Cost-Effectiveness of Pediatric Heart Transplantation Across a Positive Crossmatch for High Waitlist Urgency Candidates

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Abstract

Allosensitized children listed with a requirement for a negative prospective crossmatch have high mortality. Previously we found that listing with the intent to accept the first suitable organ offer, regardless of the possibility of a positive crossmatch (TAKE strategy), results in a survival advantage from the time of listing as compared to awaiting transplantation across a negative crossmatch (WAIT). The cost-effectiveness of these strategies is unknown. We used Markov modeling to compare cost-effectiveness between these waitlist strategies for allosensitized children listed urgently for heart transplantation. We used registry data to estimate costs and waitlist/post-transplant outcomes. We assumed patients remained in hospital after listing, no positive crossmatches for WAIT, and a base-case probability of a positive crossmatch of 47% for TAKE. Accepting the first suitable organ offer cost less ($405,904 versus $534,035) and gained more quality-adjusted life years (3.71 versus 2.79). In sensitivity analyses, including substitution of waitlist data from children with unacceptable antigens specified during listing, TAKE remained cost-saving or cost-effective. Our findings suggest acceptance of the first suitable organ offer for urgently listed allosensitized pediatric heart transplant candidates is cost-effective and transplantation should not be denied because of allosensitization status alone.

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DISCLOSURE
The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

DISCLAIMER
The data reported here have been supplied by the United Network for Organ Sharing (UNOS) as the contractor for the Organ Procurement and Transplantation Network (OPTN). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the OPTN or the US Government.
INTRODUCTION

Historically, allosensitized children requiring heart transplantation were commonly listed with a requirement for a negative donor cell crossmatch prior to transplantation [1]. Consequently, this group’s survival has been poor because fewer donor organs are “acceptable” for such patients [1, 2]. Our recent analysis showed that taking the first suitable organ offer for urgently listed, allosensitized candidates, results in a survival benefit from the time of listing when compared to a strategy of awaiting transplantation across a negative crossmatch [3]. However, the cost-effectiveness of this strategy is unknown. We used a Markov state transition model [4] to compare the relative costs and health utility outcomes of these strategies. This type of decision modeling, termed cost-effectiveness analysis, is a quantitative, probabilistic economic analysis that is used commonly in health services research to inform decision-making [5]. A key aspect of this methodology is the ability to perform sensitivity and scenario analyses in which the “base-case” model findings are reassessed after varying cost and/or event probability assumptions. This allows investigators to account for uncertainty in model assumptions and potentially define circumstances under which each strategy is cost-effective.

We compared the cost-effectiveness of two competing waitlist management strategies for allosensitized, urgently listed, pediatric heart transplant candidates: listing with a requirement for a negative prospective crossmatch (WAIT) versus acceptance of the first suitable organ offer (TAKE). We hypothesized that taking the first suitable organ offer would be more cost-effective than awaiting transplantation across a negative donor cell crossmatch. We also used waitlist outcomes data from a cohort of children who had unacceptable antigens recorded at some point during listing as a surrogate to assess cost-effectiveness of listing with a negative virtual crossmatch requirement.

METHODS

Overview and Data Sources

Cost-effectiveness analysis uses discrete health states, costs and utilities (a measure of quality of life) associated with each health state, and probabilities of transitioning from one state to another to compare outcomes between alternative management strategies [4]. Strategies are compared on the basis of the ratio of the difference in cost to the difference in effectiveness (quality adjusted life years, QALYs). A strategy is ‘dominated’ by another when it costs more and results in fewer QALYs. In the absence of a dominant strategy, the incremental cost-effectiveness ratio (ICER) is used to decide between strategies. For this analysis we considered an ICER <$100,000/QALY as cost-effective [6].

This study used data from the Organ Procurement and Transplantation Network (OPTN). The OPTN data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere [7]. The Health Resources and Services Administration (HRSA), US Department of Health and Human Services provides oversight to the activities of the OPTN contractor. The Pediatric Heart
Transplant Study (PHTS) is an organization of more than 40 centers that contribute data about children from the time of listing and after transplantation to a centralized, prospective, event-driven database [8]. HCUPnet is a publically-available on-line query system that provides access to US statistics on inpatient utilization using data from the Healthcare Cost and Utilization Project (HCUP)[9]. The Pediatric Health Information System (PHIS) database contains inpatient billing data from 43 not-for-profit children’s hospitals located in 17 major metropolitan areas and accounting for 85% of admissions to US freestanding children’s hospitals [10].

