Cost-Consequences of Ultrafiltration for Acute Heart Failure
A Decision Model Analysis

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Background—Ultrafiltration for heart failure may reduce costs associated with acute heart failure by decreasing rehospitalization rates compared to intravenous diuretics.

Methods and Results—We developed a decision-analytic model to explore the clinical outcomes and associated costs of ultrafiltration compared to intravenous diuretics for index and subsequent acute heart failure hospitalizations to 90 days from index hospitalization. We evaluated the model from societal, Medicare, and hospital payer perspectives. Base-case probabilities and costs were derived from the Ultrafiltration versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Congestive Heart Failure clinical trial, Medicare reimbursement schedules, and published data. From a societal perspective, treatment with ultrafiltration had an 86% probability of being more expensive than intravenous diuretics in probabilistic sensitivity analysis, with a base-case estimate of $13,469 per patient treated with ultrafiltration compared to $11,610 per patient treated with intravenous diuretics. Cost estimates were most influenced by length of index hospitalization, daily cost of rehospitalization, number of days rehospitalized, and number and cost of ultrafiltration filters. From a Medicare payer perspective, ultrafiltration had a >99% probability of being cost saving. From a hospital perspective, there was a 97% probability ultrafiltration was more expensive. Our model suggested similar 90-day mortality rates between treatment arms.

Conclusion—Despite a reduction in rehospitalization rates, it is unlikely ultrafiltration results in cost savings from a societal perspective. The discordance in cost between societal, Medicare, and hospital perspectives underscores the importance of payer perspective in formulating strategies and reimbursement structures to reduce heart failure hospitalizations. (Circ Cardiovasc Qual Outcomes. 2009;2:566-573.)

Key Words: heart failure • ultrafiltration • diuretics • costs and cost analysis

In the United States, the projected costs for heart failure hospitalizations in 2009 exceeded $20 billion, representing more than one half of all heart failure-related expenditures.1 More than one-third of this cost is contributed by patients readmitted for heart failure within 6 months of discharge.2-4 Heart failure disproportionately affects older individuals and is the most common cause of hospitalization among Medicare beneficiaries.5 As our population ages, acute heart failure exacerbations represent a significant financial burden that is likely to grow.

Ultrafiltration is an alternative to intravenous (IV) diuretics in the treatment of acute heart failure. In the Ultrafiltration versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Congestive Heart Failure (UNLOAD) prospective randomized trial, patients who received ultrafiltration therapy at index hospitalization were less likely than patients treated with IV diuretics to be seen in unscheduled outpatient appointments or readmitted to the hospital for heart failure in the subsequent 90 days of follow-up.6 Several hypotheses have been suggested for this observation including larger total sodium excretion, less neurohumoral activation, and clearance of inflammatory cytokines with ultrafiltration compared to IV diuretics.7-9 The cost of ultrafiltration therapy in the index hospitalization may therefore be offset by a reduced utilization of medical resources in follow-up. We undertook a cost-consequences analysis to determine the average patient clinical outcomes and associated costs with ultrafiltration therapy compared to IV diuretics for index and subsequent acute heart failure hospitalizations out to 90 days from the index hospitalization.

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WHAT IS KNOWN

- Ultrafiltration is an alternative to intravenous diuretics for the management of volume overload in acute heart failure.
- Although ultrafiltration is likely more costly in the index hospitalization, this cost may be offset by a reduction in rehospitalizations.

WHAT THE STUDY ADDS

- Our study suggests ultrafiltration is not cost savings from a societal perspective despite a presumed reduction in rehospitalizations.
- Furthermore, we demonstrated the importance of perspective in cost analysis as the cost estimate varied depending on perspective chosen (ie, societal, Medicare, and hospital).

Methods

Model Design
We used a decision-analytic approach to compare the health and economic outcomes from a societal perspective after treatment with ultrafiltration or IV diuretics at index and subsequent hospitalizations with 90 days follow-up (Figure 1). The decision analysis reflects the design and composition of the UNLOAD trial as several of the clinical outcomes in this trial were used for the base-case estimate. Patients in the UNLOAD trial were predominantly NYHA functional class III or IV and followed for 90 days after the index hospitalization. A societal perspective was chosen for the primary analysis as this perspective incorporates costs and benefits regardless of who incurs the costs and who obtains the benefits.

