Cost–Utility Analysis of Home Mechanical Ventilation in Patients with Amyotrophic Lateral Sclerosis

Ondřej Gajdoš *, Martin Rožánek ☑, Gleb Donin ☑ and Vojtěch Kamenský

Department of Biomedical Technology, Faculty of Biomedical Engineering, Czech Technical University in Prague, nám. Sítná 3105, 272 01 Kladno, Czech Republic; rozanek@fbmi.cvut.cz (M.R.); gleb.donin@fbmi.cvut.cz (G.D.); vojtech.kamensky@fbmi.cvut.cz (V.K.)
* Correspondence: ondrej.gajdos@fbmi.cvut.cz

Abstract: Amyotrophic lateral sclerosis is a disease with rapid progression. The use of mechanical ventilation helps to manage symptoms and delays death. Use in a home environment could reduce costs and increase quality of life. The aim of this study is a cost–utility analysis of home mechanical ventilation in adult patients with amyotrophic lateral sclerosis from the perspective of healthcare payers in the Czech Republic. The study evaluates home mechanical ventilation (HMV) and mechanical ventilation (MV) in a healthcare facility. A Markov model was compiled for evaluation in a timeframe of 10 years. Model parameters were obtained from the literature and opinions of experts from companies dealing with home care and home mechanical ventilation. The cost–utility analysis was carried out at the end of the study and results are presented in incremental cost–utility ratio (ICUR) using quality-adjusted life-years. Uncertainty was assessed by one-way sensitivity analysis and scenario analysis. The cumulative costs of HMV are CZK 1,877,076 and the cumulative costs of MV are CZK 7,386,629. The cumulative utilities of HMV are 12.57 quality-adjusted life year (QALY) and the cumulative utilities of MV are 11.32 QALY. The ICUR value is CZK-4,403,259. The results of this study suggest that HMV is cost effective.

Keywords: cost–utility analysis; Markov model; home mechanical ventilation; amyotrophic lateral sclerosis

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a condition characterized by degeneration of lower and upper motor neurons resulting in progressive weakness of skeletal muscles including the muscles used for breathing. This condition is rapidly progressive and, on average, within 2 to 4 years from the onset of symptoms, the failure of breathing functions due to respiratory muscle damage becomes a frequent cause of death. Only 5–10% of patients survive more than 10 years. Although there is still no existing treatment for this disease, various stages of the disease are still being studied, so some types of treatment including mechanical ventilation may help to relieve symptoms and thus delay death [1–4].

In ALS, both non-invasive and invasive mechanical ventilation is being employed. The non-invasive ventilation uses face or nose masks and a volume-cycled or two-cylinder pressure-restricted ventilator to ensure the intermittent overpressure to support ventilation. Tracheostomy ventilation is highly demanding and is associated with risks that put pressure on patients themselves and their caregivers; however, it may prolong survival for many years [3].

The results of foreign studies show that an ideal place for mechanical ventilation (MV) is home care since it lowers costs and increases the quality of life and integration in the community [5]. The cost of maintaining a patient in home care is high but certainly significantly lower than the cost of long-term hospitalization [6].

In the Czech Republic, the transfer of patients, including ALS patients, to home care began in the year 2003. However, experience has shown that the process is very lengthy...
and inefficient. This is also proved by the fact that there are only about 125 patients with various diagnoses using non-invasive home mechanical ventilation (HMV). In the case of an effective system that can ensure the provision of invasive HMV on both professional and financial levels, we could expect a 5-times higher number of patients using invasive HMV [7]. Currently (from 1 December 2019) there is only one official methodology for providing and financing invasive HMV in the Czech Republic which, however, does not take into account non-invasive HMV. As the foreign guidelines prove [8–11], it is necessary to address the provision of invasive and non-invasive approaches simultaneously, namely in patients with ALS due to the rapid progress of their condition. The non-invasive HMV may, in the Czech Republic, be covered from public health insurance through payment of the medical device using a voucher [12].

The transfer of a patient to a home environment and the subsequent care is a complex process which should be assessed comprehensively and the decision to provide care in the form of HMV should therefore be based on clear evidence. There are a large number of diagnoses for which it is appropriate to use home mechanical ventilation. Amyotrophic lateral sclerosis was used as it is the most common diagnosis from the neuromuscular group of diseases [13–15]. The aim of this study is to perform a cost–utility analysis (CUA) of home mechanical ventilation in adult patients with amyotrophic lateral sclerosis in comparison with mechanical ventilation in a healthcare facility from the perspective of a healthcare payer in the Czech Republic.

2. Materials and Methods

To evaluate the cost-effectiveness of HMV from the perspective of a healthcare payer in ALS patients, a state-transition model in the form of a Markov decision tree was created. The model was created on the basis of proposed procedures [8–11] and consultations with experts participating in HMV treatment in the Czech Republic.

The model consists of two Markov decision trees, each of them representing one method of treatment of ALS patients requiring ventilation support, in both a healthcare facility and a home environment. A state diagram of the Markov model for the home care (“HMV”) stems from 4 states and the state diagram of the Markov model for the care in a healthcare facility (“MV”) stems from 3 states (Figure 1).

![State diagram of the Markov model](image-url)

Figure 1. State diagram of the Markov model (a) home mechanical ventilation, (b) mechanical ventilation.
Due to the nature of the condition and studies analyzing survival curves, a 10-year timespan was selected for the simulation. Since there are rapid changes in a patient’s condition in the stage of the disease requiring ventilation support, the 10-year timespan was simulated in 120 cycles, i.e., one cycle corresponds to one month.

A Danish study [16] was employed to acquire the probability of transition through the death branch (“Death”), or survival/continuation in the treatment branch (“Survival”), for the health state of non-invasive HMV (“NIV”) and the health state of invasive HMV (“IV”). The probability was obtained by extracting relevant cumulative Kaplan–Meier survival curves concerning the care using non-invasive or invasive mechanical ventilation. To obtain the probability of a patient’s death while on the non-invasive mechanical ventilation (“probability_death_NIV”), a Weibull probability distribution was determined based on the value of the log-likelihood ratio. To obtain the probability of a patient’s death while on the invasive mechanical ventilation (“probability_death_IV”), log-normal probability distribution was determined based on the value of the log-likelihood ratio.