Model Parameters

The Markov model is shown in Figure 1. After assignment to either the TAKE or WAIT strategy, the hypothetical model candidate can remain in the waitlist phase of the model for up to 2 years, during which in each model cycle he/she can receive a transplant, die awaiting transplant, or be delisted. The probability of these events was varied with each cycle (defined as 1 month in our model) based on OPTN data on the occurrence of these events among children (age <18 years) who were listed status 1A between January 21, 1999 and December 2009 (n=2,937). We assumed all patients remained hospitalized until transplant, death, or delisting. Pre-transplant event probabilities and post-transplant survival were derived from candidates in the OPTN dataset as previously described [3]. We assumed no patient in the WAIT arm could have a positive donor-specific crossmatch (DSXM) whereas in the TAKE arm we assumed the probability of a positive DSXM was 47%. This was based on the mean pre-transplant panel reactive antibodies (PRA) of patients who were listed with a prospective crossmatch requirement (PXMR) throughout the entirety of their listing that were common to both the OPTN and PHTS.

Costs and Utilities

Costs and utilities used in the model are shown in Table 1. All costs were adjusted using the gross domestic product deflator method and reported in 2012 US Dollars (USD) [11]. Costs were divided into three phases: 1) pre-transplant: from listing to transplant, death or delisting; 2) perioperative: from day of transplant to 30 days post-transplant, and 3) post-transplant care. Pre-transplant costs were derived from the HCUPnet database. Specifically we divided the median cost by the median length of stay for hospitalizations in 2009 for a principal diagnosis of “congestive heart failure, nonhypertensive” among 0 to 17 year-olds at children’s hospitals and multiplied by 30 to estimate the first month pre-transplant cost. We assumed pre-transplant costs for each additional month were 75% of the first month cost in order to account for diagnostic testing and procedures performed early in the hospitalization. We also assumed that all patients remained status 1A inpatients while awaiting transplantation. Costs for perioperative transplant and post-transplant care were derived from the literature [12, 13].

Sensitivity and Scenario Analyses

To account for potential uncertainty of our model input data we performed a series of one-way sensitivity analyses [14], varying each of the waitlist and post-transplant event probabilities from 0.5 to 1.5 times their base-case estimate. The probability of a positive DSXM for the TAKE strategy was varied from 10 to 100%. The ranges over which costs and
utilities were varied are shown in Table 1. We also performed a probabilistic sensitivity analysis [15] where the model outcome was determined for 5000 iterations in which each of the model input variables were varied simultaneously and randomly across parameter distributions. We used the 95% confidence intervals of the time-dependent event probabilities and a probability of a positive DSXM of 10 to 100% as the boundaries in this analysis. Costs and utilities were bounded by distributions that approximated the mean and standard deviation of their base-case point estimates [14].

We also performed scenario analyses to assess the impact of regional differences in waitlist durations on our findings. For these analyses we determined the median time to heart transplantation for status 1A children in each United Network for Organ Sharing (UNOS) region from 1999 to 2009 and then substituted waitlist outcomes data from UNOS regions with the shortest and longest waiting times.

Because perioperative transplant cost data were derived from a relatively small sample size [13], we substituted data from the PHIS database into the model. For this scenario analysis, we only used PHIS data of children who received heart transplantation on hospital day 0 or 1 to ensure this alternate assessment of perioperative transplant costs did not “double count” costs already accounted for by the pre-transplant cost data. Because DSXM results are not captured in PHIS, we considered the use of plasmapheresis as a surrogate for transplantation across a positive crossmatch.

Lastly, we attempted to define a cohort from the OPTN dataset that represented the experience of candidates listed with a virtual crossmatch requirement. For this analysis we identified all status 1A children listed with “unacceptable antigens” in the OPTN dataset from 1999–2009 (n=64) and substituted this group’s waitlist event probabilities into the WAIT arm of the model. Of note, the OPTN dataset contains only the date and time of unacceptable antigen additions but not the occurrence or timing of removal of unacceptable antigens. Thus we were unable to determine the duration for which the virtual crossmatch requirement was in effect during each of these candidates’ waiting times.

