

Development of a Matrix of Cost Domains in Economic Evaluation of Rheumatoid Arthritis

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ABSTRACT. The aim of our study was to comprehensively review and critically appraise the cost domains used in economic evaluations of the rheumatic diseases and to use this information to propose standardization of cost domains. The literature search identified 210 abstracts, 32 of which included original cost data. The listed cost categories were grouped into 3 major areas: (direct) health care costs, other (direct) disease related costs, and productivity costs (indirect costs). The number of individual cost categories was reduced by considering the following criteria: (1) inclusion of all relevant cost domains; (2) avoidance of double counting; (3) summarizing of related categories under one representative heading; (4) feasibility of level of aggregation. After adjustment for synonymous labeling, 38 cost categories remained. The subsequent development of a classification scheme of cost categories led to a set of 19 separate cost domains including 7 outpatient, 3 inpatient, 6 other disease related, and 3 productivity cost domains. This literature review indicates that cost assessment in economic evaluations in rheumatoid arthritis lacks standardization. A preliminary scheme to categorize cost assessment in rheumatic conditions is presented. The adoption of standards for economic evaluation would greatly facilitate national and international comparisons. (*J Rheumatol* 2001;28:657–61)

Key Indexing Terms:

COST ECONOMIC EVALUATION STANDARDIZATION RHEUMATOID ARTHRITIS

BACKGROUND

Economic evaluations of health care interventions in the field of rheumatology are now performed more frequently, and inclusion of cost assessment instruments is becoming routine in newly planned studies. Usually, costs are broadly classified into 2 categories: direct and indirect costs. Beyond this there is little agreement on what to call various cost domains, what costs should or should not be required, how to best get at cost information, and the optimal level of detail.

We conducted a review of the current literature on economic evaluations of health care interventions aimed at rheumatoid arthritis (RA), to describe and classify the types of costs that were measured in the various studies. The objectives were (1) to identify and summarize the applied cost categories in economic evaluations in rheumatic conditions and (2) to develop a matrix of cost domains that can be used as a preliminary categorization scheme.

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METHODS

A set of 3 approaches was applied: (1) literature search identifying economic evaluations in rheumatoid arthritis; (2) listing of cost categories mentioned in the identified articles; (3) development of a matrix of cost domains that can be used as a preliminary categorization scheme.

To identify economic articles in rheumatic conditions a MEDLINE search covering the years January 1966 to November 1999 was conducted. A combination of the medical subject heading (MeSH) terms “rheumatoid arthritis” and “costs” and “cost analysis” was applied. Appropriate text words were employed to broaden the search (cost, costs, health care, direct, indirect). All retrieved abstracts were screened for the use of original cost data; those that did not provide originally collected cost data were excluded. Full length articles of the remaining abstracts were obtained and assessed with regard to the types of cost categories used. All identified categories were included in a comprehensive list.

Subsequently, a classification scheme was developed. As a starting point the identified cost categories were adjusted for non-homogeneous labeling. Therefore the various cost components mentioned in the reviewed articles carrying different labels but including similar contents were summarized into one cost category (e.g., travel expenses and transportation expenses were labeled transportation). In a next step the remaining categories were grouped into 3 major areas as suggested by Luce, *et al*¹: (direct) health care costs, other (direct) disease related costs, and productivity costs

(indirect costs). Finally the number of individual cost categories was reduced by considering the following criteria: (1) inclusion of all relevant cost domains; (2) avoidance of double counting; (3) summarizing of related categories under one representative heading; (4) feasibility of level of aggregation/disaggregation.

RESULTS

The MEDLINE search yielded 210 abstracts, 174 of which were excluded because they did not provide original cost data. Another 4 abstracts were excluded because they were lacking detailed cost information. Full length articles were obtained for the remaining 32 abstracts and were assessed for the costing methodology used and the types of cost categories included²⁻³³. The 32 studies were designed as cost-of-illness studies or cost comparisons (21 studies)²¹, cost-effectiveness analyses (7 studies)⁷, and cost-utility analyses (34 studies)³⁴.

