
The economic impact of gout: a systematic literature review

L. Trieste¹, I. Palla¹, F. Fusco¹, C. Tani², C. Baldini², M. Mosca², G. Turchetti¹

¹Istituto di Management, Scuola Superiore Sant'Anna, Pisa, Italy;

²Rheumatology Unit, Department of Internal Medicine, University of Pisa, Italy.

Leopoldo Trieste, PhD
Ilaria Palla

Francesco Fusco, PharmD, MSc

Chiara Tani, MD, PhD

Chiara Baldini, MD, PhD

Marta Mosca, MD, PhD

Giuseppe Turchetti, PhD, Fulbright Scholar

Please address correspondence to:

Prof. Giuseppe Turchetti,

Istituto di Management,

Scuola Superiore Sant'Anna,

Piazza Martiri della Libertà 33,

56127 Pisa, Italy.

E-mail: g.turchetti@sssup.it

Received and accepted on October 1, 2012.

Clin Exp Rheumatol 2012; 30 (Suppl. 73): S145-S148.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2012.

Key words: gout, prevention, adherence to therapy, costs, review

ABSTRACT

This article performs a systematic literature review of the last decade studies assessing the economic impact of gout. The literature review confirms the fact that gout reduces productivity and increases annual total healthcare costs, since care of gout absorbs relevant amounts of healthcare resources. One important aspect to be considered is represented by prevention and monitoring of the disease after the diagnosis, as gout is sometimes underestimated by patients and this leads to a reduced adherence to follow up and to treatment with consequences on the disease course and outcome.

In fact, the lack of prevention and the scarce adherence to monitoring increase the number and costs of hospitalisation. Prevention, monitoring the level of sUA and using a urate-lowering therapy appear to have a central role for controlling gout and reducing hospitalisation, with positive advantages in terms of healthcare costs and healthcare utilisation.

One limitation on the analysis of gout related costs, however, resides in the fact that the majority of the retrieved studies are retrospective and the definition of the economic impact of the disease is made difficult by differences in inclusion criteria, costs assessment, use of gout-related healthcare resources.

Introduction

Although its importance and consequences are underestimated if compared to other pathologies, gout is a disease that substantially impacts on patients and healthcare institutions in terms of health costs and utilisation of healthcare services. In fact, reduction of productivity and of quality of life, increasing in hospitalisation and in healthcare annual costs supported both by patients and public healthcare institutions, are associated with gout (1).

In addition, it is well known that in spite of these facts, patients tend to underes-

timate the importance of gout and a low adherence to monitoring and treatment is reported in the literature (2).

Over the last 10 years, health economic literature has highlighted the importance and impact of gout in terms both of healthcare utilisation and of the risk of an increase in complexity and costs potentially associated with the underestimation of the relevance of this condition.

The objective of this systematic literature review is to establish the economic impact of gout. The review is based on papers published over the last decade and is designed in accordance with the recommendations of the Centre for Reviews and Dissemination (3) and of the Cochrane Collaboration (4), thereby using an established rigorous and reproducible methodology. A protocol was developed to define review questions.

Methods

Published studies in English were searched using the main electronic database, PubMed MEDLINE. The search was performed for the period January 2002-September 3, 2012. The search strategy is as follows: ((“economics”[Subheading] OR “economics”[All Fields] OR “cost”[All Fields] OR “costs and cost analysis”[MeSH Terms] OR (“costs”[All Fields] AND “cost”[All Fields]) AND “analysis”[All Fields]) OR “costs and cost analysis”[All Fields]) AND (“gout”[MeSH Terms] OR “gout”[All Fields])) AND ((“2002/01/01”[PDAT]:”2012/09/03”[PDAT]) AND “humans”[MeSH Terms] AND English[lang] AND “adult”[MeSH Terms]).

The publications were assessed for inclusion by a 3-step process: i. titles and abstracts of all identified studies were assessed by one reviewer and checked by a second reviewer; ii. full texts of relevant articles were then obtained and inclusion criteria applied independently by two reviewers. Possible discords between reviewers were resolved by consensus; iii. data were extracted by one

Competing interests: none declared.

reviewer and then checked by a second reviewer.

Inclusion criteria

In the study protocol the reviewers selected publications from the mentioned database as follows:

Period: Jan. 2002–Sep. 3, 2012

Language: English

Studies: all articles related to economic analysis

Patients: adult ≥18

Outcomes: direct costs, indirect costs, quality of life costs, and cost associated with flares.

Exclusion criteria

Studies not published in English and all publications before 2002 were excluded. Conferences proceedings, case reports, reviews, systematic reviews, letters and commentaries were also excluded.