Based on the results of a foreign study [17] observing patients with the non-invasive mechanical ventilation and their transition to the invasive method, the probability of transition from non-invasive to invasive mechanical ventilation (“Transition to IV”) was determined for both Markov trees. The probability of a transition of a patient in a worsening condition while being on the invasive HMV to a hospital (“hospitalization”) and the probability of transition back to a home environment were estimated on the basis of opinions of experts and their internal data on patients. According to the expert opinion (agency ProCare Medical s.r.o.), there are no differences in clinical parameters of a patient in a home environment and a healthcare facility, therefore the Markov tree “HMV” and Markov tree “MV” use the same values for the same health conditions and transitions. Health states and probabilities of mutual transitions are presented in Table 1.

Table 1. Health states and probabilities of mutual transitions.

| Health State HMV | Branch | Probability | Data Source | Health State | Probability | Data Source |
|------------------|--------|-------------|-------------|--------------|-------------|-------------|
| NIV              | Survival | Evaluation to the sum of 1 | [16] | NIV | 0.99812 | [17] |
|                  | Death | Weibull probability | | Death | 0.00188 | [17] |
| IV               | Survival | Evaluation to the sum of 1 | – | IV | 0.999 | Expert estimation ¹ |
|                  | Death | Log-normal probability | [16] | Death | – | – |
| Hospitalization  | – | – | – | Hospitalization | 0.01 | Expert estimation ¹ |
|                  | – | – | – | IV | 0.95 | Expert estimation ¹ |
|                  | – | – | – | Death | 0.04 | Expert estimation ¹ |

| Health state MV | Branch | Probability | Data source | Health state | Probability | Data Source |
|-----------------|--------|-------------|-------------|--------------|-------------|-------------|
| NIV             | Survival | Evaluation to the sum of 1 | [16] | NIV | 0.99812 | [17] |
|                 | Death | Weibull probability | | Death | 0.00188 | [17] |
| IV              | – | – | – | IV | Evaluation to the sum of 1 | [16] |
|                 | – | – | – | Death | Log-normal probability | [16] |
| Death           | – | – | – | – | – | – |

¹ Experts from company dealing with home care and home mechanical ventilation in the Czech Republic.
The creation and evaluation of the model was performed through a computer software TreeAge Pro Healthcare [18] and through R program [19].

2.1. Cost Identification

The non-invasive HMV costs consist of the HMV technical support costs, nursing care costs and other costs. Bilevel positive airway pressure (BiPAP) devices with a backup respiratory frequency or volume support are used to provide non-invasive HMV. The average price of a BiPAP device is CZK 62,424 and its payment is limited to 7 years. The device is provided with all the accessories such as masks, hoses, humidifiers and filters. The average payment for the masks is CZK 4202, for the hoses CZK 967, for the heated humidifiers CZK 1500 and for the filters CZK 699. Payment due date for accessories is in most cases once a year. The technical support costs were calculated as average costs pursuant to Act No. 48/1997 Coll., on public health insurance [20].

Nursing care costs and other costs (payments for GP visits, payments for medication and other medical materials, rehabilitation care and acquisition costs of medical devices) were analyzed on the basis of data provided by a health insurance company (Zaměstnanecká pojišťovna Škoda) for the year 2019. The obtained data were averaged for the purposes of the model and on the basis of average annual inflation expressed by the increase in an average consumer price index; this amount was recalculated for the year 2020. The overall average costs per patient with the non-invasive HMV, along with estimated costs for the year 2020, are presented in Table 2.

Table 2. The overall average costs per patient with the non-invasive home mechanical ventilation for the year 2020.

| Type of Costs           | 1 Day  | 1 Month (30 Days) | 1 Year (365 Days) |
|-------------------------|--------|-------------------|-------------------|
| Technical support       | CZK 45 | CZK 1338          | CZK 16,286        |
| Nursing care and other costs | CZK 524 | CZK 15,720       | CZK 191,266       |
| **Total**               | CZK 569 | CZK 17,058        | CZK 207,552       |

The invasive HMV costs consist of HMV technical support costs, costs of nursing care and other costs. Technical support costs are paid according to one of two payment codes based on a patient’s condition, on the basis of the methodology of general health insurance company CR (VZP) [21]. The nursing care of a patient is ensured by a “certified” provider of HMV and a home care nurse as for the field of expertise (expertise 925). The provided care is governed by a valid payment catalogue of VZP and the relevant decree on setting a one point value for the given year [22]. For the year 2020, the point value was determined by Decree no. 268/2019 Coll., on determination of the point value, the amount of payments of provided services and regulatory restrictions for the year 2020, and it corresponds to the amount of CZK 1.07 [23]. For the purposes of the model, the highest possible use of the nursing care in the length of 180 min a day was taken into account. The analysis of personal costs (payments for GP visits, costs of medication and other medical materials, rehabilitation care and acquisition costs of medical devices) stems from the materials of a university hospital in Brno which calculated these costs for the year 2012. On the basis of average annual inflation rates expressed by the increase in the average consumer price index, this amount was recalculated for the year 2020 [24–26]. The overall costs per patient with invasive HMV with estimated costs in the year 2020 are presented in Table 3. The costs are divided according to technical support for mobile and immobile patients.
Table 3. The overall costs per patient with invasive home mechanical ventilation for the year 2020.

| Type of Costs        | Mobile Patient 1 Month (30 Days) | Mobile Patient 1 Year (365 Days) | Immobile Patient 1 Month (30 Days) | Immobile Patient 1 Year (365 Days) |
|----------------------|---------------------------------|---------------------------------|------------------------------------|-----------------------------------|
| Technical support    | CZK 20,550                      | CZK 250,025                     | CZK 23,550                         | CZK 286,525                      |
| Nursing care         | CZK 38,809                      | CZK 472,175                     | CZK 38,809                         | CZK 472,175                      |
| Other costs          | CZK 68,192                      | CZK 829,671                     | CZK 68,192                         | CZK 829,671                      |
| **Total**            | CZK 127,551                     | CZK 1,552,006                   | CZK 130,551                        | CZK 1,588,371                    |