The reviewed studies used a total of 51 cost categories, which, after adjustment for synonymous labeling, made up 38 cost categories (Table 1). All the studies considering health care costs included the domains inpatient and outpatient costs. The level of disaggregation into subcategories differed widely. While all the studies reported medication costs and costs for acute hospital facilities, the categories “emergency room visits” and “devices and aids” were only included in 4 and 7 studies, respectively. Other disease related cost components were assessed in 15 publications, most of them referring to expenses for transportation and home health care services. Productivity costs were taken into account by 14 references, considering costs due to loss of productivity in employed patients. Only 3 studies commented on the portion of out-of-pocket expenses.

The subsequent development of a classification scheme of cost categories led to a set of 19 separate cost domains (Table 2) including 7 outpatient, 3 inpatient, 6 other disease related, and 3 productivity cost domains. Out-of-pocket expenditure is listed as a distinct category since this domain might comprise parts of all other components.

DISCUSSION

The absence of valid taxonomies can in part be explained by the varying needs of those who consume the economic information; i.e., different cost information is needed for different perspectives (e.g., health care system, patient, society, etc.). Furthermore, taxonomies may depend on the costing methodology used. Gross-costing methods would lead to different taxonomies than micro-costing methods. However, the prevailing confusion definitely has repercussions on the comparability of findings from economic evaluations. In fact, there is and has been little guidance for researchers on how to comprehensively approach the measurement of costs.

Still, it is important to identify an optimal balance

Table 1. Listing of 38 identified cost categories after adjustment for synonymous labeling and number of studies that included the domains.

| Cost Categories | n = 32 |
|---|--------|
| Medication outpatient | 31 |
| Visits to physicians, outpatient | 26 |
| Outpatient surgery | 10 |
| Laboratory tests, outpatient | 17 |
| Diagnostic investigations, outpatient | 8 |
| Therapeutic measures, outpatient | 8 |
| Imaging, outpatient | 7 |
| Aids/devices | 7 |
| Non-acute hospital facilities | 15 |
| Nursing homes | 10 |
| Rehabilitation | 6 |
| Emergency room visits | 4 |
| Physiotherapy, outpatient | 8 |
| Occupational therapy, outpatient | 9 |
| Psychological therapy, outpatient | 2 |
| Visits of district nurse | 4 |
| Paramedical therapy | 3 |
| Visits to nonmedical practitioners | 6 |
| Acute hospital facilities | 31 |
| Medication, inpatient | 16 |
| Diagnostic investigations, inpatient | 15 |
| Therapeutic measures, inpatient | 15 |
| Laboratory tests, inpatient | 16 |
| Surgery, inpatient | 2 |
| Imaging, inpatient | 3 |
| Physician charges in hospital | 4 |
| Transportation | 13 |
| Home health care services | 10 |
| Lost wages | 4 |
| Home remodeling | 4 |
| Medical equipment | 4 |
| Loss of productivity due to sick leave | 14 |
| Loss of productivity due to work disability | 14 |
| Loss of productivity due to loss of work | 1 |
| Nursing family members | 1 |
| Impairments of activities of daily life | 4 |
| Impairments of housekeeping | 2 |
| Patient leisure time | 1 |

between this need for standardization in economic analysis research and the support of every investigator’s innovation. Basically, the development of the matrix of cost domains aims at providing a pool of distinct cost categories that contains components for different purposes of cost evaluation. One should be aware that assessment of all cost domains might lead to double counting depending on the perspective taken. For instance, in a societal analysis one would not count both lost productivity and lost wages to the patient, since gross earnings is often used to value the lost productivity.

