The cost-effectiveness of treatment for congenital diaphragmatic hernia
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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.

Health technology
The use of neonatal surgery and subsequent treatment, either with preoperative stabilisation, delayed repair, or extracorporeal membrane oxygenation (EMCO) (depending on the availability of treatments through time) in children with congenital diaphragmatic hernia (CDH).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with CDH.

Setting
The setting appears to have been hospital. The economic study was performed at the Sophia Children's Hospital, Rotterdam, The Netherlands.

Dates to which data relate
The effectiveness data were collected between 1997 and 1999, but corresponded to the period between 1969 and 1996. Some of the direct medical costs (those related to the period before the patients were discharged after having the diaphragm closed) were calculated for patients born between 1993 and 1996. The ECMO-related costs were obtained from a survey, the results of which were published in 1995. The direct medical costs related to the period after the patients were discharged with the diaphragm closed were obtained from a study published in 2001. The dates to which the rest of the costs related were not reported. The price year was not given.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Part of the cost data appears to have been collected retrospectively from the same, or at least partly the same, patient population as that used in the effectiveness analysis. However, some of the costs (those related to ECMO) were taken from a survey, and the sources of some other costs were not reported.

Study sample
There were 2 studies (see study design below). They shared the same intervention group, but had different control
Intervention group. No power calculations were reported if performed in the planning phase of the study in order to assure certain power. Patients who underwent treatment for CDH after 1969 were considered at analysis. The authors reported that patients born after 1996 were excluded in order to ensure a minimal follow-up period. In total, 285 patients underwent treatment for CDH, among whom 261 (92%) could be traced. Among the traced patients, 86 had died (33%) and 7 (2.7%) were mentally disabled. Questionnaires were sent to the remainder (n = 168). The response rate was 67% (n=112). Two patients were excluded from the CDH group because their CDH was not diagnosed during the neonatal period.

The first control group was a hypothetical control group, composed of CDH patients who were assumed not to have received treatment after birth, which was used to estimate the life expectancy and the quality-adjusted life years (QALYs) obtained by treated and non-treated CDH patients.

The second control group was selected from children who visited the day care department for minor day-case surgery, and was used to assess whether the problems suffered by CDH patients (such as respiratory difficulties, stomach ache and other disease-specific symptoms) were due to CDH or not. Questionnaires were sent to the caregivers of 72 children belonging to the latter control group. The response rate was 74%.

The authors did not provide evidence that the study sample used at analysis was representative of the study population.

Study design
There were two studies: first, an observational study with a hypothetical control group, carried out in a single centre and, second, a historical cohort study.

For the first study, the authors compared the historical records of the intervention group with a hypothetical control group of patients who did not receive treatment, in order to assess the effectiveness of the treatment for CDH;

For the second study, the authors compared the historical records of the intervention group with a selected control group of children who visited the hospital for minor day-case surgery. This was in order to assess whether the respiratory difficulties, stomach aches and other disease-specific symptoms suffered by CDH patients were consequences of CDH.

The period of follow-up was not reported, although it is likely to have been from birth until the moment when the effectiveness data were collected or until death.

Analysis of effectiveness
For the first study, the primary health outcomes assessed were: mean and median life expectancy of a patient with CDH among those who had already died when the effectiveness data were collected, and mean life expectancy of a patient with CDH (for all patients, assuming a life expectancy of 75.4 years for those CDH patients still alive when the effectiveness data were collected).

For the second study, when CDH and the selected control group were compared, the authors assessed: the symptom score for CDH and control group patients under the age of 19, which was calculated from numerous symptoms; the proportion of CDH and control patients under the age of 20 who were admitted to the hospital, and the proportion who consulted a physiotherapist in the 12 months prior to the questionnaires; the proportion of CDH and control patients between 20 and 44 years of age who consulted a general practitioner in the 12 months prior to the questionnaires, and the proportion who used prescribed medication during the 14 days prior to the questionnaires. The health state valuation of a life year with CDH and the number of QALYs for both treated and non-treated CDH patients were also assessed.

