4-22-2004

Delays in publication of cost utility analyses conducted alongside clinical trials: registry analysis

Dan Greenberg
Harvard School of Public Health

Allison B. Rosen
University of Massachusetts Medical School

Natalia V. Olchanski
Harvard School of Public Health

See next page for additional authors

Follow this and additional works at: http://escholarship.umassmed.edu/qhs_pp

Part of the Biostatistics Commons, Epidemiology Commons, and the Health Services Research Commons

Repository Citation
Greenberg, Dan; Rosen, Allison B.; Olchanski, Natalia V.; Stone, Patricia W.; Nadai, John; and Neumann, Peter J., "Delays in publication of cost utility analyses conducted alongside clinical trials: registry analysis" (2004). Quantitative Health Sciences Publications and Presentations. 892.
http://escholarship.umassmed.edu/qhs_pp/892

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in Quantitative Health Sciences Publications and Presentations by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Delays in publication of cost utility analyses conducted alongside clinical trials: registry analysis

Authors
Dan Greenberg, Allison B. Rosen, Natalia V. Olchanski, Patricia W. Stone, John Nadai, and Peter J. Neumann

This article is available at eScholarship@UMMS: http://escholarship.umassmed.edu/qqhs_pp/892
Economic evaluations conducted alongside randomised controlled trials enable analysis of detailed, patient level data on efficacy, cost, and quality of life in a controlled setting. They can provide timely and reliable assessments of value for money, to inform decisions on coverage and reimbursement.1–3

The BMJ recently decided to consider trial based economic evaluations for publication only if the clinical results are submitted to the journal as well.1 We assessed the extent to which cost utility analyses are conducted alongside trials, estimated the time lag between the publication of trials’ clinical and economic results, and compared the characteristics of journals publishing the clinical trial data and the cost utility analyses.

Methods and results

We conducted a systematic search for original English language cost utility analyses published in 1976–2001 by using Medline and other electronic databases. Two readers independently reviewed each study and came to a consensus on whether the analysis was conducted alongside a trial (data on both efficacy and resource use from the trial were used for the analysis). We identified the journal and publication date for each cost utility analysis and the corresponding trial. To assess the study’s potential readership and dissemination we used paired sample t tests to compare the mean impact factors of journals in which studies were published and the extent to which publications were subsequently cited by other authors.

Of 533 cost utility analyses identified, 45 (8%) were trial based economic evaluations and covered a variety of clinical areas, particularly cardiovascular disease, cancer, and psychiatry (a full list of studies is available at www.hsph.harvard.edu/eareregistry). We could not determine the lag in publication between the trial and the economic evaluation for four studies, for which a specific trial could not be identified or trial results were published only in abstract form. In cases where the clinical trial results and economic evaluation were reported in the same article or in the same issue of the journal (n = 7), we assumed no lag.

On average, cost utility analyses were published almost two years after the publication of the corresponding trial (mean (SD) 1.8 (1.4) years; range 0–7.5 years) (figure). Journal impact factors were higher for trials than for cost utility analyses (11.0 v 4.9; t = −3.951 (df = 28); 95% confidence interval for the difference −9.25 to −2.93; P < 0.001). The mean number of citations per year (total number of citations divided by number of years since the study was published) was also higher for clinical trials than for the economic evaluations (27.4 v 3.4; t = −3.197 (df = 30); 95% confidence interval for the difference −39.24 to −8.64; P = 0.003).

This article was posted on bmj.com on 20 April 2004: http://bmj.com/cgi/doi/10.1136/bmj.38036.646030.AE

Delays in publication of cost utility analyses conducted alongside clinical trials: registry analysis

Dan Greenberg, Allison B Rosen, Natalia V Olchanski, Patricia W Stone, John Nadai, Peter J Neumann

Economic evaluations conducted alongside randomised controlled trials enable analysis of detailed, patient level data on efficacy, cost, and quality of life in a controlled setting. They can provide timely and reliable assessments of value for money, to inform decisions on coverage and reimbursement.1–3

The BMJ recently decided to consider trial based economic evaluations for publication only if the clinical results are submitted to the journal as well.1 We assessed the extent to which cost utility analyses are conducted alongside trials, estimated the time lag between the publication of trials’ clinical and economic results, and compared the characteristics of journals publishing the clinical trial data and the cost utility analyses.

Methods and results

We conducted a systematic search for original English language cost utility analyses published in 1976–2001 by using Medline and other electronic databases. Two readers independently reviewed each study and came to a consensus on whether the analysis was conducted alongside a trial (data on both efficacy and resource use from the trial were used for the analysis). We identified the journal and publication date for each cost utility analysis and the corresponding trial. To assess the study’s potential readership and dissemination we used paired sample t tests to compare the mean impact factors of journals in which studies were published and the extent to which publications were subsequently cited by other authors.

Of 533 cost utility analyses identified, 45 (8%) were trial based economic evaluations and covered a variety of clinical areas, particularly cardiovascular disease, cancer, and psychiatry (a full list of studies is available at www.hsph.harvard.edu/eareregistry). We could not determine the lag in publication between the trial and the economic evaluation for four studies, for which a specific trial could not be identified or trial results were published only in abstract form. In cases where the clinical trial results and economic evaluation were reported in the same article or in the same issue of the journal (n = 7), we assumed no lag.

