Sumatriptan: economic evidence for its use in the treatment of migraine, the Canadian comparative economic analysis
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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 sumatriptan in the treatment of patients with migraine. Six alternative strategies with sumatriptan were analysed:

- Subcutaneous sumatriptan, 6mg;
- Oral sumatriptan, 100 mg;
- Oral sumatriptan, 50 mg;
- Sumatriptan nasal spray, 10 mg;
- Sumatriptan nasal spray, 20 mg;
- Sumatriptan suppository, 25 mg.

Under these sumatriptan strategies, it was considered that patients with moderate or severe migraine would be treated with sumatriptan, whereas those with mild migraine would be treated with customary therapies.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised Canadian patients with migraine.

Setting
The setting appears to have been the community, primary care and/or a hospital. The economic study was performed in Canada.

Dates to which data relate
The primary studies from which the effectiveness data were obtained were published between 1991 and 1997. The dates to which the cost data related were not reported. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.
Modelling
A Monte Carlo simulation was used to model the outcomes for a patient population of 10,000 people, with the demographic characteristics of the Canadian population. Each of the sumatriptan formulations and customary therapy were compared. The time period considered in the model was one year. The authors also made some assumptions. For example, people with moderate or mild migraine would not visit an emergency room, neither would they be hospitalised. Also, side effects would manifest themselves either as time lost, increased duration of symptoms and/or additional medical resource use.

Outcomes assessed in the review
The health outcomes assessed in the review for both customary therapy and sumatriptan were:

the severity of migraine days, in terms of the percentage of males and females experiencing mild, moderate and severe migraine days;

the frequency of migraine days, in terms of the mean annual numbers of days that male and females experienced migraine;

the effects of the strategies on the duration of symptoms, in terms of the probability of males and females having a physician visit when experiencing either a moderate or a severe migraine day; and

the probability of males and females having an emergency visit or being hospitalised when having a severe migraine day.

These health outcomes were included as key parameters in the model to estimate the annual duration of symptoms, in terms of the average number of days per year that a patient experienced migraine symptoms.

Study designs and other criteria for inclusion in the review
The effectiveness data were mainly obtained from a prospective sequential multinational study (see Other Publications of Related Interest). The authors also considered one randomised, double-blind study, an open longitudinal study, and at least ten other primary studies, the designs of which were not reported.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Some of the results obtained (i.e. the reduction in doctor visits among patients receiving sumatriptan) were compared with other published results, which may have validated part of the results reported in the study. The authors reported using data from as many trials as possible in order to minimise the potential measurement differences between the efficacy of pain relief with sumatriptan.

Number of primary studies included
At least 13 primary studies were included in the review.

Methods of combining primary studies
The results of the primary studies were combined using a narrative method. Adjustments were made to estimate the probability of visits to the doctor, to the emergency room and of being hospitalised, according to the severity of migraine.

Investigation of differences between primary studies
Some of the results reported (such as the reduction in visits to doctors among patients receiving sumatriptan, compared with patients under conventional therapy) were compared with other published and unpublished studies, in order to minimise the differences.

Results of the review
The mean annual number of days experiencing migraine under customary therapy was 82.5 days for males, and 77.4 for females. The corresponding values for patients receiving sumatriptan were 61.0 days (males) and 55.3 days (females), respectively.

Under customary therapy, 31.2% of men experienced mild migraine days, 44.1% moderate migraine days, and 24.7% severe migraine days. For women, these percentages were 24.9% (mild), 44.3% (moderate) and 30.8% (severe), respectively. For patients receiving sumatriptan, 19.4% of men experienced mild migraine days, 46.8% moderate migraine days, and 33.8% severe migraine days. Among women, these percentages were 17.9% (mild), 44.7% (moderate) and 37.4% (severe), respectively.

Under customary therapy, the probabilities of a man visiting the physician were 0.008 because of a moderate migraine day and 0.023 because of a severe migraine day. Among women, these probabilities were 0.017 (moderate) and 0.047 (severe), respectively. Among patients receiving sumatriptan, these probabilities were 0.004 (moderate) and 0.01 (severe) for men, and 0.008 (moderate) and 0.021 (severe) for women.

The probability of visiting the emergency room due to a severe migraine day was 0.007 for men receiving customary therapy and 0.013 for women receiving customary therapy. For the sumatriptan patient group, this probability was 0.003 for men and 0.006 for women.

The probability of being hospitalised when experiencing a severe migraine day was 0.003 for men and 0.002 for women under customary therapy, and 0.002 (men) and 0.001 (women), respectively, under sumatriptan therapy.