A disease-specific questionnaire was used to measure disease-specific symptoms, and it was applied directly to the patients if they were aged 12 or older, or otherwise to their parents. The Euroqol EQ-5D questionnaire was used to estimate the health values of a life-year and the number of QALYs gained, and this applied to patients aged 16 years or older, otherwise to their parents. A symptom score was constructed, considering the most relevant clinical items,
ranging from 0 to 45 (with 45 indicating the maximum number of symptoms).

For the comparison of responders and non-responders of the intervention group, age and gender were assessed.

**Effectiveness results**

For the first study, among patients who were dead when effectiveness data were collected the mean life span was 1.5 years, and the median was 3 days. The mean life expectancy of a patient with CDH (for all patients) was estimated to be 51.1 years.

The following significant differences in outcomes were found for the second study: the symptom score for CDH patients was 6.8 (n = 81; mean age = 10.3), while for control patients it was 4.9 (n = 53; mean age = 7.4).

The proportions of CDH and control patients under the age of 20 who were admitted to the hospital were, respectively, 17% and 4%.

The proportion of CDH patients who consulted a physiotherapist in the 12 months previous to the questionnaires was 13, while 7% of the control patients visited a physiotherapist during the same period.

The proportion of CDH and control patients between 20 and 44 years of age who consulted a general practitioner in the 12 months prior to the questionnaires was, respectively, 96 and 74.

In total, 41% of CDH patients used prescribed medication during the 14 days prior to the questionnaires, while for control patients this percentage was 10%.

The health state valuation of a life year with CDH was estimated to be 0.92 for CDH patients from 5 to 15 years, and 0.91 for older CDH patients. The mean health state value for all CDH patients was 0.91.

CDH patients who received treatment gained 46.5 QALYs when a lifetime period was considered, while the authors assumed that the number of QALYs for those CDH patients who did not receive treatment would be zero.

**Clinical conclusions**

CDH patients had a higher number of symptoms, admissions to the hospital, and visits to doctors (physiotherapists and general practitioners) than control patients. A higher number of CDH patients received medication, when compared to control patients.

**Methods used to derive estimates of effectiveness**

Authors’ assumptions were used to derive life expectancy measures.

**Estimates of effectiveness and key assumptions**

In order to assess the effectiveness of treatment for CDH, the authors assumed that a child with CDH would die shortly after birth due to inability to obtain sufficient oxygen, and therefore the number of QALYs for those patients would be zero. This assumption was supported by the findings about the life expectancy for non-surviving CDH patients (see 'Effectiveness Results’ section, reported above). Those patients surviving the first few years were assumed to have a normal life expectancy (75.4 years at birth, according to Statistics Netherlands, 1997).

**Measure of benefits used in the economic analysis**

The measure of benefit used in the economic analysis was QALYs, which were calculated for a lifetime period. The method of valuation used was the EQ-5D questionnaire. Questionnaires were sent to 175 patients who were alive at the time the study was performed, and 112 CDH patients returned them.
Direct costs
The direct costs included in the study were those of the health service and patient, and included: direct medical costs and direct non-medical costs. Some, but not all, of the resource quantities were reported separately from the costs. The direct medical costs included costs for hospital days, laboratory tests, diagnostic radiology, surgeries, intercollegial consultations, visits to the outpatient department, ECMO-related costs, and costs incurred after the child was discharged with the diaphragm closed (such as costs for hospital admissions, visits to the outpatient department, consultations with a general practitioner, and consultations with a physiotherapist). Direct non-medical costs included the transportation costs, which patients and their families incurred.

The direct medical costs before the patients were discharged with the diaphragm closed were obtained from a sample population of 38 patients who were born between 1993 and 1996. The costs of ECMO were obtained from a Dutch survey on ECMO in neonates. The direct medical costs relating to the period after the patients were discharged with the diaphragm closed were obtained from a published study. The authors did not report the source of the direct non-medical costs included in the analysis. Direct costs were discounted at a rate of 5% and 0%. The study reported average costs. The authors did not report the price year. No power analysis was reported.