In our model, the decision node represented the determination to treat the index hospitalization for heart failure with ultrafiltration or IV diuretics. The ultrafiltration system evaluated in the UNLOAD trial requires either midline or central venous access. The model thus incorporated catheter-related blood stream infections (CRBSI) as a significant adverse outcome of ultrafiltration therapy. Treatment with ultrafiltration also requires anticoagulant therapy with heparin to prevent clotting of the ultrafiltration filter. The probability of major bleeding or HIT related to use of intravenous heparin was included in the model. Anticoagulant therapy is not dependent on the use of midline or central venous access, thus the probability of bleeding or HIT does not vary between these arms in our model. Rehospitalized patients were assumed to receive therapy as they had at index hospitalization (ie, patients who received ultrafiltration at index hospitalization would receive ultrafiltration on rehospitalization and vice versa).

There were 9 deaths (9.6%) after ultrafiltration therapy and 11 deaths (11.6%) after IV diuretics in the UNLOAD trial. The trial was of insufficient size to fully assess the ramifications of rare complications associated with ultrafiltration therapy and comment on the significance of this mortality difference. Therefore, we explored the clinical implications of CRBSI, major bleeding, and HIT within our model to assess whether inclusion of these complications substantially increased the estimated 90-day mortality of ultrafiltration. Several inputs in our analysis required communication with investigators from the UNLOAD trial. This included unpublished prospectively collected data on the number of filters used per patient and post hoc estimates on the proportion of patients requiring central access for ultrafiltration. These investigators were not provided access to the current analysis. Our institutional committee on human research determined human subjects review was not required for our analysis. TreeAge Pro was used for model design and analyses. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Clinical Probabilities and Rates
The model required inputs for the following probabilities of clinical events: major bleeding, use of midline or central venous catheters for ultrafiltration, CRBSI, and unscheduled urgent care visit in follow-up. The probability of an unscheduled urgent care visit in follow-up for the base-case estimate was provided from the results of the UNLOAD trial.6 The probability of HIT during ultrafiltration was estimated as the weighted average of published estimates from a systematic review of HIT in the setting of hemodialysis or hemofiltration renal replacement therapy.11 Patients managed with IV diuretics were assumed to receive low-molecular-weight heparin for deep venous thrombosis prophylaxis and thus had a lower associated probability of HIT.12 Mortality for HIT was determined from a weighted average of published literature.13–15 Probability estimates of midline or central venous access use were obtained from discussion with the UNLOAD study investigators (M. Schollmeyer, unpublished data, 2007). The probability of CRBSI with midline and central venous access and associated mortality of CRBSI was estimated as the weighted average from the published literature.16–19 Patients treated with IV diuretics had a nonsignificantly increased probability of a major bleed than ultrafiltration treated patients in the UNLOAD trial (5% versus 1%).6 This likely underestimates the probability of bleeding with ultrafiltration and overestimates the risk.
of bleeding with IV diuretics. Therefore, we chose to model the risk of bleeding with ultrafiltration as the weighted average of bleeding from prior studies of anticoagulation strategies for ultrafiltration in addition to the UNLOAD trial. The risk of bleeding with IV diuretics was estimated as the weighted average from studies of deep venous thrombosis prophylaxis with low-molecular-weight heparin.24–23

Table 1 summarizes the base-case probability estimates for clinical outcomes used in this analysis.

Costs
All health care costs are presented in 2007 US dollars. Cost estimates were based on inflation-adjusted values of weighted averages from the published literature and Medicare reimbursement schedules. When available, we used Medicare reimbursement schedules as the primary estimate of cost to minimize variability in cost estimates. Use of Medicare reimbursement data in cost estimation has been previously described.24 We did not discount costs, as the impact of the potential outcome was less than 1 year.

The following cost estimates deserve emphasis. The baseline daily cost for congestive heart failure hospitalization was calculated by dividing the Medicare Diagnosis Related Group (DRG) reimbursement rate for heart failure (DRG 127) by the mean length of stay reported by the Centers for Medicare and Medicaid Services.25 The amortized cost of the ultrafiltration device per patient was calculated assuming an ultrafiltration device cost of $19,839,26 effective lifetime of 5 years,27 3% discount factor, 5% annuity factor,28 and average use of the ultrafiltration machine 3 times a week for a total of 780 patients. An annual service charge of $3,000 dollars was divided by the annual number of patients treated with the device and added to the amortized cost of the ultrafiltration device.27 The cost of ultrafiltration filters was estimated at $913 per filter.29 The daily cost of rehospitalization with IV diuretic therapy was determined as for the index hospitalization.28 The daily cost of rehospitalization with ultrafiltration was determined by dividing the average hospitalization cost as determined by the decision model by the average number of rehospitalization days.6 To determine inconvenience costs to the patient for urgent care visits or hospitalizations, we used willingness-to-pay estimates from studies of telemonitoring of outpatient heart failure. These studies determined patients are willing to pay $31 to access care at home instead of traveling to the physician’s office.29

Medical Device Utilization and Time Variables
The average patient treated with ultrafiltration in the UNLOAD trial underwent two ultrafiltration treatments with an average of 1.2 filters per treatment (M. Schollmeyer, unpublished data, 2008). The average number of ultrafiltration nursing shifts was assumed equivalent to the number of ultrafiltration treatments. The average per patient duration of index hospitalization and rehospitalization for heart failure was determined from the UNLOAD trial.6 The average medical device utilization and time variables are summarized in Table 3.

