the day-to-day substance of RA.

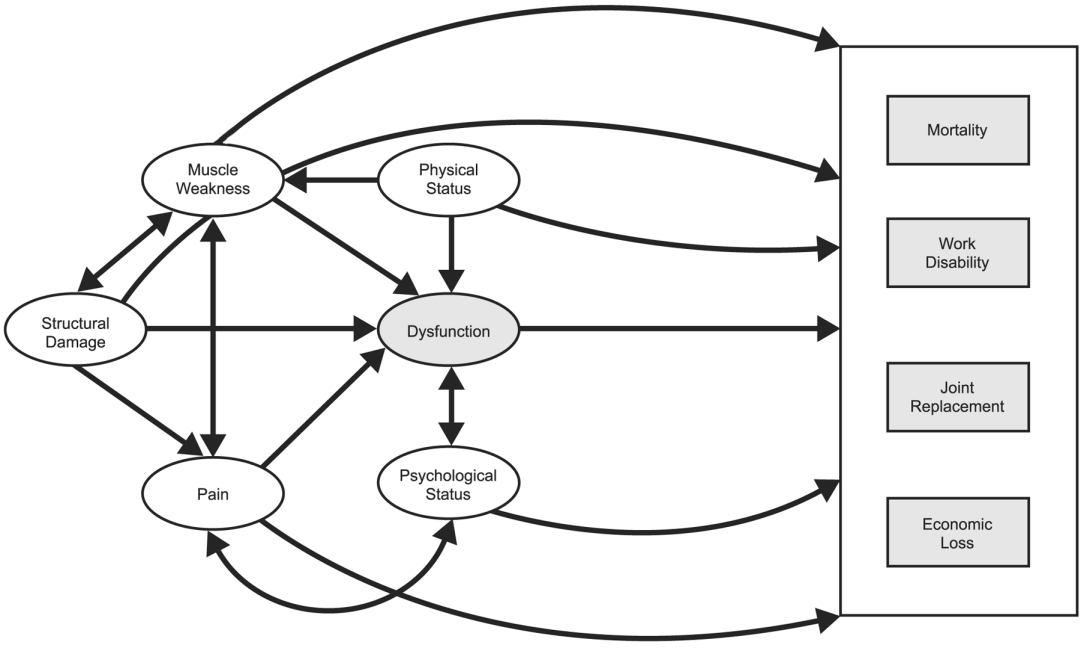
Another very common approach to outcome measurement is to use observed variables as surrogates. For functional disability, the central outcome in RA, the HAQ becomes

Figure 1



A partial causal model of disease activity and outcome in rheumatoid arthritis. Rectangles represent observed variables, and ovals and rounded rectangles represent latent (unobserved) variables. ESR/CRP, erythrocyte sedimentation rate/C-reactive protein; HAQ, Health Assessment Questionnaire; SF-36, Medical Outcomes Study Short Form 36; QOL, quality of life; JT, joint.

Figure 2



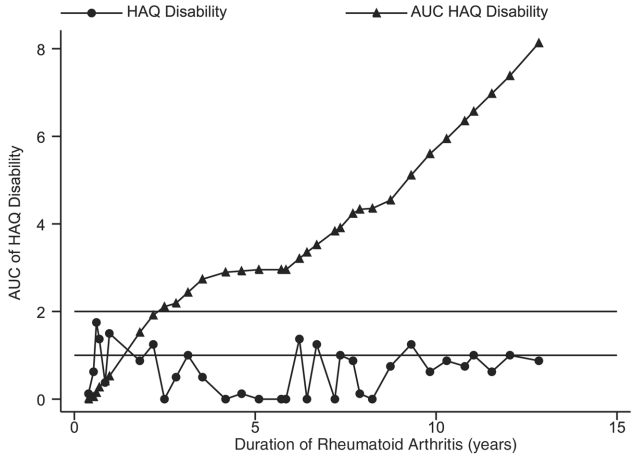
A partial causal model of disease activity and outcome in rheumatoid arthritis that includes well-defined outcomes. Rectangles represent well-defined outcomes, and ovals represent latent (unobserved) variables. The figure demonstrates the multivariate nature of outcome and the central role of disability in rheumatoid arthritis.

the key functional surrogate variable. Although we have spoken of the HAQ as the central outcome variable in RA, it is really a dual-purpose variable, one purpose representing the short-term result of the inflammatory process of the illness, as shown in Figure 1. Its usefulness in clinical trials occurs because of its primary role as a measure of the inflammatory process. It is not surprising, then, that its second purpose can be a predictor of outcome (Fig. 2). In fact, of all clinical variables, the HAQ is the best predictor of outcomes such as mortality, work disability, joint replacement, and economic loss.

