Preliminary Core Set of Domains and Reporting Requirements for Longitudinal Observational Studies in Rheumatology

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ABSTRACT. Observational and longitudinal observational studies (LOS) provide essential information about the course and outcome of rheumatic disorders that cannot be provided by randomized controlled trials, and they constitute the major clinical scientific communication in rheumatology. There has been no consensus as to the full and appropriate content of LOS. This report defines a core set of domains and reporting requirements for LOS. At the 1998 OMERACT IV Conference a consensus process evaluated the literature of rheumatology in light of the constructs, variables, and outcomes of rheumatology by using introductory lectures, nominal groups, and plenary sessions. The result of this process was to identify 5 "core" domains that should be included in every LOS: Health Status, Disease Process, Damage, Mortality, and Toxicity/Adverse Reactions. Two additional domains, Work Disability and Costs, were recognized as important, but need not be used in all LOS. Eleven subdomains were identified that divided the domains into convenient clinical and conceptual units. A set of reporting requirements was also determined. The core recommendations, which follow on the WHO ICIDH-2 outline, are not disease-specific; the substitution of different "disease process" and "damage" measures make them suitable for many rheumatic disorders. The core set is intended to serve as a core for LOS in almost all rheumatic conditions. (J Rheumatol 1999;26:484–9)

Key Indexing Terms:
OMERACT RHEUMATIC DISEASES LONGITUDINAL AND OBSERVATIONAL STUDIES

Longitudinal and observational studies (LOS) provide essential information about the course and outcome of rheumatic diseases that cannot be provided by randomized controlled trials, including addressing multiple outcomes over longer terms, and with broader based recruitment. Included in the information that may be provided by these studies are effects of treatment, sociodemographic factors, disease severity, and psychological factors on outcomes such as mortality, function and functional disability, symptoms, radiographic abnormality, joint surgery, costs, and toxicity. LOS studies constitute the major clinical scientific communication in rheumatology. In 1997, more than 95% of reports published in *Arthritis and Rheumatism* and *The Journal of Rheumatology* were in the form of observational or longitudinal observational studies.

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THE PROCESS

Prior to OMERACT IV an expert international committee with a strong publication record of longitudinal studies prepared a list of core variables thought to be useful for (1) short term and (2) longterm observational studies. In addition, essential demographic and covariates were enumerated. The recommendations were discussed and then categorized by the group as "core," "potentially important," and demographic and covariate variables. These items were presented to the conference in the form of lectures. Following the introductory plenary sessions, small groups were formed whose task it was to discuss and make recommendations as to LOS variables. Two groups considered shorter term LOS (< 2 years) and two groups discussed longterm studies (> 2 years).

The committee also acted to develop a set of recommen-

dations regarding study development and reporting. Because there was little disagreement in this area, the committee presented recommendations at the OMERACT Conference primarily through the presentation of Alan Silman and secondarily through presentations by Frederick Wolfe and Marissa Lassere. After this two groups were formed to discuss and recommend study design and reporting elements. The recommendations of Dr. Silman and Deborah Symmons, as presented elsewhere in these proceedings[1], were accepted without substantial modification. Details of these recommendations will be found in this article. Table 3 summarizes the recommendations.

As to core variables, there was initially considerable disagreement among groups. There were two main sources of disagreement. The first was whether it was appropriate to recommend what was a very large set of outcome and process measures. Some felt that it was necessary to do this, while others felt all variables were not appropriate for all studies. The second area of disagreement concerned the inclusion of specific variables that were endorsed by some groups and opposed by others.

These disputes were resolved in a conference committee, and later endorsed with slight modification by a plenary session. The adopted recommendations recognized that there was broad agreement as to domains, with somewhat less agreement as to specific items within the domains. The final recommendations, which addressed all of these issues, were congruent with the World Health Organization (WHO) International Classification of Impairments, Activities and Participation (ICIDH-2)[2].

There was little disagreement regarding study design and reporting, and no substantial changes in the group recommendations were made at the plenary session.

THE CONSENSUS

I. Core Domains for Longitudinal Observational Studies

Seven domains for LOS were identified (Table 1). Of these, 5 domains are considered as "core domains," or domains that should be included in every LOS: Health Status, Disease Process, Damage, Mortality, and Toxicity/Adverse Reactions. Two additional domains, Work Disability and Costs, were recognized as important, but it was not considered necessary that they be included in every LOS. The domains include items that may measure outcome as well as process, depending upon the study or illness. Table 1 includes a classification as to whether an item functions as an outcome, a predictor, or both.

