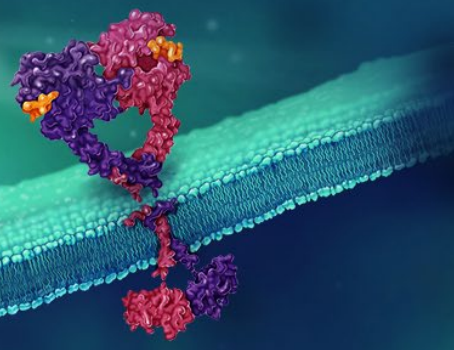

INTERNATIONAL MARKET ACCESS CONSULTING

Where expertise drives strategy

An innovative economic model: Cost-effectiveness over the short- and long-term horizon

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Scope of work and deliverables (1)

International Market Access Consulting (IMAC) was tasked with developing a unique economic model comparing the cost-effectiveness of low chloride versus high chloride crystalloid fluids used during fluid resuscitation (in the short-term) or for the maintenance of hydration (over the long-term) among patients hospitalized for critical illnesses or major surgery.

IMAC addressed the different time horizons by developing an innovative economic model consisting of two parts. First, a decision-tree design for the 90-day period after entry in the model to simulate patient flow post-surgery or once out of critical care. From there, surviving patients then entered the Markov component of the model in which outcomes and costs were modelled in annual cycles for the remainder of the cohort's lifespan. This creative design allowed the exploration of costs and outcomes over different, clinically-relevant time periods, facilitating the assessment of the short- and long-term costs associated with acute kidney injury (AKI), including renal replacement therapy (RRT). The inventive and specifically tailored final model was subsequently published in a high-profile journal; the *Journal of Health Economics and Outcomes Research*.[1]

Journal of Health Economics and Outcomes Research OPEN ACCESS

Cost-effectiveness of Chloride-liberal versus Chloride-restrictive Intravenous Fluids among Patients Hospitalized in the United States

Louise Perrault[1], Dilip Makhija[2*], Idal Beer[2], Suzanne Laplante[2], Sergio Iannazzo[3], Karthik Raghunathan[4]

Abstract

Background: Patients developing acute kidney injury (AKI) during critical illness or major surgery are at risk for renal sequelae such as costly and invasive acute renal replacement therapy (RRT) and chronic dialysis (CD). Rates of renal injury may be reduced with use of chloride-restrictive intravenous (IV) resuscitation fluids instead of chloride-liberal fluids.

Objectives: To compare the cost-effectiveness of chloride-restrictive versus chloride-liberal crystalloid fluids used during fluid resuscitation or for the maintenance of hydration among patients hospitalized in the US for critical illnesses or major surgery.