Sensitivity Analyses
We varied the clinical probabilities, cost estimates, and resource utilization of all variables in the model to identify important model uncertainties and to assess the robustness of the base-case estimate. We varied the base-case probability of CRBSI in accordance with the source literature.16 All other probability estimates were varied by 50%. All cost assumptions were varied by 25% from the base-case estimate. The number of ultrafiltration filters used per patient and ultrafiltration nursing shifts were varied by 50% from the base-case estimate. The average index hospital duration and rehospitalization days per patient were varied by 25% from the base-case estimate. Variables were adjusted individually to identify variables that most substantially affected the results. Two-way sensitivity analyses were conducted for clinical probabilities and resource utilization that were possible after either treatment modality. Monte Carlo simulation with 10^6 iterations was completed to allow multiple-way sensitivity analysis and estimation of the 95% central range cost and mortality outcomes. Probabilistic sensitivity analyses represent a range of probable outcomes and should not be interpreted as a confidence interval derived from a singular study population. Costs, medical device utilization, and time variables were specified as normal distributions and probabilities were specified as β distributions within the Monte Carlo simulation.

Medicare Payer and Hospital Perspectives
We explored the influence of Medicare payer or hospital perspectives on the cost consequences of ultrafiltration for heart failure. In the Medicare DRG reimbursement model, a set reimbursement is assigned per admission for heart failure.25 Therefore, Medicare does not incur the cost of complications from ultrafiltration therapy. In the Medicare payer perspective, the model included DRG reimbursement for heart failure for the index hospitalizations and congestive heart failure (CHF) hospitalizations occurring within 90 days of

Table 1. Probability Estimates Used in Decision-Tree Analysis

<table>
<thead>
<tr>
<th>Variable Assumption</th>
<th>Base-Case Estimate</th>
<th>Ranges Tested</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleed with UF</td>
<td>0.038</td>
<td>0.019–0.057</td>
<td>6, 20, 21</td>
</tr>
<tr>
<td>Major bleed with IV diuretics</td>
<td>0.006</td>
<td>0.003–0.009</td>
<td>23</td>
</tr>
<tr>
<td>Major bleed mortality</td>
<td>0.148</td>
<td>0.074–0.222</td>
<td>23</td>
</tr>
<tr>
<td>HIT with UF</td>
<td>0.01</td>
<td>0.005–0.015</td>
<td>11</td>
</tr>
<tr>
<td>HIT with IV diuretics</td>
<td>0.002</td>
<td>0.001–0.003</td>
<td>12</td>
</tr>
<tr>
<td>HIT mortality</td>
<td>0.08</td>
<td>0.04–0.12</td>
<td>13–15</td>
</tr>
<tr>
<td>UF via midline catheter</td>
<td>0.5</td>
<td>0.25–0.75</td>
<td>M. Schollmeyer, personal communication, 2007</td>
</tr>
<tr>
<td>UF via CVL</td>
<td>0.5</td>
<td>0.25–0.75</td>
<td>M. Schollmeyer, personal communication, 2007</td>
</tr>
<tr>
<td>CRBSI with midline catheter</td>
<td>0.004</td>
<td>0.002–0.024</td>
<td>16</td>
</tr>
<tr>
<td>CRBSI with CVL</td>
<td>0.044</td>
<td>0.02–0.07</td>
<td>16</td>
</tr>
<tr>
<td>CRBSI mortality</td>
<td>0.16</td>
<td>0.12–0.20</td>
<td>17–19</td>
</tr>
<tr>
<td>Baseline UF mortality</td>
<td>0.096</td>
<td>0.072–0.12</td>
<td>6</td>
</tr>
<tr>
<td>Baseline IV diuretic mortality</td>
<td>0.116</td>
<td>0.087–0.145</td>
<td>6</td>
</tr>
<tr>
<td>Unscheduled UC visit after UF</td>
<td>0.21</td>
<td>0.16–0.26</td>
<td>6</td>
</tr>
<tr>
<td>Unscheduled UC visit after IV diuretics</td>
<td>0.44</td>
<td>0.33–0.55</td>
<td>6</td>
</tr>
</tbody>
</table>

UF indicates ultrafiltration; CVL, central venous line; and UC, urgent care.
follow-up. From a hospital perspective, the costs of heart failure treatment included all costs as determined by the decision model from the societal perspective with the exception of patient inconvenience costs and urgent care visits. Reimbursements included DRG reimbursement for the index hospitalization and CHF hospitalizations occurring in follow-up. Sensitivity analyses were conducted using the same assumptions applied in the societal perspective model.

