Project No. 101045956
Biomarker and AI-supported FX06 therapy to prevent progression from mild and moderate to severe stages of COVID-19

Deliverable 7.5

Hospital-level budget impact tool

WP 7 – Socio-economic impact and cost effectiveness analyses (HTA)

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Revision history

Date	Authors	Revision
21-05-2025	Clazinus Veijer, Thea van Asselt (UMCG)	Draft version
04-06-2025	Benjamin Friedrichson, Elina Nürenberg-Goloub (GUF)	First revision
30-06-2025	René van Hulst, Thea van Asselt, Clazinus Veijer (UMCG)	Final version

Contents

Partner short names

GUF	Johann Wolfgang Goethe Universität Frankfurt am Main
accelCH	accelopment Schweiz AG
ESAIC	European Society of Anaesthesiology and Intensive Care
Fraunhofer	Fraunhofer Institute for Translational Medicine and Pharmacology ITMP
F4	F4 Pharma GmbH
TAU	Tampereen Korkeakoulusaatio SR
UCD	University College Dublin
UMCG	Universitair Medisch Centrum Groningen
MiDA	Medical Intelligent Data Analytics GmbH
KC	Lietuvos Sveikatos Mokslu Universiteto Ligonine Kauno Klinikos
ICS-HUB	Hospital Universitari de Bellvitge
UMFCD	Universitatea de Medicina si Farmacie Carol Davila din Bucuresti
APHP	Assistance Publique – Hôpitaux de Paris

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
BIA	Budget impact analysis
CEA	Cost-effectiveness analysis
D	Deliverable
DRG	Diagnosis-Related Group
EC	European Commission
EU	European Union
M	Month
OECD	Organisation for Economic Cooperation and Development
PPP	Purchasing Power Parity
SHEPARDS	Simulation for Health Economic Payoffs in ARDS
SOC	Standard of Care

Executive Summary

A budget impact analysis (BIA) is an important part of the economic evaluation of (new) healthcare interventions. A BIA complements a cost-effectiveness analysis (CEA) by providing the expected financial impact when implementing the studied intervention. The current deliverable constitutes a description of a user-interactive web application to analyse the budget impact of FX06 in the treatment of Acute Respiratory Distress Syndrome (ARDS). The tool provides a user-interactive web application to calculate the financial consequences at a hospital level when implementing FX06 in addition to the Standard of Care (SOC). The BIA tool is subdivided into the subpages. An explanation and screen shots of each subpage ('Start', 'Population', 'Clinical inputs', 'Cost inputs', 'Input summary', and 'Output') of the web application is described here.

1 Introduction

1.1 Budget impact analysis

Besides a new healthcare intervention's calculated cost-effectiveness, its financial impact on the budget plays an important role in the decision on whether or not to implement the intervention. It may seem obvious that a positive decision on implementing a novel intervention will follow from favourable outcomes of a cost-effectiveness analysis (CEA) that is well-designed, i.e. using robust evidence from clinical and economic sources, performed over an expansive time horizon, and incorporating multiple alternatives. However, the financial impact on the budget when purchasing the intervention may be higher than the budget taker can afford. Hence, a budget impact analysis (BIA) is an important part of the economic evaluation of (new) healthcare interventions and complements a CEA.

As has been described in D7.1, the outcome of a BIA is part of the reimbursement eligibility criteria in several countries in Europe. Moreover, guidelines on health economic evaluations across several countries recommend the use of a budget impact analysis (BIA) in addition to a cost-effectiveness analysis (CEA). Both types of analyses have different objectives. A BIA focuses on the costs and usually provides a calculation framework of the annual financial impact on the budget in a certain setting, i.e. a health system, region, or organisation, whereas a CEA examines both the cost and health effects of an intervention.