Results

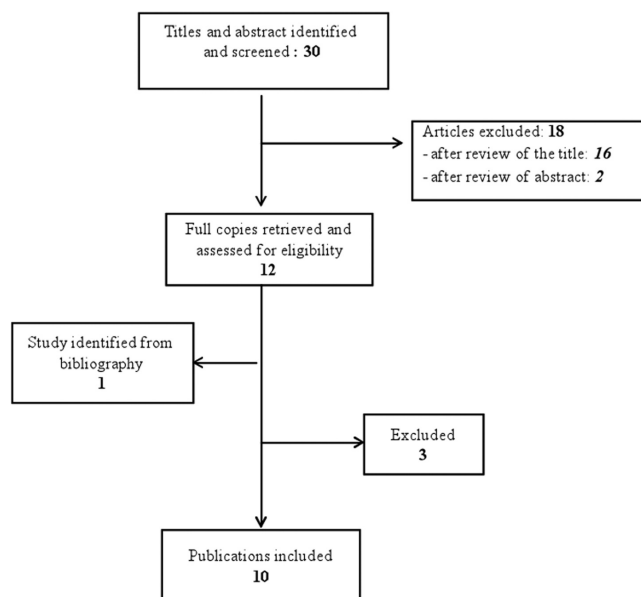
As of September 3 2012, 30 articles were extracted by the search procedure. These were reduced to 14 articles after title scrutiny. After abstract review, 12 publications were included in the analysis, one additional paper was retrieved from the bibliography. These 13 publications were examined and assessed for eligibility. On reading the full text copies, 10 publications were considered relevant to the review (Fig. 1). Two reviewers read and examined the full text of these publications.

Full details of the articles in tabular form used in the review can be obtained on request to corresponding author.

None of the articles provided a full economic evaluation (Cost Minimisation Analysis, Cost Effectiveness Analysis, Cost Utility Analysis and Cost Benefit Analysis). The review is based on 9 studies from the USA (5-13) and 1 from Canada (14); all are retrospective studies. Of the 3 excluded articles, 2 articles did not perform an analysis of economic impact of gout but reported its clinical impact (15, 17); 1 article (16) was excluded since it included data, methodology and findings that overlapped with the results of another publication (12).

Cost and healthcare utilisation of

Fig. 1. PRISMA flow diagram for cost studies in gout.



medical services and prescription drugs

Costs analysis for employed population has been evaluated by Brook *et al.* (5) and Kleinman *et al.* (6). Data are poorly comparable, in fact while Brook *et al.* assessed total annual costs, Kleinman *et al.* examined loss of productivity.

Interestingly, while the total annual costs for employees with gout is higher with respect to those without gout, data on the loss of productivity associated with gout does not show difference between employees with and without gout. Different explanations for this latter findings could be sought such as the scarcity of data on productivity referred to employees affected by gout to serve as a measure of comparison, the presence of a trade-off between the number of employees with gout and the availability of an objective measure of productivity, sample dimension (only 7.3% of employees with gout falls in the sample) and a sort of self-selection of people with gout that does not accept hard jobs. Further studies are therefore needed to better define this discrepancy.

Brook *et al.* (5) have showed that cost drivers are, among others, medical and prescriptions costs, costs associated to sick-leave and short-term diseases. The total annual costs of employees with gout is two time the annual costs for employees without gout, on average. Location of services, laboratory, hospitals, matter in the differences among

annual costs.

With a different view and approach, Wu *et al.* (7) calculate healthcare costs from a third-party payer perspective. In addition, these authors evaluate the value of uric acid levels as a control indicator of gout and its relative costs.

Their data show a trend toward an increase in health care costs among patients with either high serum urate levels, gout or tophi. In a period of one year after a diagnosis of gout, for patients aged over 65, direct costs associated to any kind of conditions (either gout or increased serum urate levels) was \$876 (5.9%) of the total health costs (\$14,734 of 2005 dollars) registered in the period, mainly related with inpatient (57.6%) and outpatient (23.6%) costs, while only a small part was related with drugs (7.1%), emergency care (2.4%) and other services (9.4%). In addition, patients with tophi had higher costs than patients without. Finally, high levels (>9 mg/dL) of serum UA are associated to an increasing of \$3,103 in costs for all-cause health and \$276 health costs associated to gout, with respect to a low level of sUA.

In line with the previous authors, Hanly *et al.* (14) examined patients with gout over 65 years of age in Nova Scotia (Canada). The study included costs associated to physician claims, hospital admissions, ambulatory visits, and Pharmicare prescriptions. In the gout cohort an average overall healthcare

cost differential of C\$134 per month was observed, which was of C\$8,020 over 5 years of follow up. Hospital utilisation was the most important item in determining costs, probably due to comorbidities associated to gout.

