Center Outcomes Reporting and the CIBMTR

Defining Quality and Value in HCT
June, 2014

Highlights of SCTOD expectations

- Collect data (and specimens)
  - ALL allogeneic HCTs with a U.S. recipient or donor
  - Related donor-recipient repository
  - Other cellular therapies
  - Quality of life data
  - Secure, efficient electronic data capture system

- Analyze data
  - Center-specific outcomes for U.S. centers: related and unrelated donor transplants
  - Perform analyses of optimal size for the adult donor registry and cord blood unit inventory
  - Conduct and support other research using the data collected under the contract

- Disseminate data
  - Within the Program
  - To the scientific and medical community
  - To patients, families and the public
What is the MAIN goal?!  

• Provide an equitable, balanced, scientific performance measurement tool(s) that can be used by the profession to define and improve quality. While:  
  – Acknowledging limitations  
  – Avoiding misuse/misinterpretation  
  – Striving for continuous improvement

Center Outcomes Analysis: Basic Concepts

• Examination of individual center specific outcomes relative to the overall network  
  – The CENTER is the unit of analysis  
• Risk Adjustment for ‘case mix’ at a given center  
• Assessment of center performance needs to account for sampling variability/sample size  
• Understandable to public audience
Statistical Methods

- Comparison of observed vs. predicted one year survival probabilities in each center
- First allogeneic HCT only
- **Observed survival probability**: Kaplan-Meier estimates of one year survival, by center
- **Predicted survival probability** (Risk adjustment):
  - Multivariate modeling accounts for the types of patients being transplanted at the center
  - Includes calculation of 95% confidence limits around the predicted survival probability
- Comparison of the observed to the 95% CI of the predicted survival
Statistical Properties

• An “average” center has a <=5% chance that they will be incorrectly identified as “over-performing” or “under-performing” (Type I error)
• Type I error rate is not dependent on
  – Case mix, as long as characteristics are included in regression model
  – Sample size (because wider intervals for small centers)

Significant Risk Factors

• Disease and stage*
• Disease sensitivity (NHL and HL only)
• Co-existing disease
• Race of recipient
• Recipient Age*
• Recipient CMV status
• Year of HCT
• Conditioning regimen intensity*
• Karnofsky/Lansky perf. score
• Time from dx to tx (ALL and AML not in CR1/PIF only)
• Donor type/graft type and HLA
• Donor Age
• Donor/recipient sex match
• Prior autoHCT
Risk adjustment model
Recent modifications

• HCT-CI (Sorror, et al)
• Refined age categories at upper end
  – 60-64, 65-69, 70+
• Nonmalignant disease categories
  – SAA, Fanconi, other inherited erythrocyte,
    inherited immune, inherited metabolic,
    histiocytic, other non-malignant
• NHL subtypes by category:
  – Indolent B, Aggressive B, Mantle cell, Nodal T,
    Extranodal T, Other B, Other T/NK
## Center Outcomes Report

### Final study population - 2013

- Centers must have >90% overall f/u at 1 year
  - One center excluded in 2013 for incomplete reporting of allogeneic HCT
  - Most centers have ≥ 99% follow-up @1 y
- 168 centers; 19,958 patients first allo HCT
- Primary outcome: One year survival
  - Overall: 65.7% (71% REL, 62% UNR)
- Center outcomes report 2013 includes 3 full years of data:
  - Unrelated and Related HCT 2009 – 2011

## Center Outcomes Report

### 2013

- 3 year rolling time window
- Outcome: 1 year survival
- Multivariate analysis adjusts for ‘risk factors’
- Full data on HCT Comorbidity Index (Sorror, et al)
- **Unblinded** Reports for 2013 sent to centers Jan 2014
  - Additional univariate descriptive reports for centers accompany report
- Reports available on web Jan 2014
  - [http://bethematch.org/access](http://bethematch.org/access)
- Reports sent directly to payers Jan 2014
How are HCT centers doing 2013?

Risk Adjusted Performance

- Above Expected: 79%
- As Expected: 13%
- Below Expected: 8%

How do we maintain engagement?

Feedback and limitations
## What is the center outcomes forum?

- Bi-annual meeting to discuss the center specific survival analysis for hematopoietic cell transplantation (HCT) – the highest impact report produced for the Stem Cell Therapeutics Outcomes Database (SCTOD)
- Invitees include:
  - HCT centers/community, ASBMT Quality outcomes committee, biostatisticians, quality and reporting methodologists, patients, payers, National Institutes of Health/Office of Naval Research/Health Resources and Services Administration representatives
- Held in MKE, MSP with average costs < $50,000
- Highly rated by attendees

## What is the purpose?

- Engage the relevant stakeholders in meaningful discourse about the process and with each other regarding uses and expectations
- Transparency and accountability
- Acquire meaningful input on statistical methodology, risk adjustment methodology, relevant data collection, meaningful display of results, appropriate use and avoiding misuse, adaptation to future trends in quality reporting.
Limitations - 2014

• Only outcome is 1 year survival
  – Only one outcome, only one year
  – Balances HCT center control, type of regimen, preferred long term outcome desired by patient/society
• Is not sufficiently ‘real-time’
• Report issued annually - Jan 2015
• Does not sufficiently adjust for risk factors associated with income
  – Balance of burden and benefit