The mechanical ventilation costs in a healthcare facility include treatment days with a point value for the follow-up intensive care unit (NIP) and follow-up ventilation care (NVP). This medical care is, pursuant to Act No. 372/2011 Coll. on healthcare services and conditions on their provision [27], defined as inpatient care, since it is not possible to provide outpatient care and hospitalization is necessary. The point value of treatment days (ODs) is also assigned on the basis of a category of a medical facility provider, with the overhead costs determined for these treatment days by Decree No. 134/1998 Coll., issuing the list of medical performances with relevant point values [28]. For the year 2020, the point value of overheads for all the mentioned ODs is set at 191.86 points. The point value is determined by Decree No. 268/2019 Coll. on the point value determination of the amount of payments for covered services and regulatory restrictions for the year 2020, corresponding to the amount of CZK 1.18 [29]. NIP may be reported only for 90 days and is followed by the report of NVP. Performances with the point values and payments including overheads for the year 2020 are presented in Table 4.

Table 4. Payments for treatment days of long-term nursing care including the value of overheads for the year 2020.

| Performance Code | Medical Performance       | Point Value | Payment for 1 Day |
|------------------|---------------------------|-------------|-------------------|
| OD 00017         | Follow-up intensive care  | 9364        | CZK 11,276        |
| OD 00015         | Follow-up ventilation care| 6150        | CZK 7483          |

The model also required the analysis of a patient’s transport costs between a healthcare facility and their home. The data were provided by the emergency medical services of Pilsen region. On the basis of consultations with various experts, a standard patient with non-invasive HMV in a condition demanding intubation and transport to a healthcare facility was first identified for the purposes of transfer costs analysis and modelling. The overall costs consist of medical performances, transport services, separately charged materials or separately charged medication. The other situation describes a patient already with invasive HMV in a condition requiring transport to a healthcare facility. After consulting the experts, this case would not require intubation and some of the medication would not be used, however, overall costs would correspond to the same amount as the patient with non-invasive HMV. The overall costs per patient with invasive and non-invasive HMV, from a healthcare payer perspective, are presented in Table 5.

Table 5. The overall transport costs.

| Type of Costs                          | Costs     |
|----------------------------------------|-----------|
| Medical performance                    | CZK 2055.46|
| Transport services                     | CZK 2725.68|
| Separately charged material or medication | CZK 450  |
| **Total**                              | CZK 5231.14|
Each health state is assigned a monthly cost incurred by healthcare payers. Furthermore, the model includes the transitional costs of the healthcare payer for the transport of the patient in case the patient needs to be hospitalized or transported to home care. A 3% discount rate was chosen to adjust future costs [25,30]. The costs used in the care model are listed in Table 6.

2.2. Utility Identification

A utility value defining health state “NIV” of the Markov tree “HMV” was derived from a foreign study [31] evaluating quality of life by using the questionnaire SF-36 every 3 months for 1.5 years. However, in order to evaluate the cost-effectiveness analysis, it is necessary to convert the obtained values to one value, namely the index value of the questionnaire EQ-5D. The conversion was performed using an algorithm from a study [32] addressing the conversion of dimensions of the SF-36 questionnaire to the values of the EQ-5D questionnaire. Since the time period was set to 10 years, it was necessary to interpolate the obtained values with a curve, which was again performed in the R program. The average age of patients with ALS (neuromuscular condition) covered by the study was 42.8 years. For the purposes of modelling by setting the lifespan at 120 years, a curve of values from 42.8 to 120 years was interpolated, by which the quality of life would correspond to the value 0.

Rousseau et al. [33], examining the quality of life between non-invasive and invasive methods of ventilation support in patients with ALS, states that the differences in the quality of life are insignificant. The health state “IV”, being “HMV” in the Markov tree, was thus assigned with the same values as the health condition “NIV”. Based on the conclusions of foreign studies [6,34–42] proving improvements in the quality of life of patients in home environments, and based on consultations with experts, the utility value for the health states “MV” in the Markov tree and the health state “Hospitalization” decreased by 10%. As with the costs, a 3% rate was selected to discount the benefits [25,30].

2.3. Selection of Initial Distribution of Patients

The initial distribution stems from a study [16] providing probabilities of transition through the death branch (“Death”), or survival/continuation in the treatment branch (“Survival”) respectively, for the health conditions of non-invasive (“NIV”) and invasive (“IV”) mechanical ventilation.

2.4. Cost–Utility Analysis

The incremental cost–utility ratio (ICUR) calculated according to the following formula was used to present the CUA results:

\[
\text{ICUR} = \frac{(\text{Cost}_1 - \text{Cost}_2)}{(\text{QALY}_1 - \text{QALY}_2)} = \frac{\Delta \text{Cost}}{\Delta \text{QALY}},
\]

(1)
Cost\textsubscript{1} and QALY\textsubscript{1} represent the evaluated intervention and Cost\textsubscript{2} and QALY\textsubscript{2} represent the comparator.

2.5. Sensitivity Analysis

A one-way sensitivity analysis was calculated. Due to the low number of probands and lack of further information, it was decided to analyze the sensitivity to the given parameters in the range of 30\%. All the input parameters except for the changes in the quality of life values in HMV were gradually changed. A sensitivity analysis in which the discount rate was changed to 0\% and 5\% was also conducted.

2.6. Scenario Analysis

A scenario analysis performs the alteration in the initial distributions entering the model. The entire population was not divided in the individual states but the whole cohort (100\%) began in the state of non-invasive (“NIV”) mechanical ventilation.

3. Results

3.1. Markov Models Analysis

The cohort of patients in the Markov model was distributed within individual cycles depending on the selected transition probabilities in the model. The distribution of the cohort in individual health states within the 10-year timespan is presented in the following figures, for Markov model “HMV” (Figure 2) and for Markov model “MV” (Figure 3).