The healthcare setting to which a BIA would apply is strictly related to the funder of the intervention. Public hospitals in Europe are mainly remunerated by Diagnosis-Related Group (DRG) payment systems (1). DRGs are financed out of the national or regional budget with a predetermined amount. The expenditure of a new treatment to be used in the hospital is generally paid out of the hospital budget. The costs of the new treatment and its additional expenditure may be integrated into the lump sum of a DRG (2). However, in case of high-priced or low-volume medicines, certain extrabudgetary payment systems and specific funds to enable reimbursement may be applied. An elaborative overview of payment and reimbursement processes across several countries can be found in D7.1. In case of new interventions to be used in a hospital setting, conducting an hospital-level BIA would be a logical first step to support decision-makers on the implementation of the intervention.

1.2 Purpose and scope of the deliverable

The aim of the COVend project is to deliver a new effective therapy against endothelial damage in ARDS for the clinical management of COVID-19 and other medical conditions involving endothelial dysfunction during mild and moderate stages, including the prevention of disease progression to severe illness. Therefore, a randomised, placebo-controlled, double-blinded, parallel, phase II clinical study was performed to investigate the efficacy and safety of FX06 in ARDS patients. The current deliverable describes the online tool to analyse the budget impact of FX06 in the treatment of ARDS. The tool provides a user-interactive web application to calculate the financial consequences at a hospital level when implementing FX06 in addition to the Standard of Care (SOC).

2 Model description

The BIA tool can be accessed by visiting the COVend webpage (https://covend-project.eu/) and navigate to 'Research & Innovation'.

A supporting paragraph on the website is given: 'An online tool was developed to analyse the budget impact of FX06 in the treatment of ARDS. The tool provides a user-modifiable calculation of the financial consequences at a hospital level when implementing FX06 in addition to the Standard of Care (SOC).'

The BIA tool is subdivided into the subpages 'Start', 'Population', 'Clinical inputs', 'Cost inputs', 'Input summary', and 'Output'. Additionally, references used in the descriptions and hyperlinks to other relevant webpages are given in the final subpage 'Other links'. An explanation and screen shots per subpage of the web application are given in the following paragraphs.

2.1 Start

The tool opens at the 'Start' subpage, where a brief description of the background and the short-term compartment of the SHEPARDS (Simulation for Health Economic Pay-offs in Acute Respiratory Distress Syndrome) model is given. The SHEPARDS model is a microsimulation of ARDS patients across the clinical pathway over a 60-day time horizon. Patients can stay in their current health state or move each day to one of the following health states:

- Intensive Care Unit, with mechanical ventilation (MV);

- Intensive Care Unit, without mechanical ventilation (ICU);

- General Ward (GW);

- Rehabilitation (REH);

- Recovered (REC).

The model is described in more detail in D7.4. A visual of the model structure is displayed in figure 1 and is also displayed on the Start subpage.