As a framework for the development of the matrix of cost domains we used the discrimination between health care costs, non-health care costs, and productivity costs¹. Luce, *et al* divide direct costs into health care costs, non-health

Table 2. The matrix of 19 cost domains that can be used as a preliminary categorization scheme. Out-of-pocket expenditure comprises cost components listed under items 1–3. Detailed assessment given as portions of these components is proposed.

| Cost Domains | |
|--------------|---|
| 1. | Health care costs (direct) |
| 1.1 | Outpatient costs |
| 1.1.1 | Visits to physicians (specialists and other) |
| 1.1.2 | Outpatient surgery |
| 1.1.3 | Emergency room visits |
| 1.1.4 | Non-physician service utilization (physiotherapist, occupational therapist, social worker, psychological therapist) |
| 1.1.5 | Medication |
| 1.1.6 | Diagnostic/therapeutic procedures and tests (radiological examinations, laboratory tests) |
| 1.1.7 | Devices and aids |
| 1.2 | Inpatient costs |
| 1.2.1 | Acute hospital facilities (without surgery) |
| 1.2.2 | Acute hospital facilities (surgery) |
| 1.2.3 | Non-acute hospital facilities (rehabilitation, nursing homes) |
| 2. | Other disease related costs (direct) |
| 2.1 | Transportation |
| 2.2 | Home health care services |
| 2.3 | Home remodeling |
| 2.4 | Medical equipment (nonprescription) |
| 2.5 | Non-medical practitioner, alternative therapy |
| 2.6 | Patient time |
| 3. | Productivity costs |
| 3.1 | Loss of productivity in employed patients (sick leave, work disability) |
| 3.2 | Opportunity costs (loss of productivity due to time spent by nursing family members, disabilities leading to impaired housekeeping or activities of daily life) |
| 3.3 | Lost wages |

care costs, and patient and caregiver-time costs¹. They recommend avoiding the term indirect costs, but refer to productivity costs instead. Productivity costs are further divided into morbidity and mortality costs, both of which lead to changes in the quality of life and are fully accounted for in the measurement of such. In a similar manner Drummond, *et al* recommend avoidance of the terms direct, indirect, and intangible costs³⁴. Instead the authors recommend simply describing various cost categories without proposing a new taxonomy.

For the term “non-health care costs” the substitute “other disease related costs” was chosen, because some of the aggregated subcategories like “home health care” or “costs for home remodeling” do not fit this definition properly, since parts of these costs are borne by social insurances (e.g., Germany).

The cost category “out-of-pocket expenses” was mentioned in only 3 articles. Despite this, patient related costs seem to be of major importance from a societal viewpoint. Liang, *et al* found them to represent a substantial part (at least 20%) of direct costs²⁹. Therefore a separate assessment of the portion of out-of-pocket expenditure of the defined cost domains is proposed.

All studies assessing health care costs distinguished the

components inpatient and outpatient costs. Although inpatient costs may account for a major part of direct costs, they are very difficult to disaggregate. The estimation of inpatient costs strongly depends on the applied valuation (effect of different payment systems, inclusion or exclusion of fixed costs); consequently, further disaggregation might render data incomparable. Frequently cited was the number of treatment days in the various inpatient facilities (separation into acute facilities with and without surgery and non-acute facilities).

The loss of the patient’s time was assessed in only one study¹⁹. Since the loss of leisure time constitutes a real change in the use of a resource by the patient and society and can be considered a part of a therapeutic intervention itself, it was defined as a direct cost component¹.

Productivity costs were divided into the subgroups “loss of productivity” (in employed patients), “opportunity costs” (due to loss of productivity concerning activities of daily life or housekeeping), and “lost wages.” About half of the reviewed studies reported on productivity costs, mainly assessing loss of productivity by means of estimating the number of days off work due to RA. Since productivity costs account for a considerable portion of overall costs in RA⁶, further standardization is required. In this context it

seems important to capture the loss of productivity concerning housekeeping or activities of daily life in terms of opportunity costs as well as loss of work place productivity (sick leave, work disability, and other work loss). Additionally, there should be a standardized approach with regard to the handling of unemployment. Another aspect of loss of productivity concerns lost wages. Since there is no standardized definition of the term "lost wages," different cost domains have been summarized into this category. Our proposal defines lost wages as losses of potential earnings as a consequence of RA. This definition is based on the approach of Meenan, *et al*, who estimated expected earnings and compared them with their actual earned incomes⁷. This cost category is important in the assessment of costs from the patient's perspective.