![Figure 2. Distribution of cohort in individual cycles of home mechanical ventilation (“HMV”).](image)

The distribution of the cohort is also connected with the division of costs and utility. The cumulative costs of the Markov model “HMV” correspond to CZK 1,877,076 after 10 years. The cumulative costs of the Markov model “HV” correspond to CZK 7,386,629 after 10 years. The cumulative costs chart is presented in Figure 4.
A one-way sensitivity analysis was calculated. Due to the low number of probands and lack of further information, it was decided to analyze the sensitivity to the given parameters in the range of 30%. All the input parameters except for the changes in the quality of life values in HMV were gradually changed. A sensitivity analysis in which the discount rate was changed to 0% and 5% was also conducted.

2.6. Scenario Analysis

A scenario analysis performs the alteration in the initial distributions entering the model. The entire population was not divided in the individual states but the whole cohort (100%) began in the state of non-invasive (“NIV”) mechanical ventilation.

3. Results

3.1. Markov Models Analysis

The cohort of patients in the Markov model was distributed within individual cycles depending on the selected transition probabilities in the model. The distribution of the cohort in individual health states within the 10-year timespan is presented in the following figures, for Markov model “HMV” (Figure 2) and for Markov model “MV” (Figure 3).

![Figure 3. Distribution of cohort in individual cycles of mechanical ventilation (“MV”).](image)

![Figure 4. Cumulative costs.](image)

When evaluating the Markov models, graphs of cumulative utility arising within the 10-year period of time were also compiled (Figure 5). The cumulative utility in the value of 12.57 quality-adjusted life year (QALY) corresponds to a home environment strategy. The cumulative utility in the value of 11.32 QALY corresponds to a healthcare facility strategy.

The distribution of the cohort is also connected with the division of costs and utility. The cumulative costs of the Markov model “HMV” correspond to CZK 1,877,076 after 10 years. The cumulative costs of the Markov model “HV” correspond to CZK 7,386,629 after 10 years. The cumulative costs chart is presented in Figure 4.
The distribution of the cohort is also connected with the division of costs and utility. The cumulative costs of the Markov model "HMV" correspond to CZK 1,877,076 after 10 years. The cumulative costs of the Markov model "HV" correspond to CZK 7,386,629 after 10 years. The cumulative costs chart is presented in Figure 4.

When evaluating the Markov models, graphs of cumulative utility arising within the 10-year period of time were also compiled (Figure 5). The cumulative utility in the value of 12.57 quality-adjusted life year (QALY) corresponds to a home environment strategy. The cumulative utility in the value of 11.32 QALY corresponds to a healthcare facility strategy.

The cohort distribution graphs (Figures 2 and 3) show that the distribution is almost identical except for the hospitalization curve, which means that both approaches are very similar, but subsequently it is shown that HMV is much cheaper and provides a higher quality of life without a high risk of rehospitalization.

### 3.2. Cost–Utility Analysis

After evaluating the Markov models, a cost–utility analysis assessing two methods of mechanical ventilation in patients with a diagnosis of ALS from the perspective of a healthcare payer was carried out. In the 10-year timespan within which the care is provided by non-invasive or invasive methods of mechanical ventilation, in both a home environment and a healthcare facility environment, the analysis showed the home environment strategy to be a cost-effective dominant intervention. The CUA results are presented in Table 7.

| Strategy | Costs [CZK] | Incremental Costs [CZK] | Utilities [QALY] | Incremental Utilities [QALY] | C/QALY [CZK] | ICUR [CZK] |
|----------|-------------|-------------------------|-----------------|-----------------------------|-------------|-----------|
| HMV      | 1,877,076   | 0                       | 12.57           | 0                           | 149,292     | 0         |
| MV       | 7,386,629   | -5,509,554              | 11.32           | 1.25                        | 652,418     | -4,403,259 |

### 3.3. Sensitivity Analysis

All the input parameters in the range of 30% were changed using a one-way sensitivity analysis. However, the ICUR would be affected in terms of a change in efficiency in the case of a change in a healthcare facility utility assumption. The initial state determines this utility value to be 10% lower than in the home care. Within the sensitivity analysis, the value was varied in the range of 30% from the value allocated to the home care. The sensitivity analysis results are presented in Table 8.
Table 8. Sensitivity analysis of utility in the healthcare facility.

| Strategy | Costs [CZK] | Utilities [QALY] | ICUR [CZK] |
|----------|-------------|-----------------|------------|
| −30% HMV | 1,877,076   | 12.57           | 0          |
|          | MV          | 7,386,629       | −1,463,995 |
| −20% HMV | 1,877,076   | 12.57           | 0          |
|          | MV          | 7,386,629       | −2,197,399 |
| −10% HMV | 1,877,076   | 12.57           | 0          |
|          | MV          | 7,386,629       | −4,403,259 |
| 0% HMV   | 1,877,076   | 12.58           | 1,143,504,522  |
|          | MV          | 7,386,629       | 1,435,504,522  |
| +10% HMV | 1,877,076   | 12.58           | 0          |
|          | MV          | 7,386,629       | 4,369,607  |
| +20% HMV | 1,877,076   | 12.58           | 0          |
|          | MV          | 7,386,629       | 2,188,986  |
| +30% HMV | 1,877,076   | 12.58           | 0          |
|          | MV          | 7,386,629       | 1,460,256  |

1 diff. < 0.01.

3.4. Scenario Analysis

Instead of dividing the entry cohort into individual health states, the entire cohort (100%) entered the health state of a non-invasive method. This scenario did not affect the CUA result, i.e., the ICUR values. There was only a significant reduction in the home mechanical ventilation costs to CZK 755,672 and an increase in mechanical ventilation costs to CZK 7,563,912. There was also a slight increase in QALY, but for both variants.

4. Discussion

With its average patient ratio of approximately 1.2/100,000, the Czech Republic is very low in comparison to the given value of 6.6/100,000 population which was published by the European Respiratory Society in the Eurovent study [43]. Since the survey by the European Respiratory Society was carried out, the use of HMV has become more widespread. There has been an increase in the number of patients, better healthcare payment systems have emerged, new indications have expanded and the technology used to provide HMV has improved overall. However, there is a lack of a clear evidence base on the use of HMV and other studies to collect data on the use of HMV in Europe [13]. As a result, and on the basis of available studies, the current prevalence of HMV is expected to be higher than described in the Eurovent study, even in countries where this practice has not been as widespread in the last decade. In addition, the organization lacks comparisons with new publications [14].