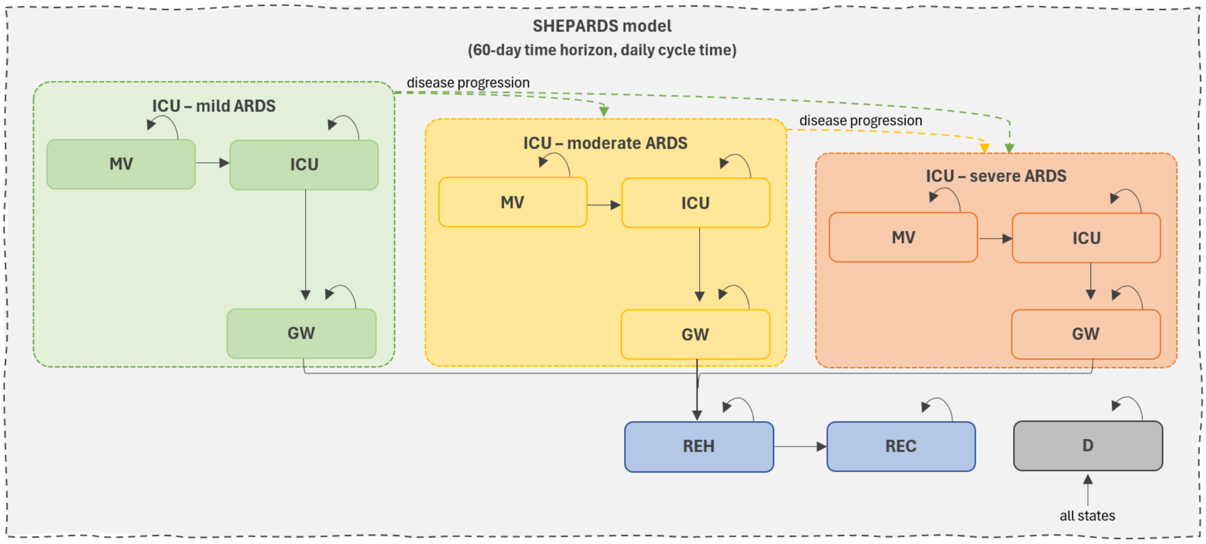

Figure 1 Schematic overview of the health states in the short-term compartment of the SHEPARDS model. SHEPARDS = Simulation for Health Economic Pay-offs in Acute Respiratory Distress Syndrome.

2.2 Population

On the subpage 'Population', the user can select the country of interest, the age distribution of the patient population, and the case-mix of the population by disease severity (i.e., mild, moderate, and severe ARDS). The current version of the BIA tool includes the countries with clinical sites where patients were recruited in IXION 2.0, i.e. Germany, Lithuania, France, and Spain. All-cause mortality rates that are applied in the 'Recovered' state as well as costs per health state are dependent per country. Mortality rates were derived from the age specific death rate per year, which were available from Eurostat (3).

The base case analysis uses data from Germany. Costs were converted for other countries using a cost conversion tool. The subpage includes a hyperlink to the online tool that was used for cost conversion (4). The user can use the tool to convert costs to other countries than the ones included in the current version. Further details about cost conversion are given in section 2.4.

The user can adjust the average age and standard deviation of the patient population, and set the minimum and maximum age of patients. Adjustments to the case mix of the patient population by disease severity is possible as well. A proportion of patients with mechanical ventilation ('MV') at the start of the simulation can be set. All simulated patients with mild, moderate, or severe ARDS start in one of the two ICU states, based on the ventilation proportion. The rest of patients starts in the ICU without ventilation ('ICU').

Figure 2 Population subpage of the web application.

2.3 Clinical inputs

The subpage 'Clinical inputs' allows the user to enter the hazard ratios that are applied to the transition probabilities for disease progression and discontinuing of mechanical ventilation. The treatment is expected to impact among others the rate of disease progression and the time with mechanical ventilation. Compared to the SOC, the hypotheses imply a hazard ratio between 0 and 1 for disease progression and a hazard ratio higher than 1 for the discontinuation of mechanical ventilation. As clinical effects of FX06 in the treatment of ARDS are unknown yet, conservative values are pre-filled as hypothetical values.

Of note, an indirect treatment effect was incorporated in the microsimulation by associating the ICU length of stay (LOS) with the time needed for rehabilitation. In other words, a hazard ratio for the time spent in ICU care was multiplied by the transition probability of moving from the 'Rehabilitation' state to the 'Recovered' state. The hazard ratio was retrieved from a Danish cohort study who identified patients who had an ICU LOS of at least 72 hours and who were working prior to the index hospitalisation. The study investigated the chance of return to work and published decreasing hazard ratios for return to work with increasing ICU LOS. The hazard ratio was applied to all patients in the model, which means that it was used as a proxy, even for patients with age > 65 years who are supposed to be not active as an employee anymore. Nonetheless, after discussion with clinical experts of the project, the association between longer ICU stays and worse functional outcomes was assumed to hold true for ARDS, making the hazard ratio conceptually applicable. No ARDS-specific data for the relation between ICU LOS and time to functional recovery was found.