The core recommendations are not disease-specific, for with the substitution of different "disease process" and "damage" measures these same core recommendations are suitable for osteoarthritis (OA) and other rheumatic disorders. For example, in OA a different set of imaging studies is required, and extraarticular manifestations and acute phase reactants are not used. In fibromyalgia, where there are no currently identifiable disease process measures or damage measures, these domains would not be assessed. In other inflammatory disorders (for example, psoriatic arthritis) deletion of items such as extraarticular measures would allow the core set to be used almost without further recommendations.

This core set, then, is intended to serve as a core for LOS in almost all rheumatic conditions.

Subdomains and Variables

Subdomains divide the domains into convenient clinical or conceptual units. Within each subdomain there maybe a number of instruments (e.g., Arthritis Impact Measurement Scales, AIMS) or individual variables (e.g., a visual analog pain scale, VAS) that can assess the subdomain. Examples of instruments and variables are listed in Table 1. At OMERACT IV no recommendations were made concerning specific instruments. The specific instruments and examples in Table 1 are included to illustrate what type of instruments could be used, without giving a complete list of all possible instruments.

Health status. The domain of health status is divided into 3 specific, and one general, encompassing subdomains. The specific subdomains include symptoms, physical function, and psychosocial function. Instruments chosen to assess the subdomain can be simple (e.g., VAS) or complex (e.g., the McGill Pain Questionnaire or a multidimensional fatigue scale). Overall health status may be measured by more comprehensive health status instruments and quality of life scales. Some of these scales may be generic [suitable for use across many illnesses (e.g., Medical Outcome Survey Short Form 36) or disease-specific (e.g., Arthritis Impact Measurement Scale, Rheumatoid Arthritis Quality of Life Scale, RAQOL)]. A number of the health status instruments and quality of life scales also assess the subdomains of symptoms, physical function, and psychosocial function. Disease-specific instruments appear to be more discriminative and sensitive to change than generic instruments. In general, LOS involving any rheumatic disease should include assessments within these subdomains, either by specific instruments or through the use of the more general health status instruments.

Disease process. Table 1 lists those items and subdomains that are most appropriate for rheumatoid arthritis (RA). With suitable changes in subdomains, the disease process domain can be appropriate for other inflammatory disorders, osteoarthritis (OA), and illnesses such as fibromyalgia. Table 1 is given as an example for RA, but should be modified for use in other disorders as long as all disease process measures are assessed.

The global subdomain may measure patient and/or physician estimates of disease "activity" and/or "severity." Activity means "inflammatory" activity, while severity reflects other aspects of the illness, including distress and

Table 1. Core domains and subdomains in longitudinal observational studies.

Domain	Type	Examples†
Health Status*		
Quality of life (QOL)/Health status instruments (HSI)	O	HUI, NHP, WHO-QOL RA-QOL/SF-36, AIMS, HLI, CLINHAQ, et.
Symptoms	O, PC	VAS and multidimensional pain fatigue and sleep scales, etc.
Physical function	O, PC	HAQ, MHAQ, FSI, etc.
Psychosocial function	O, PC	Affect, socialization, social support, etc.
Disease process		
Joint tenderness/swelling	O, PC	Short and long swelling and tenderness scales, Ritchie and modified Ritchie index, self-report joint examination scales
Global	O, PC	VAS scales; patient's severity and/or activity; physician's activity, and/or severity
Acute phase reactants	O, PC	CRP, ESR
Damage		
Radiographic or imaging	O, PC	Sharp, Larsen, Kellgren & Lawrence, etc.
Deformity	O	Radiographic or by physical examination
Surgery	O	Total joint replacement, other arthropathies
Organ damage	O, PC	Extraarticular manifestations of RA: nodules, iritis, vasculitis, etc., pulmonary, renal damage, etec.
Toxicity/adverse reactions*	O	Drug toxicity, adverse reactions to medical and surgical interventions
Mortality*	O	Number and causes of death
Work disability	O	Work disability, sick leave, days lost from work
Costs	O	Ulitization, direct and indirect costs, charges