This hypothesis seems sustained by Nitchaikulvatana *et al.* (12) showing that complications for gout in hospital also increase the length of stay with a daily cost of \$1,762. In addition, these authors observed that 29% of admissions for gout on the total examined were preventable cases. Assuming that this percentage is also true for the annual population that have a first diagnosis of gout, the annual costs for the lack of an efficient prevention and the relative use of hospitalisation would be about \$32 million.

Increasing health care costs are also related with disease severity; the studies by Wu *et al.* (10) and Park *et al.* (13) reported increased medical and pharmacy costs as the level of sUA increases. Wu *et al.* (10) analyse the correlation between gout flares and sUA levels, and the relative cost of gout flares in old people (over 65 aged). It is observed that people with high level of sUA have a higher probability of a flare in 1 year. In aggregate, the annual number of flares increases of 11.9% per unit of increasing in sUA level above 6 mg/dl. For patients with high level of sUA, the total health cost associated to gout is \$2,555 per episode with a difference of \$356 with respect to patients with a normal level of sUA.

High levels of sUA gout cases in elderly and healthcare cost increasing are positively and mutually correlated.

Similarly Halpern *et al.* (11) showed a positive association between costs for gout flare and sUA levels. For a level of sUA less than 6.0 mg/dl the average cost is \$259 (\$147 median); \$477 on average with a sUA value from 6 to 9 mg/dl (\$171 median); \$562 on average with a sUA value greater than 9 mg/dl (\$189 median).

Another important variable from an economic perspective is represented by the way patients consider their disease and patients' willingness to pay for gout care, as this also gives an indication on patients' perception of the severity of

this condition and on possible impact on future quality of life, and on future outcome and development of gout related comorbidities. In a study assessing patients with chronic gout, Khanna *et al.* (8) observed that the willing to monthly pay for gout is about \$52 on average (\$25 median) and that this value was related with income and number of gouty attacks. While gender and ethnic differences did not matter in the level of willing to pay for gout, a difference was observed with respect to age and health condition, as younger patients and people that ranked gout in the first position of their concern were willing to pay more.

On a similar type of study, Krishnan *et al.* (9) examined the magnitude of healthcare utilisation (use of ambulatories for gout treatment and visits) for gout in USA and its high economic impact. They observed that there is a small but consolidated use of healthcare services for gout in USA (3.9 million of ambulatory visits on a total of 973 million regard gout), with age and sex differences. Interestingly, Asiatic patients had a probability to have a gout visit 2.7 times higher than Caucasian patients, but a lower percentage of them was receiving allopurinol.

Discussion and conclusions

Literature data suggest that in the US every year new cases of acute gout account for a mean of \$27.4 million of direct costs (2).

The most recent literature on the economic impact of gout is not consolidated and is mainly represented by retrospective studies. Differences in patients characteristics, data retrieval and models to measure costs and gout-related healthcare resource consumption make these data difficult to be compared and summarised.

In spite of these difficulties, the present systematic literature review allows some observations. Agreement exists on the fact that the care of gout consumes a large size of resources meaning high costs.

The most important determinants of costs are represented by in and out patient's care, while drugs costs cover only a limited part. This fact could be

attributed to the fact that, up to now, the drugs largely used in the treatment of this condition are less expensive and/or off patent.

Increased disease costs are related also with the severity of the disease, as some studies have shown that higher sUA levels and flares determine an increasing in costs. In addition, patients seem to have a low utilisation of health care resources. This observation is coherent with other data showing a low adherence to therapy and follow up among gout patients in spite of emerging Recommendations developed by scientific societies, similarly to what is reported in other rheumatologic diseases (18-20).

The lack of prevention and regular monitoring increases the number and costs for hospitalisation. This factor, associated with the management of comorbidities gout-related, increases the difference in annual healthcare costs of patients with gout with respect to annual health costs for people without gout. Future studies should address, in a prospective and detailed way (21), the issue of the loss of productivity and analyse the correlations between implementation of recommendations, quality of care indicators and economic issues in gout as in other rheumatic diseases (22-28).