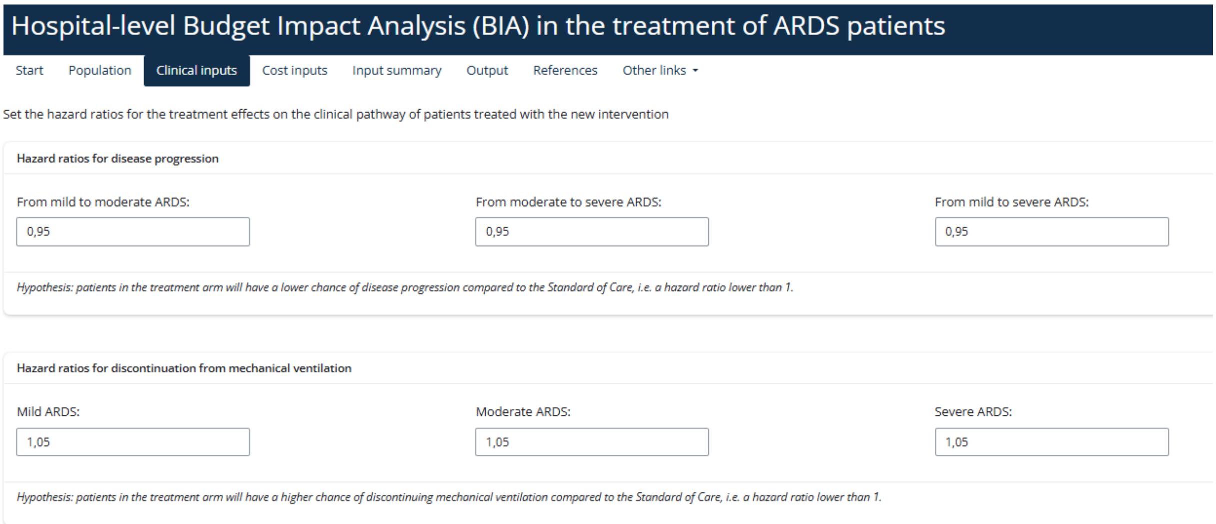

Figure 3 Clinical inputs subpage of the web application.

2.4 Cost inputs

In the subpage ‘Cost inputs’, the standard costs per health state are pre-filled, based on the country selected under ‘Population’. All daily costs can be adjusted to the user’s choice. Costs per health state were deemed to be equal between the SOC and FX06 strategies.

Daily costs of hospital stay per department have recently been studied as part of the ENVISION project and were published by Zwerwer et al (5). The study reported costs in 2020 Euros of additional days on the general ward, non-mechanically ventilated days in the ICU, and mechanically ventilated days in the ICU. Unit costs of rehabilitation per day were available from the publication of the monetary valuation of health-related consumption of resources from a societal perspective for 2020 in Germany by Muntendorf et al (6).

As described in 2.2, costs reported in Germany for 2020 were converted to the other three countries with patient inclusion (France, Spain, and Lithuania), using Purchasing Power Parity (PPP) values from the Organisation for Economic Cooperation and Development (OECD). The web-based Cost Converter tool of the Campbell & Cochrane Economics Methods Group (CCEMG) and Evidence for Policy and Practice Information (EPPI) Centre (v.1.7, last update in January 2024) was used to convert the German-based costs to the other countries (4). Then, costs per country were indexed to the year 2024, using each country’s Harmonised Index of Consumer Prices (HICP) from Eurostat (7). The adjustment for inflation follows the recommendation by the German national guideline on health economic evaluation (*General Methods 6.1*) of The Institute for Quality and Efficiency in Health Care (IQWiG) (8).

In the treatment strategy, costs of FX06 were added to the standard costs per health state during the first five cycles (= days) when the patient was in one of the three hospitalisation states (i.e. ‘MV’, ‘ICU’, or ‘GW’) of the simulation. In the base case, a hypothetical cost of EUR 240 per day is applied.