**Results**

**Societal Perspective Cost Analysis**

In the base-case from the societal perspective, the total cost for patients receiving ultrafiltration therapy at index and follow-up hospitalizations was $13,469 per patient at 90 days, whereas the cost of IV diuretic therapy was $11,610 per patient. Rehospitalization costs accounted for 39% of the total costs in patients treated with IV diuretics, whereas it accounted for only 18% of totals costs in the ultrafiltration arm. Filter costs accounted for 16% of the total cost of ultrafiltration therapy at 90 days. The component costs of the base-case estimates for the treatment arms at 90 days of follow-up are summarized in Table 4.

Varying model inputs in sensitivity analyses as described above revealed the base-case estimate was most dependent on the length of index hospitalization, daily cost of rehospitalization, days rehospitalized, number of ultrafiltration filters used per patient, and cost of ultrafiltration filters, with remaining variables resulting in smaller variation in cost estimates (Figure 2). With the exception of length of index hospitalization, ultrafiltration was more costly from a societal perspective compared to ultrafiltration for the full range of variables tested in one-way sensitivity analyses. Two-way sensitivity analyses provided ranges of values for length of index hospitalization under which ultrafiltration or IV diuretics was favored from a cost perspective. In this analysis, ultrafiltration was favored when the length of index hospitalization was 1.1 day shorter than IV diuretic treated patients (Figure 3). In 2-way sensitivity analysis on days rehospitalized after ultrafiltration of IV diuretics, ultrafiltration was more expensive in the full range of tested values. In Monte

### Table 2. Cost Estimates Used in Decision-Tree Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base-Case Cost Assumption, $</th>
<th>Ranges Tested, $</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline CHF hospitalization daily cost</td>
<td>1,185</td>
<td>889–1481</td>
<td>25</td>
</tr>
<tr>
<td>Ultrafiltration costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amortized UF machine</td>
<td>42</td>
<td>32–53</td>
<td>27</td>
</tr>
<tr>
<td>UF filter</td>
<td>913</td>
<td>685–1141</td>
<td>26</td>
</tr>
<tr>
<td>Additional nursing costs per shift*</td>
<td>102</td>
<td>77–128</td>
<td>42–44</td>
</tr>
<tr>
<td>Heparin infusion†</td>
<td>52</td>
<td>41–65</td>
<td>45, 46</td>
</tr>
<tr>
<td>Physician fees</td>
<td>115</td>
<td>86–144</td>
<td>45</td>
</tr>
<tr>
<td>Major bleed</td>
<td>5,257</td>
<td>3943–6571</td>
<td>23</td>
</tr>
<tr>
<td>HIT</td>
<td>13,041</td>
<td>9781–16 301</td>
<td>23</td>
</tr>
<tr>
<td>Midline catheter‡</td>
<td>152</td>
<td>114–190</td>
<td>Personal communication, 45</td>
</tr>
<tr>
<td>CVL§</td>
<td>205</td>
<td>154–256</td>
<td>45, 47</td>
</tr>
<tr>
<td>CRBSI</td>
<td>13,423</td>
<td>10 067–16 779</td>
<td>47</td>
</tr>
<tr>
<td>Unscheduled UC visit</td>
<td>180</td>
<td>135–225</td>
<td>45</td>
</tr>
<tr>
<td>Inconvenience cost</td>
<td>31</td>
<td>23–39</td>
<td>29</td>
</tr>
<tr>
<td>CHF rehospitalization daily cost</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic therapy</td>
<td>1,195</td>
<td>896–1494</td>
<td>Decision model</td>
</tr>
<tr>
<td>UF therapy</td>
<td>1,739</td>
<td>1304–2174</td>
<td>Decision model</td>
</tr>
</tbody>
</table>

All values in 2007 dollars. UF indicates ultrafiltration; CVL, central venous line; and UC, urgent care.

*Includes incremental salary and staffing costs.

†Includes cost of heparin (20,000 units) and PTT every 4 hours.

‡Includes materials and physician fees.