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect Costs
The indirect costs included the productivity losses of CDH patients and their parents or caregivers. This was appropriate to the study question and perspective. Quantities were reported separately from the costs (although not all the costs for the different categories of indirect costs included in the analysis were reported). The resource quantities reported were: the percentage of caregivers having paid work and the mean number of hours of paid work per week; the percentage of caregivers who had to give up paid work in order to care for their child and the mean number of hours of paid work that were given up; the percentage of caregivers who gave up paid work to care for a child as a consequence of CDH, and the percentage of hours that had to be given up; the mean number of hours spent on unpaid work per week; and the mean number of hours of unpaid work lost due to CDH and taking care of their child.

A discount rate of 5% was applied because the productivity losses were estimated for a lifetime period. The price year was not reported. The estimation of the indirect costs seems to have been based on actual data (it appears that the data were collected from the same sample population as that used for the effectiveness analysis of the symptoms of CDH).

Currency
Euro.

Sensitivity analysis
The only sensitivity analysis reported was varying the discount rate for costs and benefits between 0% and 5%.

Estimated benefits used in the economic analysis
The authors reported the incremental number of QALYs gained among CDH patients who received treatment when compared to those who did not receive any treatment. The number of QALYs gained for CDH treated patients was 46.5. This benefit was calculated considering a lifetime period. When a 5% discount rate was considered, the number of QALYs gained by CDH treated patients, when compared to non-treated patients, was 17.5.

Cost results
The total costs of treatment for CDH were Euro 42,658 (Euro 47,495 without discounting).
Synthesis of costs and benefits
The authors combined benefits and costs by means of an incremental cost-effectiveness ratio (ICER), which considered the cost per QALY gained when CDH patients were treated in comparison to "no treatment". This ICER was Euro 2,434 per QALY at a discount rate of 5%. When no discounting was considered, the ICER was Euro 1,022 per QALY.

Authors' conclusions
The authors concluded that treatment for CDH has a favourable cost-effectiveness ratio.

CRD COMMENTARY - Selection of comparators
The authors justified the comparator chosen, no treatment, because there is no realistic alternative treatment for CDH patients. You, as a user of this database, should consider if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The designs of the studies were (1) an observational study with a retrospective intervention group and a hypothetical control group, (2) a historical cohort study with a retrospective intervention group and a selected, prospective control group. The authors stated that only minor social and demographic differences were found between CDH survivors and control patients, but they were shown to be different at least in terms of age. It cannot be clearly determined whether the higher number of symptoms among CDH patients, and the higher number of CDH patients visiting the doctor and receiving medication, in comparison with control patients, were a consequence of the disease or other confounding factors not considered at analysis.

The study sample was not shown to be representative of the study population. The authors did not provide any evidence to support the assumption made regarding the life expectancy of CDH children who received treatment (that it was equal to the life expectancy of an average individual). These limitations introduce uncertainty into the reliability of the conclusions of the effectiveness analysis. Furthermore, the effectiveness results are the average outcomes from a mix of 'only surgery' and 'surgery + ECMO' which complicates the interpretation of the results. Furthermore, the effectiveness data corresponded to a long period, and there may have been some changes through time that may also have influenced the results obtained.

Validity of estimate of measure of benefit
The QALY measure was derived from the life expectancy data and the quality of life scores. Since there is uncertainty surrounding the life expectancy assumption of CDH patients, this uncertainty is also carried over into the QALY score.

Validity of estimate of costs
Future health care costs of unrelated diseases were also excluded, but this was appropriate and does not seem to have influenced the results obtained. Not all the resource quantities were reported separately from the costs, not all the dates to which costs related and their sources were reported, and the price year was not given. These points introduce uncertainty into the reliability of the conclusions and hinder reflation exercises to other settings. Moreover, no statistical analyses or sensitivity analyses of the resources and costs implied in the study were performed.

Other issues
The authors made comparisons of their findings with those from other studies. The authors questioned the usefulness of treating patients with ECMO, which may be somewhat controversial as results from previous studies have shown that it may improve survival rates in neonates, but at the same time, it may increase morbidity and late deaths. As the authors stated, the fact that some direct costs were calculated from a sub-sample of 38 patients may mean that the conclusions are not generalisable to patients born in a different period.

Implications of the study
Treatment for CDH has a favourable cost-effectiveness ratio.

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