For the HAQ to be considered as an outcome measure rather than a process measure, it must be representative of sustained impairment. But it is not easy to ascertain sustained impairment. Sustained impairment implies regular longitudinal observation, the first problem. A second problem is that HAQ values are not well conditioned and smooth, but tend to jump around. This has been the subject of a number of recent papers [2,17,18], and is illustrated in Figures 3 and 4 (inset), where HAQ values may vary significantly from observation to observation.

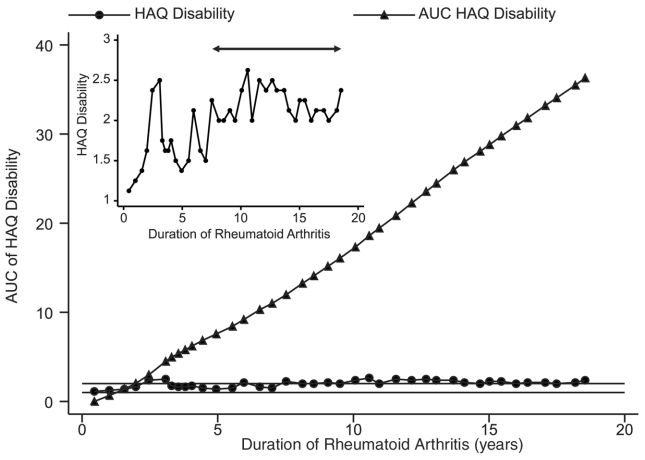
A number of approaches may be used to better define HAQ scores, including smoothing and summarizing or condensing. One method to better define HAQ scores involves measuring the area under the curve (AUC) of HAQ scores (long diagonal line of Figs 3 and 4). Notice that the irregularity of the HAQ scores (bottom of Fig. 3 and inset of Fig. 4) is removed by the AUC measurement.

Figure 3



The course of a single RA patient over 13 years of illness. Circles represent HAQ scores. Note the wide-ranging variability of the HAQ scores. Although it is difficult to give meaning to these HAQ scores or analyze them, the AUC (triangles) provides smoothing that allows further analysis. The AUC represents the total burden of RA over time, and can be used to define functional disability as an outcome. See text for details. RA, rheumatoid arthritis; HAQ, Health Assessment Questionnaire; AUC, area under the curve.

Figure 4



The course of a single RA patient over the first 19 years of illness. Circles represent HAQ scores. For increased visibility, the insert provides HAQ scores on the appropriate scale. Note the wide-ranging variability of the HAQ scores. The AUC (triangles) provides smoothing that allows further analysis. The AUC represents the total burden of RA over time, and can be used to define functional disability as an outcome. The bi-directional arrow in the insert provides another method to define functional disability: a sustained level of disability over a defined time period. In this illustration disability is defined as an HAQ score of 2 or greater over a period of at least 2 years. See text for details. RA, rheumatoid arthritis; HAQ, Health Assessment Questionnaire; AUC, area under the curve.

The AUC is a measurement of the sustained burden of functional loss on the individual. To use it as an outcome measure, a cut-off value must be chosen. For example, we might decide that a patient with 10 AUC units in 10 years or 8 AUC units in 7 years has sustained clinically important functional impairment.

One limitation of this method occurs when we are dealing with left censored data, as is often the case in rheumatology. In such an instance, we may choose to use as our measuring period (time variable) the time the patient is under our observation. We can alternatively choose to impute the AUC values before the patient came under our observation, perhaps using the average observed HAQ score. To do this, however, introduces additional error that may or may not be acceptable depending on the uses of the data.

Another method of determining outcome with the HAQ is to require that a certain value of the HAQ be sustained for a defined time period. In Figure 4 (inset), the horizontal bidirectional arrow indicates a sustained period of HAQ disability defined by a value of at least 2 for at least 2 years.

The investigator frequently does not have longitudinal data. Is it correct to take a single value or a few values and infer that they represent HAQ outcome? Given the variability of the HAQ scores in Figures 3 and 4, using a single measure will lead to an imprecise and inefficient measure of outcome. Additionally, it confounds the separate definitions of process and outcome measures.

Inferences about functional disability

All recent disease-modifying antirheumatic drugs have been shown to reduce HAQ disability over the duration of their clinical trials [19–23]. Is it reasonable to infer outcome differences based on shorter term results and results that come from clinical trials, knowing that clinical trials may not be representative of actual results in the community? The best that can be said is that it is a starting point, perhaps an indication of what we might expect to see if drugs actually worked as well in practice as they do in randomized clinical trials.

Using data from Figure 4, if the HAQ score was reduced by 0.25 units (an amount of reduction shown in most recent trials), then the total AUC of disability would be reduced from 36.28 disability years to 31.76 disability years, a reduction of 4.52 disability years. Using our definition of a HAQ score of 2 or greater for at least 2 years, disability would be postponed in this patient by 4.62 years. Small changes in HAQ levels can thus translate into important, clinically meaningful changes in outcome if all of the assumptions noted in the present paper hold.

The importance of longitudinal studies is that they provide the validation or refutation of the extrapolation of clinical results to the full population of RA patients in the community.

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