§Includes materials, physician fees, and chest x-ray for confirmation of placement for CVL.

### Table 3. Average Time and Utilization Estimates per Patient

<table>
<thead>
<tr>
<th>Variable</th>
<th>IV Diuretics (Range)</th>
<th>Ultrafiltration (Range)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index hospitalization duration</td>
<td>5.8 d (4.4–7.3)</td>
<td>6.3 d (4.7–7.9)</td>
<td>6</td>
</tr>
<tr>
<td>UF filters per patient</td>
<td>NA</td>
<td>2.4 filters (1.2–3.6 filters)</td>
<td>Personal communication</td>
</tr>
<tr>
<td>UF nursing shifts (8 hours)</td>
<td>NA</td>
<td>2 shifts (1–3 shifts)</td>
<td>Personal communication</td>
</tr>
<tr>
<td>CHF rehospitalizations</td>
<td>0.46 (0.35–0.58)</td>
<td>0.22 (0.17–0.28)</td>
<td>6</td>
</tr>
<tr>
<td>Rehospitalization days</td>
<td>3.8 d (2.9–4.8)</td>
<td>1.4 d (1.1–1.8)</td>
<td>6</td>
</tr>
</tbody>
</table>

UF indicates ultrafiltration.
Carlo simulation of $10^6$ iterations with random selection of variables from the distributions provided, the 95% central range of cost at 90 days for ultrafiltration strategy was $10,537 to $16,684 compared to $8,814 to $14,679 for IV diuretics. In 86% of iterations, ultrafiltration was more expensive compared to IV diuretics.

We explored the cost of ultrafiltration under optimal circumstances compared to IV diuretics from a societal perspective in a post hoc analysis. In the primary analysis, point estimates for initial hospital duration were assumed different for IV diuretics (5.8 days) and ultrafiltration (6.3 days). Although this difference did not reach statistical significance in the UNLOAD trial, it is consistent with another study of ultrafiltration compared to usual care.30 Given the influence of duration of hospitalization on cost in our sensitivity analyses, we assumed the initial hospital duration was the same for both treatment strategies (6.0 days) in our post hoc analysis. In the UNLOAD trial, each ultrafiltration filter was used for a maximum of 8 hours in keeping with device indications at the time.31 Current indications

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of Index Hospitalization for UF Patients</td>
<td>6.3</td>
<td>4.7-7.9</td>
</tr>
<tr>
<td>Length of Index Hospitalization for IV Diuretic Patients</td>
<td>5.8</td>
<td>4.4-7.3</td>
</tr>
<tr>
<td>Average Number of Days Rehospitalized after IV Diuretics</td>
<td>3.8</td>
<td>2.9-4.8</td>
</tr>
<tr>
<td>Daily Cost of Rehospitalization with IV Diuretics</td>
<td>$1,195</td>
<td>$896-1,494</td>
</tr>
<tr>
<td>Filters per Patient Treated with UF</td>
<td>2.4</td>
<td>1.2-3.6</td>
</tr>
<tr>
<td>Daily Cost of Rehospitalization with UF</td>
<td>$1,739</td>
<td>$1,304-2,174</td>
</tr>
<tr>
<td>Average Number of Days Rehospitalized after UF</td>
<td>1.4</td>
<td>1.1-1.8</td>
</tr>
<tr>
<td>Cost per Filter</td>
<td>$913</td>
<td>$685-1,141</td>
</tr>
<tr>
<td>Probability of CRBSI with CVL</td>
<td>0.044</td>
<td>0.02-0.07</td>
</tr>
</tbody>
</table>

Figure 2. Tornado diagram of influential variables. The horizontal bars demonstrate the difference in the total cost of ultrafiltration compared to IV diuretic therapy at 90 days when a particular input varies between its upper and lower limit of the range evaluated while other variables remain constant. All variables in the decision analysis were tested with only the most influential shown in the figure. The vertical line represents the base-case estimate. UF indicates ultrafiltration; CVL, central venous line.

Figure 3. Two-way sensitivity analysis evaluating the effect of simultaneously changing the average length of index hospitalization among patients with acute heart failure treated with IV diuretics or ultrafiltration. Pairs of values below and to the right of the line (dark gray area) favor ultrafiltration, whereas values above and to the left (light gray area) favor IV diuretics. In the UNLOAD clinical trial, the length of index hospitalization among patients treated with IV diuretics was 5.8 days compared to 6.3 days for those treated with ultrafiltration. UF indicates ultrafiltration.
allow the ultrafiltration filter to be used for greater than 8 hours in patients with volume overload.\textsuperscript{32} We explored the influence of this change by assuming the average patient used 1.5 filters for the duration of ultrafiltration therapy. Finally, our point estimate for major bleeding with ultrafiltration was a weighted average of the UNLOAD trial and other studies of ultrafiltration for nonheart failure care. This may overestimate the risk of bleeding and thus in our exploratory analysis we chose a major bleeding risk of 1% to match the rate of gastrointestinal bleeding observed in the UNLOAD trial.