Our approach faces several limitations: the selection of particular cost domains may be influenced by local, country related considerations. However, none of the articles commented on this aspect and further research is needed to clarify the generalizability of the presented cost matrix. Inhomogeneous labeling may lead to misclassification of reported cost domains.

This issue may be of particular interest in the further assessment of productivity costs. Finally, our focus was on cost assessment in RA clinical trials. The transferability of identified cost domains towards cost assessment in other rheumatic conditions remains unclear.

In summary this literature review indicates that cost assessment in economic evaluations in RA is performed rather inhomogeneously. There is a strong need for standardization of relevant cost components. A matrix of 19 cost domains that can be used as a preliminary categorization scheme is presented.

REFERENCES

- Luce BR, Manning WG, Siegel JE, Lipscomb J. Estimating costs in cost-effectiveness analysis. In: Gold MR, Russell LB, Siegel JE, Weinstein MC, editors. *Cost-effectiveness in health and medicine*. Oxford: Oxford University Press; 1996.
- Kobelt G, Jonsson L, Mattiasson A. Economic consequences of the progression of rheumatoid arthritis in Sweden. *Arthritis Rheum* 1999;42:347-56.
- Kristiansen IS, Kvien TK, Nord E. Cost effectiveness of replacing diclofenac with a fixed combination of misoprostol and diclofenac in patients with rheumatoid arthritis. *Arthritis Rheum* 1999;42:2293-302.
- Lanes SF, Lanza LL, Radensky PW, et al. Resource utilization and cost of care for rheumatoid arthritis and osteoarthritis in a managed care setting: the importance of drug and surgery costs. *Arthritis Rheum* 1997;40:1475-81.
- Magnusson S. Treatment of rheumatoid arthritis — does it affect society's cost for the disease? *Br J Rheumatol* 1996;35:791-5.
- McIntosh E. The cost of rheumatoid arthritis. *Br J Rheumatol* 1996;35:781-90.
- Meenan RF, Yelin EH, Henke CJ, Curtis DL, Epstein WV. The costs of rheumatoid arthritis. A patient-oriented study of chronic disease costs. *Arthritis Rheum* 1978;21:827-33.
- Prashker MJ, Meenan RF. The total costs of drug therapy for rheumatoid arthritis. A model based on costs of drug, monitoring, and toxicity. *Arthritis Rheum* 1995;38:318-25.
- Stone CE. The lifetime economic costs of rheumatoid arthritis. *J Rheumatol* 1984;11:819-27.
- Thompson MS, Read JL, Hutchings HC, Paterson M, Harris ED Jr. The cost effectiveness of auranofin: results of a randomized clinical trial. *J Rheumatol* 1988;15:35-42.
- Yelin E, Wanke LA. An assessment of the annual and long-term direct costs of rheumatoid arthritis: the impact of poor function and functional decline. *Arthritis Rheum* 1999;42:1209-18.
- Yelin E. The costs of rheumatoid arthritis: absolute, incremental, and marginal estimates. *J Rheumatol* 1996;23 Suppl 44:47-51.
- Bergquist SR, Felson DT, Prashker MJ, Freedberg KA. The cost-effectiveness of liver biopsy in rheumatoid arthritis patients treated with methotrexate. *Arthritis Rheum* 1995;38:326-33.
- Gabriel SE, Crowson CS, Luthra HS, Wagner JL, O'Fallon WM. Modeling the lifetime costs of rheumatoid arthritis. *J Rheumatol* 1999;26:1269-74.
- Gabriel SE, Crowson CS, Campion ME, O'Fallon WM. Direct medical costs unique to people with arthritis. *J Rheumatol* 1997;24:719-25.
- Gabriel SE, Crowson CS, Campion ME, O'Fallon WM. Indirect and nonmedical costs among people with rheumatoid arthritis and osteoarthritis compared with nonarthritic controls. *J Rheumatol* 1997;24:43-8.
- Gabriel SE, Campion ME, O'Fallon WM. A cost-utility analysis of misoprostol prophylaxis for rheumatoid arthritis patients receiving nonsteroidal antiinflammatory drugs. *Arthritis Rheum* 1994; 37:333-41.
- van Jaarsveld CH, Jacobs JW, Schrijvers AJ, Heurkens AH, Haanen HC, Bijlsma JW. Direct cost of rheumatoid arthritis during the first six years: a cost-of-illness study. *Br J Rheumatol* 1998;37:837-47.
- Verhoeven AC, Bibo JC, Boers M, Engel GL, van der Linden S. Cost-effectiveness and cost-utility of combination therapy in early rheumatoid arthritis: randomized comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone. COBRA Trial Group. *Combinatietherapie Bij Reumatoïde Artritis*. *Br J Rheumatol* 1998;37:1102-9.
- Lambert CM, Hurst NP, Forbes JF, Lochhead A, Macleod M, Nuki G. Is day care equivalent to inpatient care for active rheumatoid arthritis? Randomised controlled clinical and economic evaluation. *BMJ* 1998;316:965-9.
- Lambert CM, Hurst NP, Lochhead A, McGregor K, Hunter M, Forbes J. A pilot study of the economic cost and clinical outcome of day patient vs inpatient management of active rheumatoid arthritis. *Br J Rheumatol* 1994;33:383-8.
- Ariza-Ariza R, Mestanza-Peralta M, Cardiel MH. Direct costs of medical attention to Mexican patients with rheumatoid arthritis in a tertiary care center. *Clin Exp Rheumatol* 1997;15:75-8.
- Anis AH, Tugwell PX, Wells GA, Stewart DG. A cost effectiveness analysis of cyclosporine in rheumatoid arthritis. *J Rheumatol* 1996;23:609-16.
- Clarke AE, Levinton C, Joseph L, et al. Predicting the short term direct medical costs incurred by patients with rheumatoid arthritis. *J Rheumatol* 1999;26:1068-75.
- Clarke AE, Zowall H, Levinton C, et al. Direct and indirect medical costs incurred by Canadian patients with rheumatoid arthritis: a 12 year study. *J Rheumatol* 1997;24:1051-60.
- Helewa A, Bombardier C, Goldsmith CH, Menchions B, Smythe HA. Cost-effectiveness of inpatient and intensive outpatient treatment of rheumatoid arthritis. A randomized, controlled trial. *Arthritis Rheum* 1989;32:1505-14.
- Jonsson B, Rehnberg C, Borgquist L, Larsson SE. Locomotion status and costs in destructive rheumatoid arthritis. A comprehensive study of 82 patients from a population of 13,000.