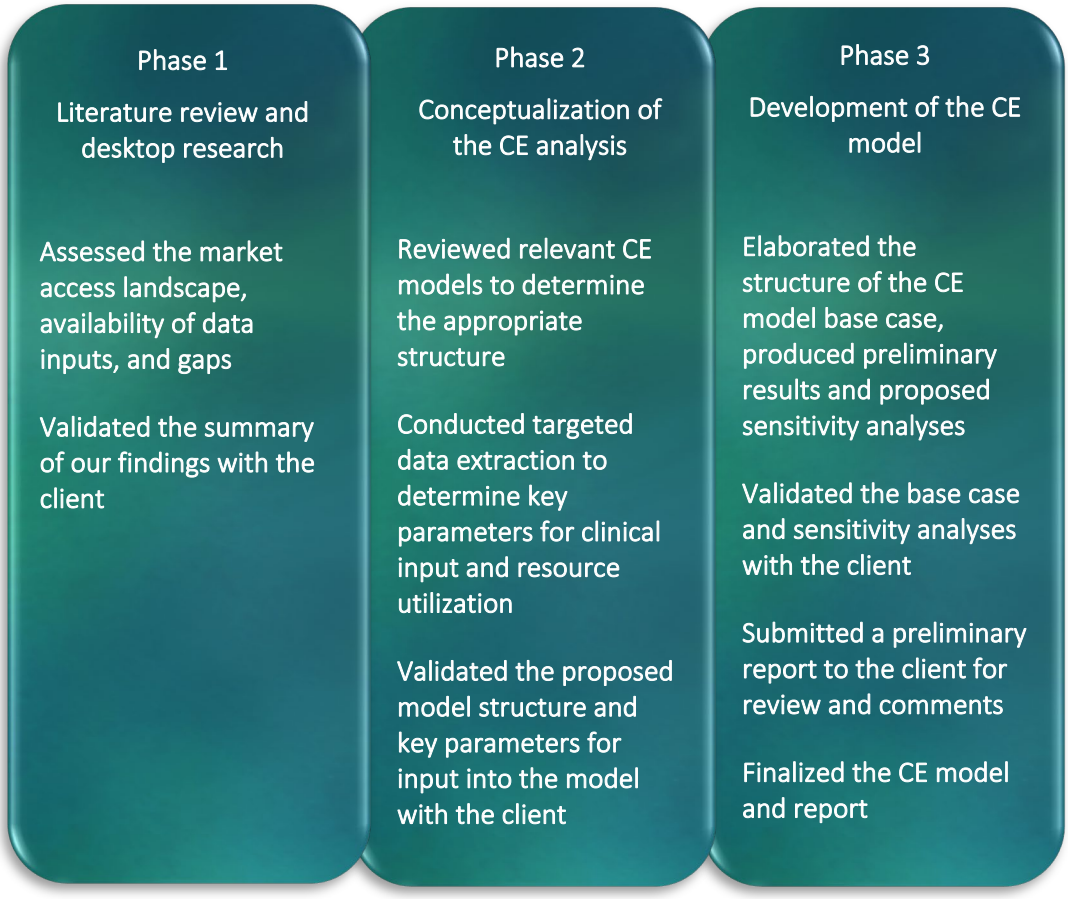
Methods: Clinical outcomes and costs for a simulated patient cohort (starting age 60 years) receiving either chloride-restrictive or chloride-liberal crystalloids were estimated using a decision tree for the first 90-day period after IV fluid initiation followed by a Markov model over the remainder of the cohort lifespan. Outcomes modeled in the decision tree were AKI development, recovery from AKI, progression to acute RRT, progression to CD, and death. Health states included in the Markov model were dialysis-free without

[1]Perrault L, Makhija D, Beer I, et al. Cost-effectiveness of chloride-liberal versus chloride-restrictive intravenous fluids among patients hospitalized in the United States. *J Health Econ Outcomes Res*. 2016;4(1):90-102.

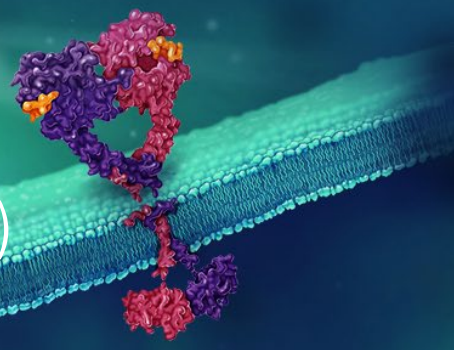
Scope of work and deliverables (2)

IMAC recommended dividing the model development into three phases, initiated on a rolling basis, in order to minimize downtime and maximize efficiency (Figure 1).

Figure 1: The three phases of the CE model development



Scope of work and deliverables (3)



PHASE 1: LITERATURE REVIEW AND DESKTOP RESEARCH

The project began with a formal kick-off meeting where the client and IMAC exchanged relevant project-related information and agreed upon the framework for the assignment.

In this first phase, IMAC recommended focusing on a review of the available literature and internal documents to identify appropriate data inputs and potential data gaps for the economic model. During this review, IMAC also initiated the conceptualization of the model.

IMAC conducted targeted market-access literature searches to categorize appropriate data for inputs and identify any data gaps that may exist. The findings of this phase were summarized in a PowerPoint slide deck which was presented during a web conference call. In collaboration with IMAC's expert Health Economic team, the client reviewed the findings and the recommended approach to move forward with the next phase.

