Increasing The Value Of Clinical Trials With Cost-Effectiveness Analysis

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Why Trial-based CEA?

Benefits from high internal validity of clinical trial design and conduct in naturalistic settings

Provides an opportunity to collect and analyse individual patient data. Such information may not be available at any other time

Produces reliable estimates of cost effectiveness at low marginal cost with resources already in place

Permits a wide range of statistical and econometric techniques with individual patient data
Objective: To assess the cost-effectiveness of brief physiotherapy intervention versus usual physiotherapy management in patients with neck pain of musculoskeletal origin in the community setting.

Randomized trial of a brief physiotherapy intervention compared with usual physiotherapy for neck pain patients: Cost-effectiveness analysis

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**Methods:** A cost-effectiveness analysis was conducted alongside a multicenter pragmatic randomized controlled clinical trial. Individuals 18 years of age and older with neck pain of more than 2 weeks were recruited from physiotherapy departments with referrals from general practitioners (GPs) in the East Yorkshire and North Lincolnshire regions in the United Kingdom. A total of 139 patients were allocated to the brief intervention, and 129 to the usual physiotherapy. Resource use data were prospectively collected on the number of physiotherapy sessions, hospital stay, specialist, and GP visits. Quality-adjusted life years (QALYs) were estimated using EQ-5D data collected at baseline, 3 and 12 months from the start of the treatment. The economic evaluation was conducted from the U.K. National Health System perspective.
RESULTS
A total of 268 participants were recruited to the study (129 and 139 randomly assigned to usual physiotherapy and the brief intervention, respectively). Of these, 101 (78 percent) in the usual physiotherapy and 113 (81 percent) in the brief intervention group returned questionnaires at both 3 months and 1 year after randomization. There was no evidence that drop-out from the trial was associated with whether patients received their choice of treatment.

Differential QALYs were 0.001 (95 percent CI, -0.028 to 0.030) in favor of usual physiotherapy, after adjusting for baseline difference in EQ-5D score between the trial arms. Similarly, the differential area under the NPQ score of 0.686 (95 percent CI, -0.255 to 1.665) was in favor of usual physiotherapy.

What likely will be your conclusion?
Which Tx will you recommend?
Methods: A cost-effectiveness analysis was conducted alongside a multicenter pragmatic randomized controlled clinical trial. Individuals 18 years of age and older with neck pain of more than 2 weeks were recruited from physiotherapy departments with referrals from general practitioners (GPs) in the East Yorkshire and North Lincolnshire regions in the United Kingdom. A total of 139 patients were allocated to the brief intervention, and 129 to the usual physiotherapy. Resource use data were prospectively collected on the number of physiotherapy sessions, hospital stay, specialist, and GP visits. Quality-adjusted life years (QALYs) were estimated using EQ-5D data collected at baseline, 3 and 12 months from the start of the treatment. The economic evaluation was conducted from the U.K. National Health System perspective.
Cost-effectiveness

on average, usual physiotherapy intervention costs more and produces slightly more QALYs than the brief intervention. Relating mean differences in costs (to the NHS) and QALYs produced an incremental cost effectiveness ratio of £68,000 (i.e., 68/0.001). This value is above the implicit threshold of £30,000 that NICE showed itself to be willing to pay in the past, suggesting usual physiotherapy may not be a cost-effective treatment compared with the brief intervention in this patient population. That is, the small additional benefit produced by a more intense physiotherapy management in this patient group, comes at a high additional cost.

What likely will be your conclusion?

Which Tx will you recommend?
What Are The Key Elements For A Trial-based CEA?
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Resource Use & Costs

- Costs in hospital
- Costs in primary sector
- Costs for patients & family
- Costs in other sectors
- Productivity Loss
- Future unrelated costs

“Hospital”  “Patient”  “Society”
Resource Use Measurement
Health care resource utilization data were collected during the study period using a combination of patient health care diaries and case record forms (CRFs). The latter were sent out at 3 and 12 months from randomization as postal questionnaires to be completed by each patient. The CRF asked participants to recall the number of National Health Service (NHS) GP, physiotherapist, hospital specialist and other outpatient visits, the number and cost of private health care consultations (excluding travel), and type and cost of anything else bought to help the person’s neck pain since the previous follow-up assessment.
Analysis

The primary economic analysis was undertaken in the form of cost-effectiveness analysis relating differential mean cost to differential mean QALYs associated with the alternative treatment strategies in the trial.

In terms of results of the analysis, the following scenarios can arise:

a) The brief intervention, on average, costs more and produces less QALYs than usual physiotherapy;

b) The brief intervention, on average, is less costly and more effective (in terms of QALYs gained) than usual physiotherapy;

c) The brief intervention, on average, is both more (less) costly and more (less) effective, in which case the decision problem is to determine whether the additional cost that needs to be born to obtain a unitary increment in the effectiveness measure (here QALYs) is worth paying. This determination is achieved by calculating the incremental cost-effectiveness ratio (calculated as the difference in mean costs divided by the difference in mean QALYs) in the trial, and comparing this ratio against the maximum amount the decision maker is willing to pay for an additional QALY.
Cost Effectiveness Plane

North West

Existing treatment more effective and less costly

A

Existing treatment more effective but more costly

C1

North East

New treatment more effective but more costly

C2

New treatment more effective and less costly

B

South West

South East

(-) Difference in Cost (+)

(-) Difference in Effect (+)
Results

**Resource Use:** In total, including initial physiotherapy sessions, the brief intervention group had fewer NHS physiotherapist visits compared with usual physiotherapy over the study period (mean visits = 2.78 (SD 4.55) versus 6.82 (SD 6.55), for the brief intervention and usual physiotherapy respectively). The use of other health care resources during 12-month follow-up period was similar between the two groups.