Our exploratory analysis demonstrated the cost of ultrafiltration was $11,957 per patient compared to $11,847 for IV diuretics. In Monte Carlo simulation, ultrafiltration was favored in 50% of iterations suggesting neither strategy was favored from a cost perspective in this analysis. As in our primary analysis, the probability of rare events was determined from published literature given the small size of the UNLOAD trial. Reducing the probability of rare events such as CRBSI to match event rates observed in the UNLOAD trial and HIT to match event rates estimated for treatment with IV diuretics decreased the cost of ultrafiltration to $11,692. This was not a substantial cost-savings with ultrafiltration as it was favored to IV diuretics in only 54% of iterations in Monte Carlo simulation.

Cost From Medicare and Hospital Perspectives
Changing the payer perspective significantly impacted the results of the model. The total 90-day costs from the Medicare perspective for patients receiving ultrafiltration therapy was $7230 compared to $6852 for patients treated with IV diuretics. From a hospital perspective, ultrafiltration was associated with a $6157 shortfall between cost and revenues compared to $2820 for patients treated with IV diuretics.

One-way sensitivity analyses from the perspective of Medicare demonstrated that the cost results were most influenced by the reimbursement rate for CHF admissions. Ultrafiltration dominated IV diuretics from a Medicare perspective throughout the ranges tested in sensitivity analyses. In the probabilistic sensitivity analysis, the 95% central range of cost at 90 days for ultrafiltration strategy was $5405 to $7905 compared to $6423 to $10,959 for IV diuretics. Ultrafiltration was cost-saving relative to IV diuretics in greater than 99% of iterations from a Medicare perspective. From a hospital perspective, 1-way sensitivity analyses suggested the base-case estimate was most influenced by reimbursement for CHF admission, length and cost of index hospitalization, daily cost of rehospitalization with IV diuretics, and the average number of days rehospitalized after IV diuretics. In Monte Carlo simulation from a hospital perspective, the 95% range of cost in excess of revenue for ultrafiltration was $2789 to $9689 compared to $826 of revenue above cost to $6606 in excess of revenue. From a hospital perspective, ultrafiltration therapy was more expensive that IV diuretics in 97% of iterations.

Mortality Estimates at 90 Days
In the base-case, 90-day mortality with ultrafiltration was 10.85% compared to 11.75% with IV diuretics. Contributors to absolute mortality above the baseline estimate for ultrafiltration included a 0.69% increase attributed to major bleeding, a 0.10% increase attributed to HIT, and a 0.47% increase attributed to CRBSI. For IV diuretics, contributors to absolute mortality above the baseline estimate included a 0.13% increase from major bleeding and a 0.02% increase from HIT. In Monte Carlo simulation, the 95% range of mortality at 90 days for ultrafiltration therapy was 8.4 to 13.6% compared to 9.0 to 14.8% for IV diuretics. In 68% of iterations, ultrafiltration had a lower 90-day mortality compared to IV diuretics.

Discussion
From this cost-consequences analysis, it appears unlikely that ultrafiltration therapy for index and subsequent acute heart failure hospitalizations is cost-saving from a societal perspective compared to IV diuretics at 90 days from index hospitalization. Sensitivity analyses demonstrated ultrafiltration to be more expensive throughout the majority of variable ranges. This was confirmed in probabilistic sensitivity analyses, which demonstrated higher costs with ultrafiltration compared to IV diuretics in 86% of iterations. Changing the payer perspective was highly influential on the relative costs of ultrafiltration and IV diuretic therapy at 90 days. From a Medicare perspective, ultrafiltration was cost-saving in 99% of Monte Carlo simulations due to differences in cost between therapies being only related to differences in rehospitalization rates. Conversely, ultrafiltration therapy was unfavorable from a hospital perspective because of the additional costs associated with ultrafiltration therapy that are not captured in a DRG reimbursement system and a reduction in revenue from fewer rehospitalizations.