PHASE 2: CONCEPTUALIZATION OF THE CE ANALYSIS (MODEL DESIGN AND SPECIFICATIONS) DETERMINATION OF THE CE MODEL DESIGN

IMAC sourced comparable models through review of the existing economic literature from the SLR and additional targeted literature reviews. IMAC prepared a slide presentation of suggested model design and specifications, and in collaboration with the client, determined the most appropriate approach to build the economic model for the product.

PHASE 3: DEVELOPMENT OF THE CE MODEL

After the structure and inputs for the CE model were reviewed and approved by the client, IMAC began building the model. The CE model base case along with a preliminary draft of the CE model report including the model structure, assumptions, perspective, horizon, and inputs, but not the results, were presented during a web conference. In collaboration with IMAC, the client had the opportunity to review and approve the model specifications, base case, and to discuss the scenario and sensitivity analyses to be performed. IMAC and the client worked together to determine the final model parameters. Once approved, IMAC finalized the model and CE model report.

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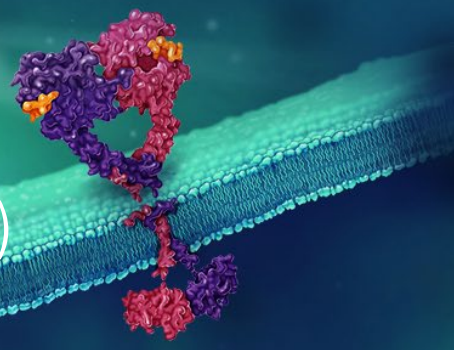
Scope of work and deliverables (4)



MODEL VALIDATION (EXTERNAL VALIDITY)

IMAC recommended that the CE model be validated by a minimum of 3 external experts since the aim was to produce a credible analysis that was applicable to the patients in the US.

QUALITY ASSURANCE (INTERNAL VALIDITY)

The economic model was audited for quality assurance. An IMAC pharmacoeconomic specialist who had not built the model checked all formulae and data entered in the model to ensure its internal validity.

CE MODEL REPORT

IMAC produced a transparent and detailed comprehensive report. Enough information was provided to enable the audience to critically evaluate the validity of the analysis. The report also included a list of all the parameters and assumptions required to build the model and a discussion section describing the main findings, strengths, and weaknesses of the analysis.

As outlined above, a preliminary draft of the report, outlining the CE model base case (eg, model structure, assumptions, perspective, horizon, and inputs) but not the results, was presented prior to the finalization of the CE model. The final report was completed once the client had signed-off on the final CE model.

INTERNATIONAL MARKET ACCESS CONSULTING

Related Experience

IMAC has considerable experience developing economic models for products across a wide range of therapeutic areas, including nephrology. IMAC has supported strategic global submissions for products in Europe and North America including developing and adapting cost-effectiveness and budget impact models for the UK, Canada, and select European markets.

Additionally, IMAC has considerable experience developing health-technology submissions in the UK, Europe, South America, and North America. IMAC has successfully developed submissions to the National Institute for Health and Care Excellence (NICE) for products in many therapeutic areas. Recently, IMAC developed a successful Highly Specialised Technology (HST) submission for an innovative gene therapy for an ultra-rare disease and Single Technology Appraisal (STA) submissions for a first-line oncology product and a first-in-class monoclonal antibody.

"We've been running on repeat business for the last 12 years. We know how to really build a strong story that links both clinical & economic aspects of your therapy together"
– Louise Perrault, President & CEO

"IMAC consists of a team of people that are experienced in not only developing submissions, but also in rescuing submissions that are struggling for different reasons. We are able to quickly assess the challenge(s), strategize a plan for optimising the value proposition of a product and continue our support throughout the submission process. Because we are a team of experts, we are able to work quickly under tight deadlines that are often challenging for larger firms. We produce the highest quality products, on time and on budget, and we have an excellent success rate."
– Nicole Tunstall, Senior Consultant, HTA and Medical