Data were analyzed with SAS v9.2 (SAS Institute Inc, Cary, NC, USA) and R (R Foundation for Statistical Computing, Vienna, Austria). Decision modeling was performed using TreeAge Pro Suite 2012 (TreeAge Software, Inc, Williamstown, MA). Costs and health benefits were discounted at 3% annually [16]. This study was conducted with the approval of the University of Pittsburgh Institutional Review Board, OPTN, PHTS, and PHIS.

RESULTS

Base-case analysis

Characteristics of the patient cohorts used in the model are shown in Table 2. Patients who had a PXMR throughout listing were older and more commonly had a diagnosis of congenital heart disease. Waitlist competing outcomes and post-transplant survival data that were used in the model are shown graphically as cumulative event curves in Figure 2. Under
base-case assumptions TAKE was dominant; it cost less ($405,904 versus $534,035) and
gained more QALYs (3.71 versus 2.79) than WAIT.

**Sensitivity Analyses**

TAKE remained dominant after varying the probability of a positive DSXM of the TAKE
group from 10 to 100%. The TAKE strategy was also generally dominant or cost-effective
when each of the waitlist monthly event probabilities were varied between 0.5–1.5 times
of base-case. The only exception was when the monthly event probability of transplantation for
the TAKE strategy was between 0.63 and 0.5 times base-case (ICER $101,261 to $291,524/
QALY gained). When each of the costs and utilities were varied according to the ranges
shown in table 1, the TAKE strategy also remained dominant or cost-effective. Taking the
first suitable donor organ offer also remained the dominant strategy when post-transplant
survival estimates for either a positive or negative DSXM were varied between 0.5–1.5 times
base-case. To put this into a more clinically applicable context, we assumed constant annual
probabilities of death after transplantation across a negative (4.5%/year) and positive (7.5%/year)
DSXM that were equal to our 10-year OPTN survival estimates of 63% and 46%,
respectively (figure 2c). Under these circumstances, TAKE remained dominant as long as
annual mortality for transplantation across a positive DSXM was <37%/year (equivalent to
median post-transplant survival of >1.6 years).

In probabilistic sensitivity analysis the TAKE strategy cost an average of $67,603 less than
WAIT and gained an average of 0.61 QALYs more than WAIT. At a willingness-to-pay of
$100,000/QALY gained, the TAKE strategy was 1.6 times more likely to be favored than the
WAIT strategy.

**Scenario Analyses**

When we examined the effect of regional differences in waitlist durations on strategy
preference, the TAKE strategy remained cost-effective. In the regions with the longest
median waiting times, TAKE was dominant (Table 3). In the regions with the shortest
median waiting times, TAKE was favored; it cost more ($387,195 versus $326,283) but
 gained more QALYs (3.68 versus 2.82) than WAIT and had an ICER of $70,384/QALY
 gained. Substitution of multicenter PHIS cost data for the perioperative transplant phase
showed that costs were higher among recipients who received plasmapheresis [$720,148
(445,008 – 1,042,621) versus $355,578 (265,144 – 524,093); p<0.001]; however, the TAKE
strategy was still dominant ($432,197 versus $542,894 and 3.71 versus 2.79 QALYs).

Finally, when we substituted waitlist outcomes of candidates who had unacceptable antigens
indicated at some point during listing into the WAIT strategy we found that WAIT gained
more QALYs than TAKE (3.94 versus 3.80); however, it was far more costly ($798,432
versus $405,904) and thus not cost-effective (ICER $2,777,763/QALY gained).

**DISCUSSION**

Our model predicts that taking the first suitable organ offer, regardless of the potential for a
positive crossmatch, is cost-effective at a willingness-to-pay threshold of $100,000/QALY
 gained for allosensitized pediatric heart transplant candidates who are listed at high urgency
(i.e. UNOS status 1A). Under base-case assumptions and in all but one of the sensitivity analyses, a strategy of taking the first suitable organ offer resulted in both lower costs and greater survival from the time of listing. The results of the probabilistic sensitivity analysis confirmed these findings.

It appears that taking the first suitable organ offer was cost-effective for two reasons. First, the cost savings of transplantation across a negative DSXM were generally offset by the higher cost of pre-transplant care accrued during the longer waiting times associated with awaiting transplantation across a negative prospective crossmatch. Second, the inferior survival observed after transplantation across a positive DSXM was more than offset by enhanced waitlist survival.