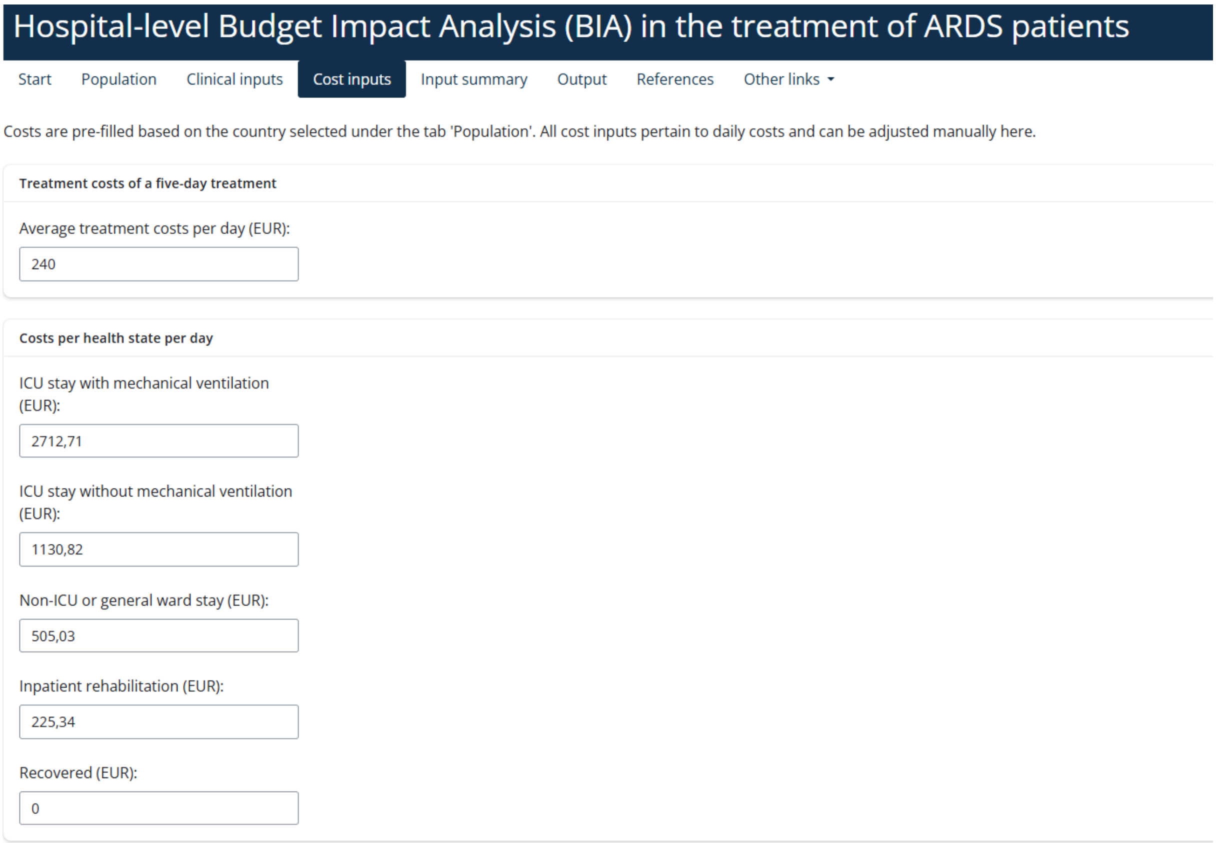

Figure 4 Costs input subpage of the web application.

2.5 Input summary

A describing summary of the selected inputs is given in the subpage 'Input summary'. The user can read and check the scenario chosen in the preceding subpages. The content of the subpage automatically adjusts to the user's input. The input summary may serve as an explanation to others than the user(s) when disseminating the outcome of the BIA.