**Costs:** The usual physiotherapy group displayed higher average NHS direct costs compared with the brief intervention group in the first 3 months of the study period, which was mainly driven by the cost of physiotherapy visits (£78 versus £37). NHS and private health care costs other than physiotherapists’ visits were similar between the two arms. By the end of the study period, the brief intervention compared with usual physiotherapy resulted in a reduction of direct NHS mean costs (i.e., cost saving) per patient (£−68; 95 percent CI, −103 to −35).
Results

**Cost Effectiveness:** On average, brief intervention produced lower costs (£-68; 95 percent confidence interval [CI], £-103 to £-35) and marginally lower QALYs (-0.001; 95 percent CI, -0.030 to 0.028) compared with usual physiotherapy, resulting in an incremental cost per QALY of £68,000 for usual physiotherapy. These results are sensitive to patients’ treatment preferences.
Willingness To Pay (WTP)

- Difference in Cost (+)
- Difference in Effect (+)

North West
Existing treatment dominates
North East
Not Cost Effective
Cost Effective
South West
Existing treatment more effective but more costly
South East
New treatment dominates
Maximum Willingness To Pay
Results

Cost Effectiveness: On average, brief intervention produced lower costs (£ -68; 95 percent confidence interval [CI], £ -103 to £ -35) and marginally lower QALYs (-0.001; 95 percent CI, -0.030 to 0.028) compared with usual physiotherapy, resulting in an incremental cost per QALY of £68,000 for usual physiotherapy. These results are sensitive to patients’ treatment preferences.

On average, usual physiotherapy intervention costs more and produces slightly more QALYs than the brief intervention. Relating mean differences in costs (to the NHS) and QALYs produced an incremental cost effectiveness ratio of £68,000 (i.e., 68/0.001). This value is above the implicit threshold of £30,000 that NICE showed itself to be willing to pay in the past, suggesting usual physiotherapy may not be a cost-effective treatment compared with the brief intervention in this patient population. That is, the small additional benefit produced by a more intense physiotherapy management in this patient group, comes at a high additional cost.
Cost Effectiveness

WTP = 30,000
Result

Cost-effectiveness: on average, usual physiotherapy intervention costs more and produces slightly more QALYs than the brief intervention. Relating mean differences in costs (to the NHS) and QALYs produced an incremental cost effectiveness ratio of £68,000 (i.e., 68/0.001). This value is above the implicit threshold of £30,000 that NICE showed itself to be willing to pay in the past, suggesting usual physiotherapy may not be a cost-effective treatment compared with the brief intervention in this patient population. That is, the small additional benefit produced by a more intense physiotherapy management in this patient group, comes at a high additional cost.

Furthermore, even if the decision maker were willing to pay £68,000 or more for additional QALY in this patients’ population, Figure 1 shows that there is still considerable uncertainty regarding the cost-effectiveness in this result. The cost-effectiveness acceptability curve (Figure 1) shows that, for values of the decision maker’s maximum “willingness to pay” for additional QALYs greater than 20,000, the probability that usual physiotherapy is cost-effective is only 50 percent.
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Subgroup Analysis

Effect of Patient Preference

It was not possible to blind patients or physiotherapists with regard to the treatment allocation. This raises the possibility that the observed treatment effect (on costs and health outcomes) may be influenced by patients’ a priori preferences as well as therapeutic efficacy. In this trial, patient preferences were elicited before randomization and used as the basis of a subgroup analysis.

For patients preferring the brief intervention, the latter was associated with lower NHS costs (−£96) and improved health outcomes (+0.039).

For patients who did not have a treatment preference, there was a small increase in costs (+£14) and QALYs (+0.023) for usual physiotherapy compared with the brief intervention, resulting in an incremental cost per QALY of £609 (obtained as 14/0.023).

Finally, the group of participants who expressed a preference toward usual physiotherapy produced higher mean costs (£206 versus £70) and lower mean QALYs (0.711 versus 0.724) compared with the group who expressed a preference toward the brief intervention.
In conclusion, giving the brief intervention to neck pain patients will lead to a reduction in costs albeit with a small reduction in quality of life. In circumstances in which physiotherapy resources are scarce, then the brief intervention could be a cost-effective alternative to usual physiotherapy.

For patients with a preference for brief intervention, this therapy is the dominant treatment and such patients should receive this treatment.
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<th>CTs</th>
<th>CEA</th>
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<tr>
<td><strong>Audience</strong></td>
<td>Regulatory authorities and clinicians</td>
<td>Payers and decision makers</td>
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<tr>
<td><strong>Objective</strong></td>
<td>Assess safety and efficacy</td>
<td>Assess value for money</td>
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<tr>
<td><strong>Comparison</strong></td>
<td>Placebo / best alternatives in current practice</td>
<td>Usual care / best alternatives in current practice</td>
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<tr>
<td><strong>Outcome</strong></td>
<td>Efficacy / effectiveness (e.g. mortality)</td>
<td>Effectiveness and efficiency (e.g. ICER)</td>
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<tr>
<td><strong>Timeframe</strong></td>
<td>Driven by occurrence of clinical events, usually for years</td>
<td>Long enough to measure “downstream” consequences, can be lifetime</td>
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Summary

• Clinical trials can provide an efficient opportunity for economic evaluation, taking advantages of the rigorous experimental design and data collect infrastructure

• Suitability of study design and analysis for economic evaluation needs to be considered carefully

• No single method for dealing with uncertainty will provide all information required for decision making
Projects

- Cardiology
- Oncology
- Diagnostic Test
- Mental Health
- Infectious Disease
- Gastroenterology
Thank You

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