*A core domain. O: outcome; PC: predictor or covariate. Depending on the purpose of the study, these variables may be measured once or many times, but are usually measured multiple times.
†These examples are provided for clarification only. OMERACT IV did not recommend any specific instruments in view of the limited data available on their use in LOS.
HUI: Health Utilities Index; NHP: Nottingham Health Profile; WHOQOL: World Health Organization Quality of Life; HLI: Health and Lifestyle Index; VAS: visual analog scale; CLINHAQ: Clinical Health Assessment Questionnaire; SF-36: Medical Outcome Survey Short Form 36; FSI: Functional Status Index; CRP: C-reactive protein; AIMS: Arthritis Impact Measurement Scale; ESR: erythrocyte sedimentation rate.

illness consequences. Severity shares concepts with health status, above, and damage, below, but appears to fit best in the disease process domain.

Damage. Damage refers to physical and physiological consequences of disease. Different rheumatic diseases will have different damage abnormalities, and the seriousness of the abnormalities will differ among diseases as well.

Toxicity and adverse reactions. Toxicity and adverse reactions are non-disease-specific. They refer to consequences of interventions rather than to consequences of disease. Disease consequences can be categorized under organ damage, above.

Mortality. Many rheumatic diseases are associated with increased mortality even if the mortality does not appear to be a direct result of the rheumatic disease. Therefore LOS studies should record deaths and causes of death.

Work disability. Work disability was recognized as an important outcome domain in rheumatic disorders, but it was not felt that it must be recorded in every study. Work disability and its methods of measurement vary significantly among countries and social systems.

Costs. As with work disability, costs were not recognized as a requirement for all LOS. Costs and the distribution of costs will vary according to country and social system. Utilization of services (including drug use) also assesses costs of rheumatic conditions.

Demographic and Covariate Variables

Table 2 lists demographic and covariate variables that are important to collect since they may influence and/or modify the outcomes and predictors of LOS. Items listed with an asterisk should be collected in all studies. Those without an

asterisk should be used dependent on the disease under study and the aim and possibilities of the study. All items in the Table are covariates or predictor variables, but income can also be an outcome variable.

SPECIAL ISSUES

LOS Variables and Domains

The development of a core set of domains for rheumatic disorders implies that there is a common set of important outcomes that are germane to all patients, and that longitudinal studies of rheumatic illnesses should address those outcomes. These domains are not just those that are restricted to "medical" outcomes, but also include outcomes related to social and psychological factors. Although OMERACT IV did not recommend the collection of work disability and costs as outcomes to be collected for all studies, the group recognized and recommended the importance of such outcomes. Where possible, those outcomes should be a part of LOS.

Studies should be differentiated from reports. A study may address all of the outcomes we have suggested, but report separately on individual or groups of outcomes. Even so, the nature of studies will differ. For example, questionnaire surveys will not ordinarily address joint examination or radiographic examination, and some narrowly focused studies of damage may not address toxicity. The OMERACT recommendations recognize these differences, and we do not mean to imply that such studies are inappropriate or too narrowly drawn. Instead, the OMERACT IV recommendations indicate that, where possible, the OMERACT core set of domains be considered in the planning of future studies. The longer the study the more important it is to include the suggested domains.

OMERACT IV did not recommend specific assessment instruments. Although much is known about instruments used in controlled trials in terms of the OMERACT filter of truth, discrimination, and feasibility[3], there is limited information when instruments are used in LOS. Validity (or truth) may be surmised from shorter term studies, and feasibility can also be determined, but the comparative discriminatory ability and efficiency of instruments has not been clearly elucidated in LOS. While one instrument might be better than another, issues of feasibility, national and language differences, and differences in study purposes suggest that many instruments are acceptable. The selection of specific instruments for LOS should be the subject of another OMERACT Conference.

Although Table 1 lists variable examples, not all such outcome variables may be appropriate to the study at hand, and the role of psychosocial variables and variables such as fatigue and sleep disturbance is not fully established. These concerns extend to some of the covariates in Table 2. Body mass index, for example, has a problematic role in some studies, but may be useful in OA studies. The committee recommended that rheumatoid factor and HLA/DNA be collected in all RA LOS, but recognized that this was not appropriate for studies of OA, for example.

Many variables and subdomains cited in Table 1 as

Table 2. Core and potentially important variables: demographics, covariate, and predictors.