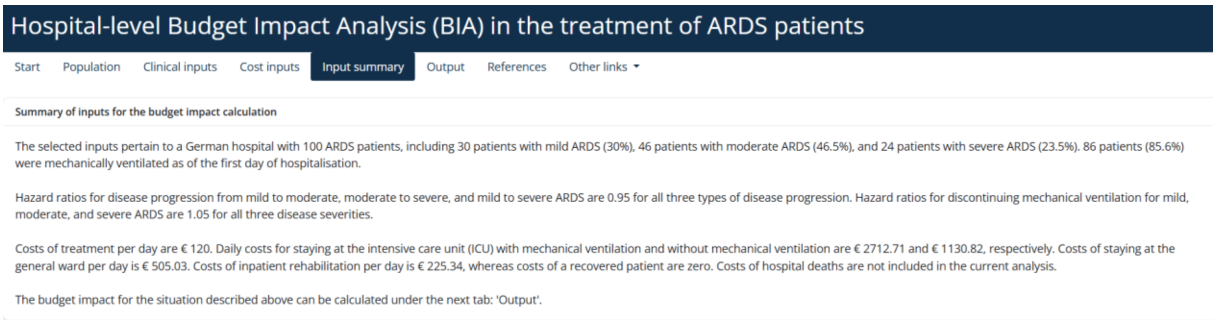

Figure 5 Input summary subpage of the web application.

2.6 Output

The 'Output' subpage has a 'Calculate' button. The analysis will run upon each button click. The subpage provides a summary of the budget impact in total values and average values per patient. The total budget impact is calculated as the difference of total costs of both strategies. The total treatment costs reflect the investment done by multiplying the cost of treatment by the number of days on treatment. The percentual mutation after adding FX06 to the SOC is also displayed.

The table below the summary shows the budget impact on daily costs per health state. In other words, the average costs per health state are shown, including the extra costs of the five-day treatment with FX06.