Virtual crossmatching has become increasingly more commonly utilized in pediatric heart transplantation [17]. While our unacceptable antigen scenario analysis finding that WAIT resulted in slightly greater quality-adjusted survival over TAKE may be interpreted as evidence to support the use of virtual crossmatching in pediatric donor heart selection, two important details should be recognized. First, the WAIT strategy in this scenario far exceeded the conventional $100,000/QALY gained threshold for cost-effectiveness. While there is debate as to the most appropriate willingness-to-pay threshold, an incremental quality-adjusted survival benefit of over $2.7 million per QALY gained is 5 to 10-fold higher than the debated range [6]. Second, this analysis almost certainly under-represents the true severity of the waitlist experience for those in whom a negative virtual crossmatch is required. This is because the occurrence and timing of changes in unacceptable antigen requirements could not be factored into this scenario analysis model cohort. With any removal of unacceptable antigens or of the virtual crossmatch requirement entirely, the cohort becomes less reflective of the WAIT strategy and more reflective of the TAKE strategy. Assuming that outcomes for candidates with a virtual crossmatch requirement lie somewhere between those estimated by the unacceptable antigen cohort in the scenario analysis and the cohort listed with a prospective crossmatch requirement in the base-case model, taking the first suitable organ offer is almost certain to be cost-effective for patients with a virtual crossmatch requirement.

This analysis adds important cost and quality of life information to our previous work [3]. In the current healthcare environment there is strong pressure to limit costs, particularly for services with little to no expected benefit over other treatments [18]. Thus, the knowledge that taking the first suitable organ offer for allosensitized pediatric heart transplant candidates is not only expected to result in greater survival, but is also economically advantageous provides justification for this approach. From a clinical perspective this is critically important. Allosensitization is present in up to 9% of adult [19] and 16% of pediatric heart transplant candidates [2, 20], and increases in the prevalence of allosensitization are likely with the growing use of ventricular assist devices [21]. Also, increased use of highly sensitive and specific antibody detection assays [22] will further augment the detection, and thus prevalence, of allosensitization.

Our model considered only costs and health benefits from the perspective of the pediatric heart transplant candidate. It does not consider the broader implications of organ allocation...
to allosensitized versus non-allosensitized patients. From the perspective of any high-risk, urgent-need candidate, even a small chance at meaningful post-transplant survival with a reasonably good quality of life would make transplantation desirable. However, the need for donor organs far exceeds supply [23] and from the societal perspective, decisions made about transplant candidacy must not only consider risk and benefit of individual candidates, but must also be made within the framework of societal expectations for opportunity and bearable costs [24].

Other important limitations to consider are our use of registry data to estimate model parameters. To account for this we varied parameter values widely around our point estimates of waitlist and post-transplant outcomes and supplemented our base-case analysis with multiple scenario analyses in which we utilized alternate sources or assumptions. Our findings are only relevant to urgent transplant candidates and should not be applied to candidates listed at lesser urgency (i.e. UNOS statuses 1B and 2). Also, we based the cost of pre-transplant care on the cost of pediatric inpatient heart failure care and thus assumed that all patients remained hospitalized from listing to transplant. While hospitalization was not a requirement for pediatric status 1A candidacy during this time period, 90% of patients in our model cohort were in hospital at the time of transplant. Also, our daily pre-transplant cost estimate was 33% less than that of Dayton et al (after conversion to 2012 USD) for 78 primary pediatric heart transplant recipients [12]. Finally, our model estimates may not be consistent with the results of a prospective assessment of these competing waitlist strategies.

In summary, taking the first suitable organ offer for allosensitized pediatric heart transplant candidates listed urgently is cost-effective at a willingness-to-pay of $100,000/QALY gained and may in fact be cost saving. Data that fully describe the waitlist experience for candidates listed with a virtual crossmatch requirement are lacking, however our analysis suggests that even for these candidates a strategy of taking the first suitable organ offer is likely to be cost-effective. While the broader implications of these conclusions with respect to organ allocation should be studied further, we believe that candidacy for pediatric heart transplantation should not be denied on the basis of sensitization status alone.