For the evaluation of HMV, a model working with health conditions, including Markov models, was selected. In another study, Chandra [44] also used a Markov model to evaluate the effectiveness and cost-effectiveness of individual interventions used in a chronic obstructive pulmonary disease (COPD) patient population. Another study [43], using the findings of a previous study, evaluated cost-effectiveness using a Markov model comparing home mechanical ventilation with the usual care of COPD patients in the United Kingdom.

A Markov model was compiled for the environment of the Czech Republic so that the recommended procedures [8–11] concerning home mechanical ventilation and care of patients with ALS were followed. In these patients, mechanical ventilation plays a major role in prolonging their lives and it is necessary to start non-invasive mechanical ventilation in time. This is also proven by studies [8,43,45–47] examining the correct time of HMV initialization and the use of optimal ventilation techniques. The model ensures the continuity of home mechanical ventilation care, from non-invasive to invasive home.
mechanical ventilation, which should work in the provision of care for patients with ALS [8–11].

The results indicate the costs of HMV to be multiple times lower than when providing MV in a healthcare facility. This was already proven by authors in a study examining the results of a long-term mechanical ventilation in patients with ALS [48]. Studies [15,34,49] examining the initial part of home mechanical ventilation also emphasize the cost savings. Initiation during hospitalization is advantageous from the point of view of better patient observation in the adaptation process, but on the other hand there are high costs associated with hospitalization of the patient or even a waiting list. Pallero et al. [50] concluded that outpatient patient adaptation is a more cost-effective strategy for the healthcare system than the adaptation process during hospitalization, as confirmed by the results of a Spanish study [49]. In comparison to non-invasive ventilation, invasive ventilation is more expensive [51]. Bach [52] states that in the environment of the US healthcare system, there is a reduction of costs in home care by about 77%, and confirms again the already mentioned positive benefits of home mechanical ventilation in both non-invasive and invasive forms. In pediatric patients, the benefit is also the contact with parents and family, which again has a positive effect on their development and relationships. The transition also affects the number of intensive care unit hospital beds for other acutely ill patients and further reduces the exposure to nosocomial infections [53].

As proved by foreign studies [6,34–42], HMV is associated with the benefits of longer survival and improved quality of life. Assessing health-related quality of life is becoming an increasingly important criterion in research and healthcare, especially in the evaluation of the cost–benefit ratio of medical devices or patients with chronic, incurable disorders [37,41]. Therefore, a cost–utility analysis examining its benefits in terms of quality of life was selected to evaluate HMV and MV variants in patients with ALS. On the basis of the mentioned studies [6,34–42] and the opinion of experts, the assumption of a 10% reduction in the quality of life of a patient in a hospital environment was chosen for the cost–utility analysis. The value of the reduction was subsequently varied in the sensitivity analysis and changed the significance of ICUR as the only input, and HMV as the only dominant variant became cost-effective, if we assume that both variants fall below the willingness to pay threshold as they are already covered. Furthermore, a second scenario was analyzed when the distribution of the initial cohort of patients changed. The baseline scenario corresponds to the distribution based on a study [16] used to obtain the probability of survival, in respect to patient deaths in the Markov model. However, the change in the distribution of the input cohort again did not lead to any changes in the results.

The ICUR value, determined on the basis of the payer’s perspective over 10 years of healthcare in patients with ALS, falls into the incremental cost–utility plane quadrant, in which the new intervention has lower costs and a higher effect than the comparator. Thus, this is a cost-effective and dominant intervention. The conclusions of HMV being cheaper and having a greater effect are also proved by the above-mentioned studies with their results of different diagnoses [6,15,34–42,48–50,52], although none of them directly performed a cost–utility analysis comparing hospital and home use of mechanical ventilation including non-invasive and invasive approaches.

The average survival according to one study [16] used to obtain the survival probability corresponds to 22.9 months without the use of mechanical ventilation, 25.8 months with non-invasive HMV alone, 56.8 months if the initial non-invasive HMV was followed by invasive HMV and 33.8 months if only invasive HMV was used. This study was chosen because of the large number of patients in a European country, a comparison of several approaches and, in particular, because of the monitoring of patients until the end of their lives over a 15-year timeframe. However, other studies, such as the 2016 study on non-invasive HMV or a study [54] on invasive HMV, also provide similar survival results for ALS patients using mechanical ventilation. Bourke [55] addressed various characteristics of patients such as the state of bulbar functions, which, according to the results, affect the quality of life and survival of patients with ALS on MV. These differences were not taken
into account in our Markov model. However, it stems from all the results of these studies that life is prolonged with the use of mechanical ventilation, and in addition, the use of HMV increases the quality of life, which can again affect life expectancy. It is possible to further expand the Markov model to the specific part of the therapy before using mechanical ventilation and to deal in more detail with various diseases. With this entry into the Markov model, ALS can be further examined and evaluated in more detail according to progression [56], either between individual types of progression or again from the point of view of the use of home care or healthcare.

The main limitation of this study is the selected perspective of a healthcare payer, as the social system and informal caregivers play a major role in providing HMV. The social system spends a large part of its funding on supporting this care in the form of various social benefits, allowances or pensions. This is furthermore related to the costs of informal care, which is often provided by family members, who may lose their own jobs due to the care provided, incurring informal caregiver costs from a societal perspective. This may be confirmed by the results of a study [57] examining the quality of life of ventilated ALS patients and their caregivers. Job loss occurred with the non-invasive approach of HMV in 19% of cases, and with the invasive approach in up to 60% of cases. According to this study, the average time spent caring for a given patient is 12.6 h for the non-invasive approach and 14.4 h for the invasive approach, which affects other activities of an informal caregiver. Although Mustfa [58] states that a non-invasive approach has no impact on the quality of life of the caregiver and does not place a significant burden on the caregiver, the guidelines [2] state that there is a gradual loss of independence during the illness and assistance with daily activities is needed. This leads to an increase in the burden on informal caregivers and can lead to social, psychological and emotional problems. The quality of life of caregivers caring for patients with HMV is reduced, which is accompanied by physical weakness, and couples may experience reduced sexual activities. Gelinas [59] also reports a significant burden and a significant limitation on other activities.