Methods used to derive estimates of effectiveness
The authors made assumptions to derive estimates of the effectiveness.

Estimates of effectiveness and key assumptions
The authors stated that, in order to estimate outcomes for the oral, nasal and suppository formulations, some factors were assumed to be equal between the sumatriptan formulations. For example, medical service usage, frequency of migraine days, severity of migraine days and any adverse event with sumatriptan.

Measure of benefits used in the economic analysis
The measure of health outcome used in the economic analysis was the duration of migraine symptoms. This was modelled using Monte Carlo simulation for a patient population of 10,000 individuals during one year of follow-up.

Direct costs
Some, but not all, of the resource quantities were reported separately from the costs. The direct costs included in the analysis were those of the health service. Also considered were physician visits, emergency room visits, hospitalisation costs and drug costs. These costs were estimated according to the severity of the symptoms. The costs were estimated from actual data (both published and unpublished). The source of the costs of the physician visits, emergency room
visits and hospitalisations were obtained from the Canadian physician fee schedules, and the Ontario Case Costing Project (unpublished). The sources of the drug cost data were the provincial drug formularies. Proxy costs were used to estimate nasal sumatriptan 10 mg and suppository sumatriptan 25 mg, since these drugs were not available in Canada. Discounting was not performed, but, as the authors stated, it was irrelevant as they considered a time horizon of one year. The price year was 1998.

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

**Indirect Costs**
When a societal perspective was considered, the indirect costs included in the analysis were those derived from the time lost due to migraine (both paid and unpaid work time), and leisure time. In the baseline analysis, leisure time was valued with a cost equal to zero. The time lost was estimated using results from the Monte Carlo simulation. The quantities were reported separately from the costs. The authors did not report the source used to value the indirect costs. The price year may have been the same as for the direct costs (1998).

**Currency**
UK pounds sterling (£) and Canadian dollars ($). The conversion rate used was Can$1 = 0.46.

**Sensitivity analysis**
Sensitivity analyses were conducted on some of the key parameters included in the Monte Carlo simulation. These included the efficacy of sumatriptan in reducing time lost due to migraine symptoms, the frequency of migraine days, the acquisition price of sumatriptan, non-prescription medical costs, time lost, proportion of wages lost, value of unpaid and paid work, and value of leisure time. One-way sensitivity analyses appear to have been carried out. The area of uncertainty investigated was variability in the data.

**Estimated benefits used in the economic analysis**
It was estimated that the average number of hours per year with migraine symptoms was:

- 632 hours for patients treated with customary therapy;
- 317 hours for patients treated with subcutaneous sumatriptan, 6 mg;
- 395 hours for patients treated with oral sumatriptan, 50 mg;
- 355 hours for patients treated with oral sumatriptan, 100 mg;
- 444 hours for patients treated with sumatriptan nasal spray, 10 mg;
- 397 hours for patients treated with sumatriptan nasal spray, 20 mg; and
- 407 hours for patients treated with sumatriptan suppository, 25 mg.

The authors reported that the costs of side effects were excluded since they were included in other areas, as time lost, increased duration of symptoms and/or additional medical resource use. The authors also reported the average time lost (in terms of work time, unpaid work time and leisure time) due to migraine under each treatment strategy, although they did not specify the time period considered for this estimation.

**Cost results**
The total medical costs and total costs (including indirect costs, i.e. paid and unpaid work) were, respectively:
for customary therapy, 130 (Can$282) and 1,037 (Can$2,255);
for subcutaneous sumatriptan, 6 mg, 940 (Can$2,043) and 1,346 (Can$2,926);
for oral sumatriptan, 100 mg, 391 (Can$849) and 849 (Can$1,845);
for oral sumatriptan, 50 mg, 365 (Can$793) and 875 (Can$1,903);
for sumatriptan nasal spray, 10 mg, 351 (Can$763) and 928 (Can$2,018);
for sumatriptan nasal spray, 20 mg, 358 (Can$778) and 872 (Can$1,895); and
for sumatriptan suppository, 25 mg, 349 (Can$759) and 876 (Can$1,904).

From a societal perspective, the incremental costs (or incremental savings), when compared with customary therapy,
were:
for subcutaneous sumatriptan, 6 mg, 309 (Can$671);
oral sumatriptan, 100 mg, -189 (-Can$410);
oral sumatriptan, 50 mg, -162 (-Can$352);
sumatriptan nasal spray, 10 mg, -109 (-Can$237);
sumatriptan nasal spray, 20 mg, -166 (-Can$360); and
sumatriptan suppository, 25 mg, -161 (-Can$351).