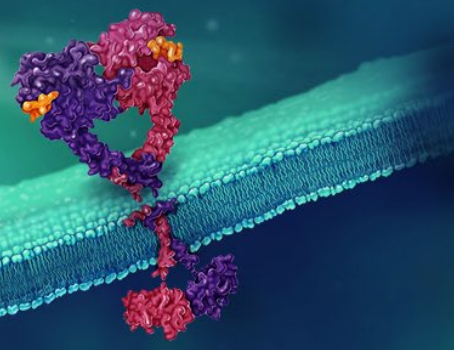
"We are people with experience, when we speak with our clients, we understand what you're talking about. We know how to develop products that stand up to review because of our expertise."
– Veronique Lauzon, Senior Health Economist

"IMAC is made up of more experienced qualified consultants who understand how to deal with the challenges many companies face when seeking market access for a new therapy. Because of this everything is completed on time, to a high level of quality, and a very good success rate."
– Eva Tsakonas, Senior Epidemiologist, Health Economist

"IMAC is above all a company of experts who are concerned about quality service throughout the duration of your project. We are a team of competent professionals who listen to and care about your needs and will successfully see your products through various evaluation processes while respecting the deadlines imposed."
– Ange Christelle Iliza, Research Assistant

"Working with IMAC is like adding a team of experts to your company for the duration of the project. From the project initiation to the final follow-up, you deal with the same experienced consultants who are there to advise and optimize the project whether it be an economic model, systematic literature review, HTA submission, global value dossier, manuscript, or conference presentation."
– Sarah-Gabrielle Béland, Senior Pharmacoepidemiologist

Background



Acute kidney injury (AKI) may result from critical illness or as a serious complication of major surgery, and impacts patient morbidity and mortality in the short- and long-term.[2,3,4] The treatment of AKI may require renal replacement therapy (RRT), an invasive procedure associated with high cost and extensive healthcare resource use.[4,5,6]

Intravenous (IV) fluids, used for resuscitation in the perioperative setting and in the management of critically ill patients, may play a role in reducing the risk of developing AKI.[8] IV crystalloids are recommended for resuscitation in critical illness, or during recovery from trauma and major operations.[9,10,11] Physiologically balanced IV crystalloids provide chloride in the physiologic range of human plasma and concentrations of anions that maintain electrical neutrality and act as buffers (eg, lactate, acetate, gluconate). As opposed to chloride-liberal IV fluid therapy, balanced IV crystalloid solutions avoid the increase in plasma chloride concentration and metabolic acidosis.[12] A meta-analysis of 6253 patients from 21 studies who received chloride-restrictive versus chloride-liberal IV fluids in perioperative or critical care settings reported that the use of chloride-liberal IV fluids was associated with a significantly higher risk of AKI (relative risk [RR] 1.64, 95% confidence interval [CI] 1.27, 2.13; P<0.001).[8]

Despite the substantial clinical evidence supporting the lowered risk of AKI with chloride-restrictive IV fluid therapy, there is a lack of analysis of the economic consequences of IV fluid choice. No studies have assessed the cost-effectiveness (CE) of chloride-restrictive vs chloride-liberal crystalloids by accounting for the most important difference in clinical impact, the variation in long-term renal function.

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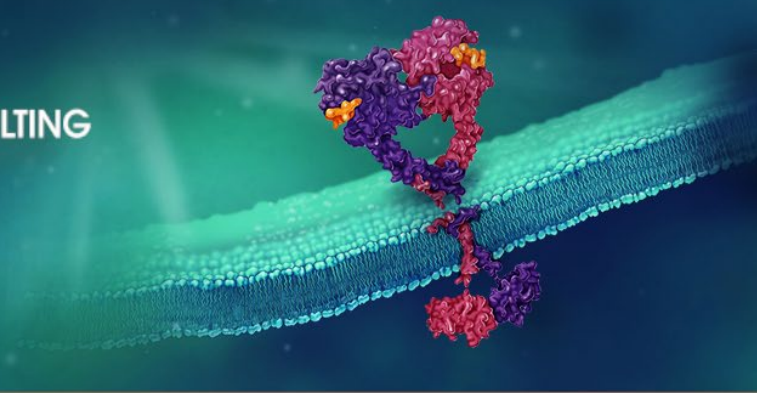

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