Based on these limitations, it is appropriate to recommend and conduct further research from a societal perspective, considering all costs associated with HMV and analyzing the quality of life of informal caregivers. However, the already created Markov model can still be used for this. The model can also be subsequently used for other diagnoses or another country, by altering the input data such as transition probabilities, costs and benefits. This study could also be suitable for assessing the situation where certain areas do not have good accessibility in terms of distance to medical facilities. It is therefore also possible to evaluate other diseases typical of HMV and different perspectives according to the created model. Currently, in connection with COVID-19, it would be possible to consider the benefit of HMV, in which in the longer term there would be a release of beds in hospital facilities for acute patients with COVID-19 using mechanical ventilation.

5. Conclusions

The results of the cost–utility analysis show that in the given setting of the study we can consider HMV as cost effective. Subsequent results of the sensitivity analysis and scenario analysis do not show significant changes in the results. Nevertheless, it is recommended to continue the research from a societal perspective and to use the created model for the research of typical HMV diseases.

Author Contributions: Conceptualization, O.G. and G.D.; methodology, O.G.; software, O.G.; validation, O.G. and V.K.; formal analysis, M.R.; investigation, O.G.; resources, O.G.; data curation, G.D.; writing—original draft preparation, O.G.; writing—review and editing, O.G., G.D. and V.K.; visualization, O.G.; supervision, M.R.; project administration, M.R.; funding acquisition, O.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Grant Agency of the Czech Technical University in Prague, grant No. SGS20/086/OHK5/1T/17 and No. SGS20/148/OHK4/2T/17.

Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.

Data Availability Statement: Data sharing not applicable.

Acknowledgments: Authors acknowledge the healthcare payer (Zaměstnanecká pojišťovna Škoda), Emergency Medical Service (Zdravotnická záchranná služba Plzeňského kraje) and home healthcare agency (ProCare Medical s.r.o.).

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

1. Rimmer, K.P.; Kaminska, M.; Nonoyama, M.; Giannouli, E.; Maltaias, F.; Morrison, D.L.; O’Connell, C.; Petrof, B.J.; McKim, D.A. Home mechanical ventilation for patients with Amyotrophic Lateral Sclerosis: A Canadian Thoracic Society clinical practice guideline. Can. J. Respir. Crit. Care Sleep Med. 2019, 3, 9–27. [CrossRef]
2. Andersen, F.M.; Abrahams, S.; Borasio, G.D.; de Carvalho, M.; Chio, A.; Van Damme, P.; Hardiman, O.; Kollewe, K.; Morrison, K.E.; Petri, S.; et al. EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MAL5)—Revised report of an EFNS task force. Eur. J. Neurol. 2012, 19, 360–375. [CrossRef]
3. Radunovic, A.; Annane, D.; Raffiq, M.K.; Brassington, R.; Mustfa, N. Mechanical ventilation for amyotrophic lateral sclerosis / motor neuron disease. Cochrane Database Syst. Rev. 2017, 28, CD004427. [CrossRef]
4. Sorrentino, P.; Russo, R.; Francesca, J.; Troisi, F.; Anna, L.; BasilecFabio, F.; Femiano, C.; Santangelo, G.; Granata, C.; Vettoliere, A.; et al. Brain functional networks become more connected as amyotrophic lateral sclerosis progresses: A source level magnetoencephalographic study. NeuroImage Clin. 2018, 20, 564–571. [CrossRef]
5. Marchese, S.; Lo Coco, D.; Lo Coco, A. Outcome and attitudes toward home tracheostomy ventilation of consecutive patients: A 10-year experience. Respir. Med. 2010, 102, 430–436. [CrossRef]
6. MacIntyre, E.J.; Asadi, L.; Mckim, D.A.; Bagshaw, S.M. Clinical Outcomes Associated with Home Mechanical Ventilation: A Systematic Review. Can. Respir. J. 2016, 2016, 1–10. [CrossRef]
7. Čabanová, A. Doma by mohlo žíti více ventilovaných pacientů. Med. Trib. 2018, 18, 1–2.
8. Windisch, W.; Geiseler, J.; Simon, K.; Walterspacher, S.; Dreher, M.; Windisch, W.; Dreher, M.; Geiseler, J.; Siemon, K.; Brambring, J.; et al. German National Guideline for Treating Chronic Respiratory Failure with Invasive and Non-Invasive Ventilation—Revised Edition 2017: Part 2. Respiration 2018, 96, 171–203. [CrossRef][PubMed]
9. Windisch, W.; Geiseler, J.; Simon, K.; Walterspacher, S.; Dreher, M.; Brambring, J.; Dellweg, D.; Grolle, B.; Hirschfeld, S.; Köhnlein, T.; et al. German National Guideline for Treating Chronic Respiratory Failure with Invasive and Non-Invasive Ventilation—Revised Edition 2017—Part 1. Respiration 2018, 96, 66–97. [CrossRef][PubMed]
10. McKim, D.A.; Road, J.; Avendano, M.; Abdoool, S.; Côté, F.; Duguid, N.; Fraser, J.; Maltais, F.; Morrison, D.L.; O’Connell, C.; et al. Home mechanical ventilation: A Canadian Thoracic Society clinical practice guideline. Can. Respir. J. 2011, 18, 197–215. [CrossRef][PubMed]
11. Make, B.J.; Hill, N.S.; Goldberg, A.I.; Bach, J.R.; Dunne, P.E.; Heffner, J.E.; Keens, T.G.; O’Donohue, W.J.; Oppenheimer, E.A.; Robert, D. Mechanical Ventilation Beyond the Intensive Care Unit. Chest 1998, 113, 2895–3445. [CrossRef][PubMed]
12. Všeobecná zdravotní pojišťovna ČR. Úhradový katalog VZP-ZP-Metodika; VZP ČR: Prague, Czech Republic, 2020.
13. Simonds, A.K. Home Mechanical Ventilation: An Overview. Ann. Am. Thorac. Soc. 2016, 13, 2035–2044. [CrossRef][PubMed]
14. Valko, L.; Baglyas, S.; Gal, J.; Lorx, A. National survey: Current prevalence and characteristics of long-term survival with noninvasive ventilation and factors affecting the transition to invasive ventilation in amyotrophic lateral sclerosis. Muscle Nerve 2018, 58, 770–776. [CrossRef]
15. TreeAge Pro Healthcare R2.1, Software for health economic modelling to analyze medical treatment decisions; TreeAge Software: Williamstown, MA, USA, 2020.
16. A Language and Environment for Statistical Computing; R Core Team: Vienna, Austria, 2020.
17. Parliament České Republiky. Zákon č. 48/1997 Sb., o Veřejném Zdravotním Pojištění a o Změně a Doplňení Některých Souvisejících Zákonů; Tiskárna Ministerstva Vítrna: Prague, Czech Republic, 1997; pp. 1–118.
18. Všeobecná Zdravotní Pojišťovna ČR. METODIKA—Postup Při Realizaci Invaziční Domácí Umělé Plicní Ventilace (DUPV) u Nových Pacientů; VZP ČR: Prague, Czech republic, 2019.
19. Všeobecná Zdravotní Pojišťovna ČR. Zdravotní Výkony. Available online: https://www.vzp.cz/poskytovatele/ciselniky/zdravotni-vykony (accessed on 20 March 2020).
23. Ministerstvo Zdravotnictví ČR. Vyhláška Č. 201/2018 Sb., o Stanovení Hodnot Bodu, Výšce Úhrad Hrazených Služeb a Regulačních Omezení pro Rol 2019; Tiskárna Ministerstva Vnitra: Praha, Czech Republic, 2019.