The authors stated that the costs of side effect were included in areas such as time lost, increased duration of symptoms
and/or additional medical resource use.

**Synthesis of costs and benefits**

Cost-effectiveness ratios (CERs) were calculated for those sumatriptan strategies that did not dominate customary
therapy. Cost benefit ratios (CBRs) were also estimated, which related the increase in pharmaceutical treatment costs to
the decrease in the costs of time lost from activities and other medical costs.

When a societal perspective was considered, the CER for subcutaneous sumatriptan 6 mg, compared with customary
therapy, was 98p (Can$2.13) per reduced hour of symptoms. All the remaining sumatriptan alternatives presented
higher benefits and lower societal costs when compared with customary therapy.

When only the direct costs were considered, the CER for subcutaneous sumatriptan 6 mg was 2.57 (Can$5.59) per
reduced hour of symptoms. The CER ranged from 94p (Can$2.04) to 1.18 (Can$2.56) for the remaining sumatriptan
strategies.

The CBR for subcutaneous sumatriptan 6 mg was 71p (Can$1.55). For the remaining sumatriptan strategies, less than
46p (Can$1) had to be spent in incremental drug costs in order to achieve the same savings.

Results of the sensitive analyses showed that for a decrease of 50% in the time lost due to migraine symptoms, the
incremental costs related to subcutaneous sumatriptan 6 mg remained positive. With a 50% increase in the time lost, the
incremental savings of the other sumatriptan strategies were maintained. The unpaid work (valued at 5.28 or Can$11.48
per hour in the baseline analysis) needed to be valued at 17/hour (Can$36/hour) for subcutaneous sumatriptan in order
to reach a cost neutral position. If leisure time was valued at 2.76/hour (Can$6/hour), the costs of subcutaneous
sumatriptan would drop to 134 (Can$292), while there would be savings ranging from 229 (Can$497) to 347 (Can$754)
for the other sumatriptan alternatives. For subcutaneous sumatriptan to be cost neutral, leisure time should be valued at
17/hour (Can$36/hour).
Authors' conclusions
Sumatriptan is expected to reduce considerably the impact of migraine episodes on the patients' work and non-work activities, with significant savings associated with a lower lost productivity.

CRD COMMENTARY - Selection of comparators
It appears that the comparator (customary therapy) was chosen because it represented current practice in the authors' setting. However, the authors did not report what this customary therapy consisted of, which presents difficulties in interpreting any comparison of sumatriptan with this customary therapy. You should consider what health technologies for the treatment of patients with migraine are available in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken, and, as such, may not have been conducted in a systematic fashion to identify relevant research and minimise bias. The authors appear to have mainly chosen a single study on which to base the collection of the effectiveness data to be included in the Monte Carlo simulation, validating some of the results according to those from other studies.

As the authors stated, the probability distributions constructed for the analysis were based on documented data, which may have made the results of the study more realistic. The validity of the assumption that all formulations of sumatriptan were equal in terms of medical service usage, frequency and severity of migraine days, and adverse events was unclear, and was not justified by the authors. The authors also assumed some factors to be equal between the sumatriptan formulations in order to estimate outcomes for the oral, nasal and suppository formulations, but they did not justify this assumption.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a Monte Carlo simulation, which seems to have been appropriate.

Validity of estimate of costs
All the categories of cost relevant to the perspectives adopted appear to have been included in the analysis. Not all of the resource quantities were reported separately from the costs, which hinders reflation exercises to other settings. The price year was given. The authors reported that they adopted a conservative approach, which favoured the customary therapy since they did not assign a monetary value for leisure time. For the calculation of the societal costs, the authors reported the number of lost hours from paid work, unpaid work and leisure due to migraine symptoms, separately from the cost values assigned to them. However, the total time lost did not coincide with the annual duration of symptoms, and the authors did not state what proportion of the duration of symptoms was considered as time lost.

Other issues
The demographic characteristics of the Canadian population were considered when running the Monte Carlo simulation. Therefore, the results are not directly generalisable to other settings with demographic characteristics different from those for Canada. Moreover, as the authors did not report what the customary therapies consisted of, it would be difficult to extrapolate the results of the study to other settings. Some comparisons of the results of the study with those from other studies were presented.

Implications of the study
The results of the study suggest that sumatriptan may be a good strategy for the treatment of patients with migraine. However, it is difficult to reach clear conclusions to extrapolate to other settings considering that customary therapy was not defined, the study was based on demographic characteristics of the Canadian population, and there were other weaknesses in the study.
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