Acknowledgments

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Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>congenital heart disease</td>
</tr>
<tr>
<td>DSXM</td>
<td>donor-specific crossmatch</td>
</tr>
<tr>
<td>ECMO</td>
<td>extra-corporeal membrane oxygenation</td>
</tr>
<tr>
<td>gov’t</td>
<td>government</td>
</tr>
<tr>
<td>HCUP</td>
<td>Healthcare Cost and Utilization Project</td>
</tr>
<tr>
<td>HRSA</td>
<td>Health Resources and Services Administration</td>
</tr>
</tbody>
</table>
References


Figure 1.
Markov decision model of cost effectiveness for two competing waitlist management strategies of allosensitized pediatric heart transplant candidates. Following assignment to either the WAIT or TAKE strategy, the hypothetical model cohort was at risk each cycle (month) for transition from the “Awaiting Transplant” state to any state directly connected by an arrow. Waitlist probabilities for transition (p₁ through p₆) were not constant for each cycle, but varied monthly and were derived from OPTN data on waitlist outcomes of candidates who were listed with a prospective crossmatch requirement throughout the entirety of listing (WAIT strategy; figure 2a) or who never had a prospective crossmatch requirement (TAKE strategy; figure 2b). For the WAIT strategy there was no probability of transitioning to transplant across a positive DSXM state (i.e. p₆=0). Post-transplant survival was also modeled using OPTN data on mortality after transplantation across a positive DSXM (p₈) or negative DSXM (p₉) and varied (monthly until 2 years, then annually; figure 2c). For simplicity, costs and utilities associated with each transition state are not illustrated in the figure but are as shown in Table 1. Note: p₄ = [1−(p₁+p₂+p₃+p₅+p₆)], p₈ = 1−p₇, and p₁₀ = 1−p₉. Tx, transplant; DSXM, donor specific crossmatch; OPTN, Organ Procurement Transplantation Network; PXMR, prospective crossmatch requirement.
Figure 2.
Graphical representation of OPTN outcomes data on status 1A pediatric heart transplant candidates (1999–2009) that were used to derive model probabilities of waitlist outcomes and post-transplant survival. Upper competing risk graphs depict waitlist outcomes for candidates who (A) maintained a requirement for a PXMR throughout listing (WAIT strategy) and (B) never had a PXMR during listing. Lower graph (C) depicts post-transplant survival for status 1A recipients, stratified by DSXM result. DSXM, donor specific crossmatch; OPTN, Organ Procurement Transplantation Network; PXMR, prospective crossmatch requirement.
Table 1

Costs and Utilities

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Case Estimate</th>
<th>Range</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Costs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preTx (1st month)</td>
<td>80,852</td>
<td>49,627 – 127,688a</td>
<td>[9]</td>
</tr>
<tr>
<td>preTx (month 2 to 24)</td>
<td>60,639</td>
<td>37,221 – 95,766a</td>
<td>[9]</td>
</tr>
<tr>
<td>Tx across positive XM</td>
<td>240,000</td>
<td>119,787 – 384,017</td>
<td>[13]</td>
</tr>
<tr>
<td>Tx across negative XM</td>
<td>187,255</td>
<td>91,889 – 784,062</td>
<td>[13]</td>
</tr>
<tr>
<td>Post Tx (months 1–12)</td>
<td>2,378</td>
<td>500 – 5,000b</td>
<td>[12]</td>
</tr>
<tr>
<td>Post Tx (months 13+)</td>
<td>1,817</td>
<td>500 – 5,000b</td>
<td>[12]</td>
</tr>
<tr>
<td><strong>Utilities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PreTx</td>
<td>0.5</td>
<td>0.2 – 0.95</td>
<td>[25]</td>
</tr>
<tr>
<td>Tx</td>
<td>0.55</td>
<td>—</td>
<td>Estimate</td>
</tr>
<tr>
<td>PostTx months 1–3</td>
<td>0.7</td>
<td>0.5–0.8b</td>
<td>Estimate</td>
</tr>
<tr>
<td>PostTx months 4–12</td>
<td>0.8</td>
<td>0.55–0.85b</td>
<td>Estimate</td>
</tr>
<tr>
<td>PostTx months 13+</td>
<td>0.87</td>
<td>0.4 – 0.98b</td>
<td>[26]</td>
</tr>
</tbody>
</table>

Pre and post-Tx costs are per model cycle (monthly). Costs expressed in 2012 USD. Tx, transplant; XM, crossmatch

\(^a\)Range corresponds to the standard error for costs and length of stay for children’s hospitals stays in 2009 for a principle diagnosis of “congestive heart failure, nonhypertensive” in the HCUPnet database.