Variable	Requirement	Measurement Time
Age	*	O
Sex	*	O
Education	*	O
Ethnicity	*	O
Disease duratin	*	O
Comorbidity	*	O
Arthritis & non-arthritis treatment	*	O, M
Occupation	*	O, M
Referral setting	*	O
Social status	*	O
HLA/DNA		O
Rheumatoid factor		O, (M)
Smoking status		O
Marital status		O, (M)
Body mass index		O, M
Pregnancies		O, (M)
Oral contraceptive/hormonal status		O, M
Income		O, M
Access to and/or financing of health care		O
Family history		O, (M)

*A core variable suggested for all studies. Items with no asterisk should be collected dependent on the disease under study and the study aim and possibilities.
O: measure once; M: measure many times; (M): can be measured many times but is usually measured just once.

outcomes can also function as predictors and covariates. For example, functional disability is predictive of work disability and mortality, but also is an outcome on its own. This overlap extends the usefulness of variables like fatigue. Although it may not be a clearly useful outcome, fatigue can be an important predictor of service utilization or work disability. With increasing use of variables like these in LOS, a better understanding of their role will be gained. Investigators and clinicians who use these variables in LOS should understand when they will be used as outcomes and when they will be predictors or covariates. Covariates, whether defined in Table 1 or Table 2, have a particularly important role in LOS because they influence outcomes strongly, and it is very important that covariates be collected.

II. Study Design and Reporting

Poor study design and inadequate reporting lead to uninterpretable studies and uninterpretable results. OMERACT IV reached universal consensus about the need to improve design and reporting. The following guidelines regarding reporting of LOS were adopted. Table 3 presents an abbre-

Table 3. OMERACT IV recommendations for reporting of longitudinal observational studies.

Item	Information to be specified
Study, rationale	State research question and importance
Study design	Prospective, retrospective or mixed
Sources of and selection of cases	True population-based, catchment population or consecutive series. Describe calender time, geographic, referral and access factors. Case control studies: method of case and control identification and selection
Timing of recruitment	Describe timing of recruitment in relation to disease onset: cases followed from disease onset, cases followed from first presentation, or prevalent cases
Inclusion criteria	Describe minimal criteria and when criteria were satisfied?
Assessment measures	Provide data on reliability and validity of instruments and study assessments
Assessment methods	Describe principal and subsidiary outcome measures. Indicate means of followup data collection (clinical examination, clinic interview, questionnaire, mail or telephone). Report number of observers, nature of training, observer variability and blindness
Baseline clinical data collected	Specify data collected at baseline. Distinguish between items ascertained from routine medical records and those collected prospectively using a standard proforma
Description of demographic and baseline characteristics	Describe demographic and baseline characteristics of participants
Followup data collection	Specify frequency of followup, decision rules about timing of assessments. Full description of missing patients at each stage of followup. Indicate means of followup data collection (clinical interview, questionnaire, mail or telephone)
Analyses	Describe missing data and missing subjects. Specify strategies used to limit missing data, and to analyze missing data and loss to follow-up. Indicate the power to detect clinically meaningful change. If a statistical model is generated, indicate performance in a validation sample. Describe key model assumptions. Where appropriate, perform sensitivity analyses to account for loss to followup. Utilize appropriate time dependent variable based analyses and survey methods. Describe rationale for statistical methodology
Biases and potential problems	Identify and discuss possible sources of bias and misinterpretation

viated outline of the recommendations. Full details on the recommendations can be found elsewhere in these proceedings[1].

Summary. The OMERACT IV conference identified 5 domains that are to be considered as "core" domains, or domains that should be included in every LOS: Health Status, Disease Process, Damage, Mortality, and Toxicity/Adverse Reactions. Two additional domains, Work Disability and Costs, were recognized as important, but it was not considered necessary that they be used in all LOS. Eleven subdomains were identified that divided the domains into convenient clinical and conceptual units. We also identified a set of reporting requirements whose use should improve the quality and generalizability of LOS. The core recommendations, which follow on the WHO ICIDH-2 outline, are not disease-specific. With the substitution of different disease process and damage measures, these core recommendations are suitable for RA, OA, fibromyalgia, and other rheumatic disorders. Thus the set is intended to serve as a core for LOS in almost all rheumatic conditions.

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