On average, cost utility analyses were published almost two years after the publication of the corresponding trial (mean (SD) 1.8 (1.4) years; range 0–7.5 years) (figure). Journal impact factors were higher for trials than for cost utility analyses (11.0 v 4.9; t = −3.951 (df = 28); 95% confidence interval for the difference −9.25 to −2.93; P < 0.001). The mean number of citations per year (total number of citations divided by number of years since the study was published) was also higher for clinical trials than for the economic evaluations (27.4 v 3.4; t = −3.197 (df = 30); 95% confidence interval for the difference −39.24 to −8.64; P = 0.003).

This article was posted on bmj.com on 20 April 2004: http://bmj.com/cgi/doi/10.1136/bmj.38036.646030.AE
Comment
We found a substantial delay in the publication of cost utility analyses, suggesting that reliable economic data are usually not available, at least in peer reviewed journals, for decision makers when decisions on adoption and reimbursement are typically made. Moreover, compared with trial results, dissemination of cost utility analyses takes place in journals with lower readership and influence. Several factors may contribute to this phenomenon: economic evaluations may be time consuming to construct, as they typically involve projections of trial data over time and across populations through use of modelling techniques and data from external sources; trial sponsors and investigators are eager to report important clinical results first, and more resources are initially allocated to interpreting and publishing these results; given that most readers of clinical journals are physicians, and not economists or policy makers, manuscripts presenting important clinical results are more often assigned by editors to an accelerated review and publication process.

Efforts have recently been made to keep the clinical and economic results of a trial together. Further efforts (for example, fast track review process) should be made to promote timely dissemination of results of economic evaluations concurrent with or soon after the completion and publication of the trial.

We thank Richard H Chapman for his contribution to the design and analysis of the Harvard School of Public Health Cost-Effectiveness Analysis Registry.

Contributors: DG had the original idea for the study, drafted the first version of the manuscript, did the statistical analysis, and is the guarantor. All authors extracted data, interpreted the findings, critically revised the report, and approved the final version.

Funding: Supported by grant number R01 HS10919 from the Agency for Health Care Research and Quality.
Competing interests: None declared.

What is already known on this topic
To identify cost effective interventions, decision makers need timely and reliable information about the clinical and economic consequences of treatments

Economic evaluations conducted alongside clinical trials enable analysis of detailed, patient level data on efficacy, cost, and quality of life in a controlled setting

What this study adds
A substantial delay in the publication of economic evaluations suggests that reliable economic data are usually not available when decisions have to be made

(Accepted 30 January 2004)
doi 10.1136/bmj.38079.502326.AE

DRUG POINTS
Guillain-Barré syndrome seen in users of isotretinoin
J Pritchard, R Appleton, R Howard, R A C Hughes

We report Guillain-Barré syndrome in people taking oral isotretinoin, a retinoid drug used in secondary care for severe acne. The Committee on Safety of Medicines has received one other report of Guillain-Barré syndrome after oral isotretinoin (Committee on Safety of Medicines, private communication).

Case 1—A 31 year old man took 80 mg of oral isotretinoin a day for five weeks, during which he had epistaxis, dry lips, cough, and arthralgia before developing parasthesia in his feet and influenza-like symptoms. The next day he could not stand due to an areflexic tetraparesis and needed ventilatory support. Within four days he could only blink.

Case 2—A 13 year old boy took 50 mg of oral isotretinoin a day for two months, stopped for one week, and then took 30 mg a day for six weeks but had epistaxis, lethargy, and headaches. After stopping isotretinoin again for 10 days he developed a flaccid areflexic tetraparesis needing ventilatory support.

Both patients displayed cerebrospinal fluid albuminocytological dissociation. Nerve conduction studies in case 1 showed a motor axonal neuropathy with unrecordable sensory potentials and F waves, those in case 2, done after 21 months, showed borderline increased F wave latencies. Both patients received intravenous immunoglobulin IVIg 2 g/kg and left hospital within three months. Neither patient has been rechallenged with oral isotretinoin, although the first continued to use topical isotretinoin gel 0.05% which is not absorbed.

Retinoids affect the development, differentiation, and function of the central nervous system. Sensory neuropathy has been described in patients taking the retinoid drug acitretin. Over a 19 year period, an estimated 375 000 patients have been treated with oral isotretinoin in the United Kingdom (Roche, personal communication), and the annual incidence of Guillain-Barré syndrome is about 2 in 100 000. This is insufficient to establish a causal association between Guillain-Barré syndrome and isotretinoin. We hope to alert others to report similar cases.

We thank the guarantors of Brain.

Funding: JP was funded by a Medical Research Council training fellowship and Roehn neurology entry fellowship.
Competing interests: None declared.

1. Webster GE. Acne vulgaris. BMJ 2002;325:475-6

Department of Clinical Neurosciences, Guy’s, Kings, and St Thomas’s School of Medicine; Guy’s Hospital, London SE1 1UL
J Pritchard
neurology research registrar
R A C Hughes
professor of neurology
Royal Liverpool Children’s NHS Trust, Liverpool
R Appleton
consultant paediatric neurologist
St Thomas’s Hospital, London
R Howard
consultant neurologist
Correspondence to: J Pritchard jane.pritchard@kcl.ac.uk
BMJ 2004;328:1157