\(^b\)Estimated range
# Table 2

Characteristics of the cohorts used to estimate base-case waitlist and post-transplant outcomes.

<table>
<thead>
<tr>
<th></th>
<th>No PXMR During Listing “TAKE” (n=2650)</th>
<th>PXMR Throughout Listing “WAIT” (n=109)</th>
<th>Post-Transplant Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>19.0 ± 22.9</td>
<td>26.5 ± 25.9</td>
<td>23.5 ± 25.7</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>4.1 ± 5.7</td>
<td>6.4 ± 6.6</td>
<td>5.2 ± 6.2</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>1184 (45)</td>
<td>50 (46)</td>
<td>560 (45)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1473 (56)</td>
<td>58 (53)</td>
<td>718 (58)</td>
</tr>
<tr>
<td>Black</td>
<td>534 (20)</td>
<td>25 (23)</td>
<td>246 (20)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>486 (18)</td>
<td>19 (17)</td>
<td>202 (16)</td>
</tr>
<tr>
<td>Other</td>
<td>157 (6)</td>
<td>7 (6)</td>
<td>77 (6)</td>
</tr>
<tr>
<td><strong>Listing diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>1304 (49)</td>
<td>67 (62)</td>
<td>508 (41)</td>
</tr>
<tr>
<td>non-CHD</td>
<td>1316 (50)</td>
<td>39 (35)</td>
<td>721 (58)</td>
</tr>
<tr>
<td>ReTx</td>
<td>30 (1)</td>
<td>3 (3)</td>
<td>14 (1)</td>
</tr>
<tr>
<td>Inotropes at listing</td>
<td>1738 (66)</td>
<td>70 (64)</td>
<td>751 (60)</td>
</tr>
<tr>
<td>Ventilator at listing</td>
<td>1082 (41)</td>
<td>42 (39)</td>
<td>358 (29)</td>
</tr>
<tr>
<td>ECMO at listing</td>
<td>470 (18)</td>
<td>25 (23)</td>
<td>135 (11)</td>
</tr>
<tr>
<td>VAD at listing</td>
<td>177 (9)</td>
<td>14 (17)</td>
<td>175 (18)</td>
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<tr>
<td><strong>Primary payer</strong></td>
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<td></td>
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<tr>
<td>Public/gov’t insurance</td>
<td>1190 (45)</td>
<td>50 (46)</td>
<td>605 (49)</td>
</tr>
<tr>
<td>Private insurance</td>
<td>1367 (52)</td>
<td>58 (53)</td>
<td>594 (48)</td>
</tr>
<tr>
<td>Other</td>
<td>91 (3)</td>
<td>1 (1)</td>
<td>41 (3)</td>
</tr>
</tbody>
</table>

Superscript notes:

- ^a^ TAKE n=2647, WAIT n=105;
- ^b^ TAKE n=1948, WAIT n=83, Negative DSXM n=971, Positive DSXM n=181;
- ^c^ TAKE n=2648, WAIT n=109, Negative DSXM n=971, Positive DSXM n=1240, Negative DSXM n=239.

CHD, congenital heart disease; DSXM, donor specific crossmatch; ECMO, extra-corporeal membrane oxygenation; gov’t, government; PXMR, prospective crossmatch requirement; ReTx, re-transplant; VAD, ventricular assist device
Table 3

Median time to heart transplantation by UNOS region and results of regional waiting-time scenario analyses.

<table>
<thead>
<tr>
<th>UNOS Region</th>
<th>“shortest”</th>
<th>“longest”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Days to HTx</td>
<td>28 30 33 37.5 39 40 47 48 49 50 51</td>
<td></td>
</tr>
</tbody>
</table>

| Model Outcome | TAKE favored (ICER $70,394/QALY) | n/a | TAKE Dominant |

HTx, heart transplant; ICER, incremental cost-effectiveness ratio; n/a, not assessed; UNOS, United Network for Organ Sharing