References

1. ROUBENOFF R: Gout and hyperuricemia. *Rheum Dis Clin Ther* 1990; 16: 539-50.
2. KIM KY, SCHUMACHER R, HUNSCH E, WERTHEIMER AL, KONG SX: A literature review of the epidemiology and treatment of acute gout. *Clin Ther* 2003; 25: 1593-617.
3. Centre For Reviews And Dissemination, CRD's guidance for undertaking reviews in health care, 2008, University of York.
4. Cochrane Handbook for Systematic Reviews of interventions, HIGGINS JPT, GREEN S (Eds.), 2008, Wiley-Blackwell.
5. BROOK R, KLEINMAN N, PATEL P *et al.*: The economic burden of gout on an employed population. *Curr Med Res Opin* 2006; 22: 1381-9.
6. KLEINMAN N, BROOK R, PATEL P *et al.*: The impact of gout on work absence and productivity. *Value in Health* 2007; 10: 231-7.
7. WU E, PATEL P, YU A *et al.*: Disease-related and all-cause health care costs of elderly patients with gout. *J Manag Care Pharm* 2008; 14: 164-75.
8. KHANNA D, AHMED M, YONTZ D, GINSBURG S, TSEVAT J: Willingness to pay for a cure in patients with chronic gout. *Med Decis Making* 2008; 28: 606-13.

9. KRISHNAN E, LIENESCH D, KWOH C: Gout in ambulatory care settings in the United States. *J Rheumatol* 2008; 35: 498-501.
10. WU E, PATEL P, MODY R *et al.*: Frequency, risk, and cost of gout-related episodes among the elderly: does serum uric acid level matter? *J Rheumatol* 2009; 36: 1032-40.
11. HALPERN R, FULDEORE M, MODY R, PATEL P, MIKULS T: The effect of serum urate on gout flares and their associated costs. an administrative claims analysis. *J Clin Rheumatol* 2009; 15: 3-7.
12. NITICHAIKULVATANA P, UPCHURCH K, HARROLD L: Impact of deficits in gout care on hospitalizations. *J Clin Rheumatol* 2011; 17: 389-91.
13. PARK H, RASCATI K, PRASLA K, TYRONE MCBAYNE: Evaluation of health care costs and utilization patterns for patients with gout. *Clin Ther* 2012; 34: 640-52.
14. HANLY J, SKEDGEL C, SKETRIS I *et al.*: Gout in the elderly – a population health study. *J Rheumatol* 2009; 36: 822-30.
15. NOVAK S, MELKONIAN A, PATEL A, KLEINMAN N, JOSEPH-RIDGE, BROOK R: Metabolic syndrome-related conditions among people with and without gout: prevalence and resource use. *Curr Med Res Opin* 2007; 23: 623-30.
16. HALPERN R, MODY R, FULDEORE M, PATEL P, MIKULS T: Impact of noncompliance with urate-lowering drug on serum urate and gout-related healthcare costs: administrative claims analysis. *Curr Med Res Opin* 2009; 25: 1711-9.
17. DALBETH N, PETRIE K, HOUSE M *et al.*: Illness perceptions in patients with gout and the relationship with progression of musculoskeletal disability. *Arthritis Care Res* 2011; 11: 1605-12.
18. TANI C, CARLIL, MOSCA M *et al.*: Adherence to cervical cancer screening in an Italian SLE cohort. *Reumatismo* 2011; 63: 11-7.
19. MOSCA M, TANI C, ARINGER M *et al.*: Development of quality indicators to evaluate the monitoring of SLE patients in routine clinical practice. *Autoimmun Rev* 2011; 10: 383-8.
20. CABANA MD, RAND CS, POWE NR *et al.*: Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999 20; 282: 1458-65.
21. TURCHETTI G, SPADONI E, GEISLER E: Health technology assessment. Evaluation of biomedical innovative technologies. *IEEE Engineering in Medicine and Biology Magazine* 2010; 29: 70-6.
22. TURCHETTI G, SCALONE L, DELLA CASA ALBERIGHI O *et al.*: The rationale of pharmacoeconomic analysis in rheumatologic indications. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S64-S71.
23. FURNERI G, MANTOVANI LG, BELISARI A *et al.*: Systematic literature review on economic implications and pharmacoeconomic issues of rheumatoid arthritis. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S72-S84.
24. TURCHETTI G, YAZDANY J, PALLA I, YELINE, MOSCA M. Systemic lupus erythematosus and the economic perspective: a systematic literature review and points to consider. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S116-S122.
25. MOSCA M, BOUMPAS D, BRUCE IN *et al.*: Treat-to-target in systemic lupus erythematosus: where are we today? *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S112-S115.
26. PALLA I, TRIESTE L, TANI C *et al.*: A systematic literature review of the economic impact of ankylosing spondylitis. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S136-S141
27. TRIESTE L, PALLA I, BALDINI C *et al.*: Systemic vasculitis: how little we know about their societal and economic burden. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S154-S156.
28. CORTESI PA, SCALONE L, D'ANGIOLELLA L *et al.*: Systematic literature review on economic implications and pharmacoeconomic issues of psoriatic arthritis. *Clin Exp Rheumatol* 2012; 30 (Suppl. 73): S126-S131.