24. Mičudová, E.; Lorenc, V. Srovnání Ekonómických Nákladů Na Pacienta v Programu Domácí Úmělá Plicní Ventilace a Pacienta Hospitalizovaného Na Jednotce Dlouhodobé Intenzivní Pěče; FN Brno: Brno, Czech Republic, 2012.

25. Česká Farmakoekonomická Společnost. Doporučené Postupy Pro Zdravotně-Ekonomické Hodnocení v ČR: Česká Společnost Pro Farmakoekonomiku a Hodnocení Zdravotnických Technologií (ČFES); Česká Farmakoekonomická Společnost: Prague, Czech Republic, 2020.

26. Český statistický úřad Inflace-druhy, definice, tabulky. Available online: https://www.czso.cz/cs/czso/mira_inflace (accessed on 20 March 2020).

27. Parlament České republiky. Zákon Č. 372/2011 Sb., o Zdravotních Službách a Podmínkách Jejich Poskytování (Zákon o Zdravotních Službách); Tiskárna Ministerstva Vnitra: Prague, Czech Republic, 2011.

28. Ministerstvo Zdravotnictví ČR. Vyhláška Č. 134/1998 Sb. Kterou Se Výkází Seznam Zdravotních Výkonn s Bodovými Hodnotami; Tiskárna Ministerstva Vnitra: Praha, Czech Republic, 1998.

29. Ministerstvo zdravotnictví ČR Zákonník č. 268/2019 Sb., o stanovení hodnot bodu, výšce úhrad hrazených služeb a regulačních omezení pro rok 2020; Tiskárna Ministerstva Vnitra: Praha, Czech Republic, 2019.

30. Goodman, C.S. HTA 101: Introduction to the health technology assessment; National Library of Medicine: Bethesda, MD, USA, 2014.

31. Nauffal, D.; Doménech, R.; Martínez García, M.A.; Compte, L.; Macián, V.; Perpiñá, M. Noninvasive positive pressure home ventilation in restrictive disorders: Outcome and impact on health-related quality of life. Respir. Med. 2002, 96, 777–783. [CrossRef]

32. Ara, R.; Brazier, J. Deriving an algorithm to convert the eight mean SF-36 dimension scores into a mean EQ-5D preference-based score from published studies (where patient level data are not available). Value Health. 2008, 11, 1131–1143. [CrossRef]

33. Rousseau, M.C.; Pietra, S.; Blaya, J.; Catala, A. Quality of life of ALS and LIS patients with and without invasive mechanical ventilation. J. Neurol. 2011, 258, 1801–1804. [CrossRef]

34. Chatwin, M.; Nickol, A.H.; Morrell, M.J.; Polkey, M.I.; Simonds, A.K. Randomised trial of inpatient versus outpatient initiation of home mechanical ventilation in patients with nocturnal hypoventilation. Respir. Med. 2008, 102, 1528–1535. [CrossRef]

35. Windisch, W. Impact of home mechanical ventilation on health-related quality of life. Eur. Respir. J. 2008, 32, 1328–1336. [CrossRef] [PubMed]

36. López-Campos, J.L.; Failde, I.; Jiménez, A.L.; Jiménez, F.M.; Cortés, E.B.; Benítez Moya, J.M.; García, R.A.; Windisch, W. Health-Related Quality of Life of Patients Receiving Home May Mechanical Ventilation: The Spanish Version of the Severe Respiratory Insufficiency Questionnaire. Arch. Bronconeumol. 2006, 42, 588–593. [CrossRef]

37. Euteneuer, S.; Windisch, W.; Suchi, S.; Köhler, D.; Jones, P.W.; Schönhofer, B. Health-related quality of life in patients with chronic respiratory failure after long-term mechanical ventilation. Respir. Med. 2006, 100, 477–486. [CrossRef] [PubMed]

38. Doménech-Clar, R.; Nauffal-Manssur, D.; Compte-Torrero, L.; Rosales-Almazán, M.D.; Martínez-Pérez, E.; Soriano-Melchor, E. Adaptation and follow-up to noninvasive home mechanical ventilation: Ambulatory versus hospital. Respir. Med. 2008, 102, 1521–1527. [CrossRef] [PubMed]

39. Doménech-Clar, R.; Nauffal-Manzur, D.; Perpiñá-Tordera, M.; Compte-Torrero, L.; Macián-Gisbert, V. Home mechanical ventilation for restrictive thoracic diseases: Effects on patient quality-of-life and hospitalizations. Respir. Med. 2003, 97, 1320–1327. [CrossRef] [PubMed]