These findings highlight important implications in considering strategies to reduce readmission after heart failure hospitalization. Approximately 1 in 4 patients are readmitted within 30 days of heart failure hospitalization.\textsuperscript{33} As demonstrated in our analysis from a Medicare payer perspective, a reduction in readmission rates after CHF hospitalization could profoundly impact costs to Medicare. A number of in-hospital and postdischarge interventions that reduce the risk of rehospitalization after admission for heart failure have been identified.\textsuperscript{34,35} In contrast to our analysis of ultrafiltration for treatment of heart failure, many of these interventions have been demonstrated to be cost-saving from a societal perspective.\textsuperscript{34,37,38} Despite the clinical and cost benefits of these interventions, many of these interventions are discontinued at the conclusion of their individual study periods due to financial considerations.\textsuperscript{39} These financial considerations are highlighted by the discordance between societal, Medicare, and hospital perspectives in our study. Reimbursement structures that reward for reductions in rehospitalization rates may reduce this cost disparity for heart failure interventions, encourage implementation of these strategies, and maintain a cost-savings from a Medicare perspective.

Our model allowed for estimation of mortality attributed to rare events that the UNLOAD trial was inadequately powered to detect. In our model, the absolute mortality associated with rare complications was 1.25% for ultrafiltration and 0.15% for IV diuretics. Despite the greater risk of complications with ultrafiltration in our model, overall mortality between therapies was similar with ultrafiltration having a lower
mortality rate in 63% of Monte Carlo simulations. Studies of long-term outcomes with recurrent use of ultrafiltration for acute heart failure are needed to fully understand the potential implications of this therapy.

Our sensitivity analyses demonstrated the number of ultrafiltration filters used per patient and length of index hospitalization were highly influential on our cost-estimate of ultrafiltration therapy. Increasing clinical experience with ultrafiltration for heart failure may allow for longer ultrafiltration filter life and fewer filters to be used per patient. Additionally, the longer duration of hospitalization associated with the use of a new technology may be eliminated with increasing familiarity. Finally, approaches to minimize complications associated with ultrafiltration, such as chlorhexidine dressings after central line placement to reduce CRBSI, could reduce costs as well. Our exploratory analysis demonstrated ultrafiltration was cost-equivalent to IV diuretics in the setting of optimized ultrafiltration filter use, minimization of adverse consequences, and equal duration of index hospitalization. Optimization of these factors was insufficient to favor ultrafiltration from a cost perspective.

There are several limitations to our analysis. First, costs were extrapolated from previously published studies and Medicare reimbursement schedules because of a lack of patient level cost data. It is possible that some patient costs were not captured in this approach. Second, ultrafiltration therapy may require intensive care unit monitoring or greater levels of nursing care than estimated in our analysis and would add additional cost not modeled in our analysis. Third, our baseline daily cost estimate includes the cost of IV diuretics. Patients treated with ultrafiltration did not receive IV diuretics in the first 48 hours of care in the UNLOAD trial. We did not discount the cost of IV diuretics for patients treated with ultrafiltration because of uncertainty on dose and type of diuretic used. Assuming furosemide to be the most frequently used diuretic at an average total dose of 480 mg IV in the first 48 hours, this would comprise less than 0.2% ($18) of the cost of ultrafiltration and is unlikely to significantly influence our model estimates. Fourth, our model did not include several of the prespecified secondary outcomes recorded in the UNLOAD trial as we intentionally limited the scope and frame of our analysis to outcomes we felt were most closely associated with potential risk of mortality and cost of care. Fifth, use of probability and resource utilization estimates from a randomized controlled trial may not represent the clinical outcomes and costs associated with ultrafiltration therapy in general use. Sixth, Medicare reimbursement rates were used as an estimate of payment to hospitals in our analysis from a hospital perspective. Private insurers likely provide a greater reimbursement to hospitals for heart failure. We feel use of Medicare reimbursement rates is reasonable given that the burden of heart failure is among the elderly. Seventh, although our use of probabilistic sensitivity analyses to evaluate the overall uncertainty in the analysis follows recommended guidelines, the results represent a range of probable outcomes and should not be interpreted as a confidence interval derived from a singular study population. The uncertainty for the key parameters in the model was estimated from a range of sources where available, however covariance estimates were not available. Finally, we chose to present our results as a cost-consequences analysis with 90-day costs and mortality reported separately as opposed to a cost-effectiveness analysis with results presented as cost per life-year or cost per quality-adjusted life-year. Although a cost-effectiveness methodology is often preferred to allow comparison of the incremental health benefit associated with the incremental cost of alternate therapies, the current data on ultrafiltration for heart failure are too limited in length of follow-up to extrapolate cost and survival estimates for a reasonable comparison of cost per life-year or cost per quality-adjusted life-year gained. Additional studies are needed to define long-term cost and mortality differences between therapies that will be essential in the final considerations of the utility of ultrafiltration.