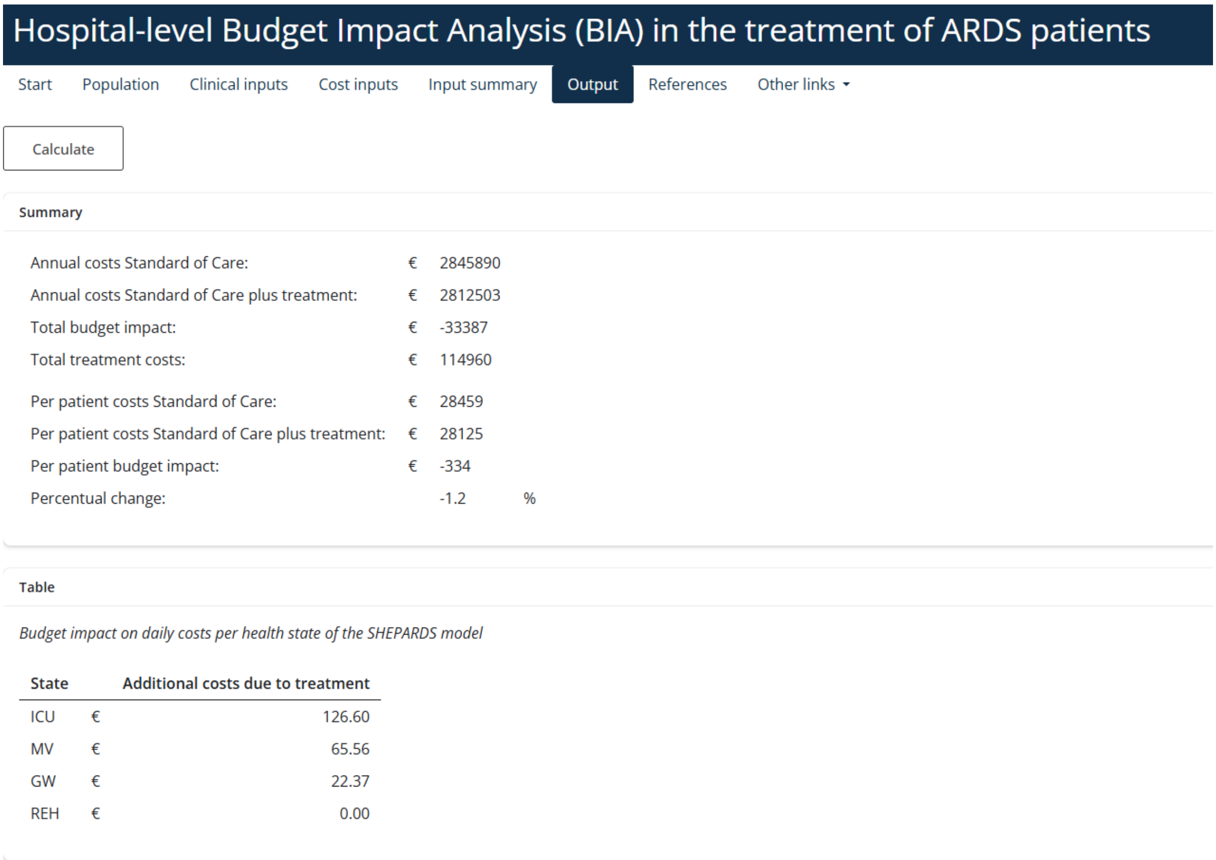

Figure 6 Output subpage of the web application.

Below the summary output, a graphical output of costs for both strategies is presented. The line charts show the proportion of patients per health state and the cost development per day. The left graph explains the distribution of patients over health states in the SHEPARDS model, whereas the right graph explains the total expenses of the analysis over the time horizon of 60 days.

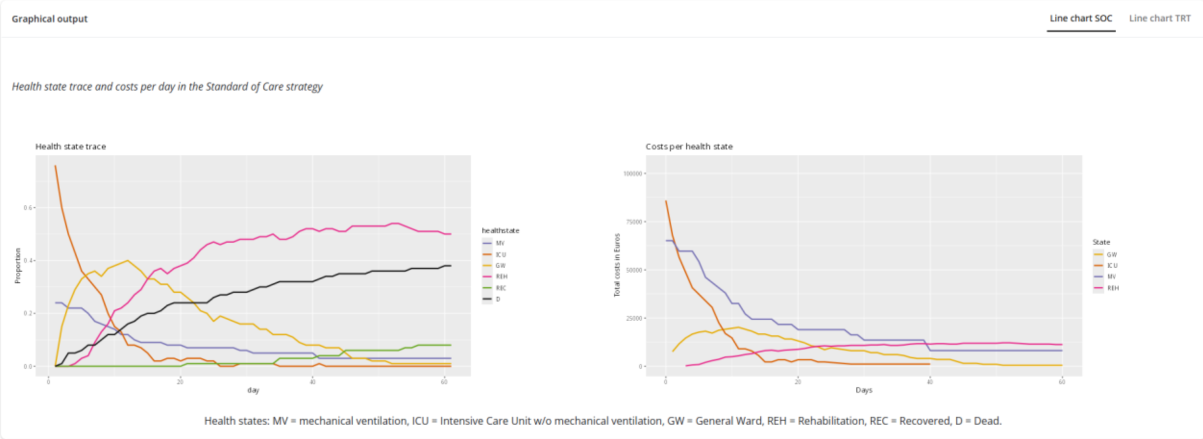

Figure 7 Line chart of the health state trace and of the total costs per health state over time in the Standard of Care strategy.

3 Final remarks

To properly interpret the output of a BIA, one should consider the potential market dynamics when implementing a new intervention. The treatment modalities may be expanded, may be (partly) substituted by the new intervention, or the SOC may be combined with the intervention. This is dependent on the comparator treatments and strategies that are considered in the health economic evaluation. For the BIA as described here, the uptake of FX06 per year may be added to the analysis. However, uptake of FX06 was not included in the current version of the BIA, as more evidence is required to estimate the market dynamics of ARDS treatments when implementing FX06.

The BIA uses terms like ‘patients per year’ and ‘annual budget impact’. In contrast, the SHEPARDS model takes a time horizon of 60 days. Presenting outcomes at an annual level was chosen to conform to the usual budgetary periods and to enable users to enter the annual number of ARDS patients. This does not interfere with the shorter time horizon of the model. In theory, all patients start at the same time and incur costs until day 60 (~2 months). As the simultaneous start of all ARDS patients is highly unlikely in practice, the line charts should be interpreted with caution. Furthermore, for similar reasons, users should not use the output of the BIA for capacity planning.

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