Cost-effectiveness of treating upper limb spasticity due to stroke with botulinum toxin type A: results from the Botulinum Toxin for the Upper Limb after Stroke (BoTULS) trial


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The objective was to assess the cost-effectiveness of botulinum toxin type A, for treating upper limb spasticity, after stroke. The authors concluded that their analysis provided no evidence to suggest that botulinum toxin type A plus therapy was a cost-effective alternative to therapy alone. The study methods were good, and they and the results were well reported. Given the scope of the analysis, the authors’ conclusions appear to be reasonable.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of botulinum toxin type A, for treating upper limb spasticity, after stroke.

Interventions
Intramuscular injection of botulinum toxin type A, plus a four-week upper limb therapy programme, comprising of one hour of therapy twice weekly, was compared with the upper limb therapy programme alone.

Location/setting
UK/primary care.

Methods
Analytical approach:
The effectiveness and resource use data were from a pragmatic multicentre randomised controlled trial – the Botulinum Toxin for the Upper Limb after Stroke (BoTULS) trial (Shaw, et al. 2011, see Other Publications of Related Interest). The time horizon was three months. The authors stated that the UK NHS and social services perspective was adopted.

Effectiveness data:
The effectiveness data were from the BoTULS trial, in which 333 adults with spasticity and reduced upper limb function, due to stroke, were randomised to receive either botulinum toxin plus upper limb therapy (170 patients) or upper limb therapy alone (163 patients). Patients were assessed at baseline and at one, three, and 12 months. The primary outcome in the trial was the improvement in active upper limb function (as measured by the Action Research Arm Test). In total, 283 participants (85%) had outcome data at three months, with 150 randomised to botulinum toxin and 133 to therapy alone.

Monetary benefit and utility valuations:
The utilities were assessed in the BoTULS trial, using the EQ-5D. Responses from the EQ-5D were converted to utilities using UK population tariffs.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the measure of benefit. These were calculated for the three-month time horizon, using the area-under-the-curve method.

Cost data:
The direct costs included those of botulinum toxin type A; upper limb therapy sessions, provided by chartered physiotherapists; other antispastic medication; the management of adverse events, from botulinum toxin or upper limb therapy, requiring hospitalisation; and other health care and social services, including day-patient hospital treatment, home care services, day care centre, general practitioner and nurse visits, therapy, and house modifications. The resource use was from case records, adverse event monitoring forms, and participant responses to specific resource use questions. The unit costs were from UK national sources. The costs were in UK £, for the year 2007.

Analysis of uncertainty:
Uncertainty in the mean cost-effectiveness was estimated using non-parametric bootstrapping and the construction of a cost-effectiveness acceptability curve. The impact of missing data on the results was investigated, using multiple imputation techniques.

Results
The average cost of botulinum toxin plus therapy was £2,170 (SD 2,007) per patient compared with £1,796 (SD 1,944) per patient on therapy alone. The QALYs gained over three months, with the addition of botulinum toxin, compared with therapy alone, were 0.004 per patient.

Compared with therapy alone, therapy plus botulinum toxin had an incremental cost-utility ratio of £93,500 per QALY gained.

The addition of botulinum toxin type A was cost-effective at a threshold of £50,000 per QALY gained in 41% of simulations, and at £100,000 per QALY gained in 42% of simulations. Imputing missing data had little impact on the results.

Authors' conclusions
The authors concluded that their analysis provided no evidence to suggest that botulinum toxin type A plus therapy was a cost-effective alternative to therapy alone.

CRD commentary
Interventions:
The interventions were reported clearly and in detail. The rationale for the selection of the comparators was clear, as the two treatments were the comparators in the randomised controlled trial, which supplied most of the evidence.

Effectiveness/benefits:
The effectiveness data were from the randomised controlled BoTULS trial. This was described, including the patient sample, randomisation, primary outcome measures, and follow-up rates. Well-conducted randomised controlled trials are considered to be the gold standard for assessing health care interventions; it seems that the effectiveness data were internally valid. QALYs were a valid benefit measure to capture the impact of the disease on the patients’ health, and they allow cross-disease comparisons. The utilities were estimated using a valid measure (EQ-5D) and they were appropriate to the UK setting.

Costs:
The authors explicitly reported that the perspective was that of the UK NHS and social services. For this perspective, all the relevant costs were included. The authors reported how the resource use was collected in the trial, and the sources for the unit costs. The price year and time horizon were given.

Analysis and results:
The outcome and cost data were from the BoTULS trial. The impact of uncertainty on the results was adequately tested, using non-parametric analyses. The authors assessed the impact of missing data on the results, using recommended methods. They reported that the relatively short time horizon for the analysis (three months) was the main limitation of their study. This was used rather than 12 months, because of the loss of participant responses, due to curtailment of the 12-month follow-up.

Concluding remarks:
The study methods were good, and they and the results were well reported. Given the scope of the analysis, the authors’
conclusions appear to be reasonable.

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