In summary, our cost-consequences analysis suggests ultrafiltration is unlikely to be cost-saving from a societal perspective compared to IV diuretics at 90 days from index hospitalization. Further study is needed to determine whether ultrafiltration may result in survival benefit or improvement in quality of life to support use of this therapy. Medicare and hospital perspectives demonstrated opposing cost implications for ultrafiltration therapy that were highly influenced by rehospitalization rates. Understanding how perspective influences cost of heart failure interventions has implications for formulating reimbursement structures that encourage strategies to reduce CHF hospitalization rates while reducing costs to society and payers such as Medicare.

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References


Cost-Consequences of Ultrafiltration for Acute Heart Failure: A Decision Model Analysis
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SUPPLEMENTAL MATERIAL.

Supplemental Methods

Additional Cost Estimates

The costs of intravenous access, heparin infusion and associated laboratory monitoring, and nursing costs associated with ultrafiltration were determined as follows. Professional fees from 2007 Medicare reimbursement schedules were used as a surrogate for the professional cost of hemofiltration evaluation (CPT 90947) and placement of central venous line (CPT 36556) or midline venous access (CPT 36569). Material costs for central venous lines were estimated from published literature and cost of midline catheters from personal communication with UNLOAD study investigators (Schollmeyer M., unpublished data, 1/31/08). We estimated patients would receive 20,000 units of heparin over 8 hours with PTT monitoring every four hours during ultrafiltration. The cost of heparin infusion was estimated from average wholesale drug prices ($11 for 20,000 units of heparin). Costs of partial thromboplastin time laboratory monitoring (CPT 85730) and x-ray confirmation of line placement (CPT 71010) were estimated from 2007 Medicare reimbursement schedules. We estimated nursing costs would include staffing costs resulting from a higher nurse to patient ratio and higher salaries for nurses trained in hemodialysis. We estimated a general ward nurse to patient ratio of 1:3 and a nurse to patient ratio of 1:2 for patients undergoing ultrafiltration. Using weekly base salaries for hemodialysis nurses, we divided by 4 shifts per week to determine shift salaries. Finally, the cost of urgent care visits was estimated from Medicare reimbursement schedules (CPT 99285). The overall estimated cost per ultrafiltration treatment was larger in our analysis than previously published cost estimates, mostly due to a greater cost for ultrafiltration filters in our analysis.
Supplemental Tables

**Table A.** Reimbursement, and Cost Estimates Used in Medicare Payer and Hospital Perspectives

<table>
<thead>
<tr>
<th>Variable Assumption</th>
<th>Base-Case Estimate</th>
<th>Ranges Tested</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement for CHF Admission</td>
<td>$5,926</td>
<td>$4,445-$7,408</td>
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<tr>
<td>Daily Cost of CHF Admission with UF</td>
<td><strong>$1,739</strong></td>
<td><strong>$1,304-$2,174</strong></td>
<td>Decision model</td>
</tr>
<tr>
<td>Daily Cost of CHF Admission with IVD</td>
<td>$1,195</td>
<td>$896-$1,494</td>
<td>Decision model</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; UF, ultrafiltration; and IVD, intravenous diuretics.
**Table B.** Base-Case Estimate of Average Patient Costs for IV Diuretics and Ultrafiltration Therapy at 90-days Follow-up from Medicare Payer and Hospital Perspectives

<table>
<thead>
<tr>
<th>Component</th>
<th>IV Diuretics</th>
<th>Ultrafiltration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medicare Perspective</strong></td>
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<td></td>
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<tr>
<td>Index CHF Hospitalization</td>
<td>5,926</td>
<td>5,926</td>
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<tr>
<td>CHF Rehospitalizations</td>
<td>2,726</td>
<td>1,304</td>
</tr>
<tr>
<td>Total Cost at 90-days</td>
<td>$8,652</td>
<td>$7,230</td>
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<tr>
<td><strong>Hospital Perspective</strong></td>
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<td></td>
</tr>
<tr>
<td>Baseline CHF Hospitalization Costs</td>
<td><strong>6,931</strong></td>
<td><strong>10,952</strong></td>
</tr>
<tr>
<td>Reimbursements</td>
<td>5,926</td>
<td>5,926</td>
</tr>
<tr>
<td>CHF Rehospitalizations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs</td>
<td>4,541</td>
<td>2,435</td>
</tr>
<tr>
<td>Reimbursements</td>
<td>2,726</td>
<td>1,304</td>
</tr>
<tr>
<td>Total Cost at 90-days</td>
<td>$2,820</td>
<td>$6,157</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure.
Supplemental References