- Acta Orthop Scand 1992;63:207-12.
28. Jacobs J, Keyserling JA, Britton M, Morgan GJ Jr, Wilkenfeld J, Hutchings HC. The total cost of care and the use of pharmaceuticals in the management of rheumatoid arthritis: the Medi-Cal program. *J Clin Epidemiol* 1988;41:215-23.
 29. Liang MH, Larson M, Thompson M, et al. Costs and outcomes in rheumatoid arthritis and osteoarthritis. *Arthritis Rheum* 1984;27:522-9.
 30. Lubeck DP, Spitz PW, Fries JF, Wolfe F, Mitchell DM, Roth SH. A multicenter study of annual health service utilization and costs in rheumatoid arthritis. *Arthritis Rheum* 1986;29:488-93.
 31. Kavanaugh A, Heudebert G, Cush J, Jain R. Cost evaluation of novel therapeutics in rheumatoid arthritis (CENTRA): a decision analysis model. *Semin Arthritis Rheum* 1996;25:297-307.
 32. Wolfe F, Kleinheksel SM, Spitz PW, et al. A multicenter study of hospitalization in rheumatoid arthritis. Frequency, medical-surgical admissions, and charges. *Arthritis Rheum* 1986;29:614-9.
 33. Pullar T, Capell HA, Millar A, Brooks RG. Alternative medicine: cost and subjective benefit in rheumatoid arthritis. *BMJ* 1982;285:1629-31.
 34. Drummond M, O'Brien B, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press; 1997.