40. Oga, T.; Windisch, W.; Handa, T.; Hirai, T.; Chin, K. Health-related quality of life measurement in patients with chronic respiratory failure. Respir. Investig. 2018, 56, 214–221. [CrossRef]

41. Huttmann, S.E.; Windisch, W.; Storre, J.H. Invasive home mechanical ventilation: Living conditions and health-related quality of life. Respir. Investigation 2015, 89, 312–321. [CrossRef]

42. Huttmann, S.E.; Magnet, F.S.; Karagiannidis, C.; Storre, J.H.; Windisch, W. Quality of life and life satisfaction are severely impaired in patients with long-term invasive mechanical ventilation following ICU treatment and unsuccessful weaning. Ann. Intensive Care 2018, 8. [CrossRef]

43. Lloyd-Owen, S.J.; Donaldson, G.C.; Ambrosino, N.; Escarabill, J.; Farre, R.; Fauroux, B.; Robert, D.; Schoenhofer, B.; Simonds, A.K.; Wodzica, J.A. Patterns of home mechanical ventilation use in Europe: Results from the Eurovent survey. Eur. Respir. J. 2005, 25, 1025–1031. [CrossRef]

44. Chandra, K.; Blackhouse, G.; McCurdy, B.R.; Bornstein, M.; Campbell, K.; Costa, V.; Franek, J.; Kaulback, K.; Levin, L.; Sehatzadeh, S.; et al. Cost-effectiveness of interventions for chronic obstructive pulmonary disease (COPD) using an Ontario policy model. Ont. Health Technol. Assess. Ser. 2012, 12, 1–61.

45. Masefield, S.; Vitacca, M.; Dreher, M.; Kampelmacher, M.; Escarabill, J.; Paneroni, M.; Powell, P.; Ambrosino, N. Attitudes and preferences of home mechanical ventilation users from four European countries: An ERS/ELF survey. ERJ Open Res. 2017, 3. [CrossRef] [PubMed]

46. Pomares, X. Noninvasive Mechanical Ventilation. Reflections on Home. 2014, 50, 85–86.

47. Fernández-Alvarez, R.; Rubinos-Cuadrado, G.; Cabrera-Lacalzada, C.; Galindo-Morales, R.; Guillón-Blanco, J.A.; González-Martín, I. Home mechanical ventilation: Dependency and burden of care in the home. Arch. Bronconeumol. 2009, 45, 383–386. [CrossRef]

48. Moss, A.H.; Oppenheimer, E.A.; Case, P.; Cazzolli, P.A.; Roos, R.P.; Stocking, C.B.; Siegler, M. Patients with amyotrophic lateral sclerosis receiving long-term mechanical ventilation: Advance care planning and outcomes. Chest 1996, 110, 249–255. [CrossRef]
49. Luján, M.; Moreno, A.; Veigas, C.; Pomares, X.; Domingo, C. Non-invasive home mechanical ventilation: Effectiveness and efficiency of an outpatient initiation protocol compared with the standard in-hospital model. *Respir. Med.* 2007, 101, 1177–1182. [CrossRef]

50. Pallero, M.; Puy, C.; Güell, R.; Pontes, C.; Martí, S.; Torres, F.; Antón, A.; Munoz, X. Ambulatory adaptation to noninvasive ventilation in restrictive pulmonary disease: A randomized trial with cost assessment. *Respir. Med.* 2014, 1014–1022. [CrossRef]

51. Geiseler, J.; Karg, O.; Bürger, S.; Becker, K.; Zimolong, A. Invasive home mechanical ventilation, mainly focused on neuromuscular disorders. *GMS Health Technol. Assess.* 2010, 6, 1–10.

52. Bach, J.R. The ventilator-assisted individual. Cost analysis of institutionalization vs rehabilitation and in-home management. *Chest* 2015. [CrossRef]

53. MacIntyre, N.R.; Epstein, S.K.; Carson, S.; Muldoon, S.R. Management of patients requiring prolonged mechanical ventilation: Report of a NAMDRC Consensus Conference. *Chest* 2006, 128. [CrossRef]

54. Vianello, A.; Arcaro, G.; Palmieri, A.; Ermani, M.; Bracconi, F.; Gallan, F.; Soraru, G.; Pegoraro, E. Survival and quality of life after tracheostomy for acute respiratory failure in patients with amyotrophic lateral sclerosis. *J. Crit. Care* 2011, 26. [CrossRef]

55. Bourke, S.C.; Tomlinson, M.; Williams, T.L.; Bullock, R.E.; Shaw, P.; Gibson, G.J. Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: A randomised controlled trial. *Lancet Neurol.* 2006, 5, 140–147. [CrossRef]

56. Ackrivo, J.; Hansen-Flaschen, J.; Jones, B.L.; Paul Wileyto, E.; Schwab, R.J.; Elman, L.; Kawut, S.M. Classifying Patients with Amyotrophic Lateral Sclerosis by Changes in FVC A Group-based Trajectory Analysis. *Am. J. Respir. Crit. Care Med.* 2019, 200, 1513–1521. [CrossRef]

57. Kaub-Wittemer, D.; Von Steinbuechel, N.; Wasner, M.; Laier-Groeneveld, G.; Borasio, G.D. Quality of life and psychosocial issues in ventilated patients with amyotrophic lateral sclerosis and their caregivers. *J. Pain Symptom Manage.* 2003, 26, 890–896. [CrossRef]

58. Mustfa, N.; Walsh, E.; Bryant, V.; Lyall, R.A.; Addington-Hall, J.; Goldstein, L.H.; Donaldson, N.; Polkey, M.I.; Moxham, J.; Leigh, P.N. The effect of noninvasive ventilation on ALS patients and their caregivers. *Neurology* 2006, 66, 1211–1217. [CrossRef] [PubMed]

59. Gelinas, D.F.; O’Connor, P.; Miller, R.G. Quality of life for ventilator-dependent ALS patients and their caregivers. *J. Neurol. Sci.* 1998, 160, 134–136. [CrossRef]