Limitations - 2014

• Does not address value (beyond outcome)
  – No cost data – increasingly of interest to payers, patients, policy makers
  – Costs among most rapidly growing (AHRQ Report 2010)
  – About $500,000 billed first 180 days after alloHCT (Friedman, Optum 2012)
    – Cost variation ??? related to risk
• Cannot be used to predict future performance
• Translating results into performance improvement is challenging
Limitations - 2014

• Adult and pediatric centers can be combined
• Autologous HCT are NOT included
  – Full representation essential
• Conveying data to the non-statistician
  – Misunderstandings & misrepresentation
• Unintended consequences
  – Not intended to directly compare centers, may inappropriately affect patient selection for HCT
  – May stifle investigational approaches

Where do we go from here?
Changes Ahead

• Re-incorporation of zipcode into data collection
  – Facilitates several future uses for adjustment
• More disease and cytogenetic refinement
• Expansion of data sharing

Can we identify center characteristics that affect performance?

• A primary goal of center survival reporting is to promote performance improvement at centers
• What do we know about:
  – Volume
  – Modifiable factors that can be adopted
• What can we learn from high-performing centers that can be used by other centers to improve
Why don’t we offer benchmarks?

• Comparisons of centers to each other very problematic
  – Heterogeneity of HCT recipients at centers
  – Incomplete measurement of risk factors
  – If a benchmark were created with a “standard” group of patients, the smaller numbers will lead to very large confidence intervals

Is the Center Outcomes Report a full proxy for quality at US HCT centers?

• Not really. It is part of larger picture.
• However…..As ONE performance measurement tool it is:
  – Fair
  – Transparent
  – Guided by the profession and stakeholders
  – Relies on deep, specific registry data (as opposed to claims data)
  – Uses very good (not perfect) risk adjustment
  – A solid starting point to investigate and improve quality
Slides to keep for questions
Risk Adjustment Model

- Fit a (pseudovalue) logistic regression model for one year survival to all patients in entire network to predict patient outcomes based on individual patient characteristics alone
- Compute pseudovalues for each recipient by individually removing each recipient from a pooled KM 1 year survival estimate
- Fit fixed effects censored data logistic regression model to the pseudo-values with no center effect
  - Each pt characteristic associated with OR of 1 yr survival
- Direct model for 1 year survival probability which is an alternative to Cox model for hazard rate

Prediction

- Define risk score (log-odds of survival) and predicted survival for each recipient based on the odds ratios for their patient characteristics from the regression model
  - Compute case mix score for each center by averaging the risk scores for all recipients at the center
- Generate the predicted survival by center based on recipient characteristics by averaging the estimated survival for all recipients at the center
- Generate the observed one year survival using KM estimation
Statistical Methods

• Predicted survival outcome at a given center is based on the average predicted survival of patients actually transplanted at that center
  – Directly comparable to unadjusted K-M estimate to assess center performance
• This represents what we would have expected to happen to the patients at that center if they had been transplanted at a “generic” center in the network (i.e. no center effect)
• Need to account for sampling variability in comparing observed and predicted outcomes

Statistical Methods

• 95% confidence interval constructed
  – Range of plausible values for survival probability, if those patients had been transplanted at a generic center in the network
  – Constructed by resampling pseudovalues (Logan et al, Lifetime Data Analysis, 2008)
• If observed survival is outside confidence interval, the center appears to be under- or over-performing relative to the overall network
Statistical Methods

- We also provide a case mix score (1-5)
  - Describes the sickness/severity of patients transplanted at that center NOT the center outcome itself
  - Compute predicted log-odds of survival outcomes for each center by averaging across patients at that center.
  - Scores are quintiles of center predicted outcomes
  - Score=1 is 20% of centers with highest predicted survival outcomes according to their case mix of patient characteristics

Statistical Methods

- Case mix score (1-5)
  - Descriptive information only – not used explicitly in center outcomes analysis
  - Risk adjustment is done on individual patient basis instead
  - Not related to a summary of center performance
Case Mix Score
• Quintiles of centers based on the predicted survival outcomes of pts at center

![Graph showing expected 1 year survival by case mix score quintiles]

Exploratory Analysis 2010

Table 8: Results of addition of exploratory variables to the risk adjustment model

<table>
<thead>
<tr>
<th>Variable Level</th>
<th>N</th>
<th>Odds ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>p value</th>
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<tr>
<td>AML cytogenetics (Form 2000 only)</td>
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<tr>
<td>Adverse</td>
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<td>Intermediate</td>
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<td>1.24</td>
<td>1.01</td>
<td>1.53</td>
<td>0.040</td>
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<tr>
<td>Favorable</td>
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<td>2.41</td>
<td>1.41</td>
<td>4.15</td>
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<td>0.71</td>
<td>0.46</td>
<td>1.10</td>
<td>0.125</td>
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</table>

<table>
<thead>
<tr>
<th>Median household income by ZIP code (Form 2000 or Legacy Form only)</th>
<th>N</th>
<th>Odds ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 35 K</td>
<td>2423</td>
<td>1.00</td>
<td></td>
<td></td>
<td>0.236</td>
</tr>
<tr>
<td>35 to 45 K</td>
<td>2837</td>
<td>1.00</td>
<td>0.88</td>
<td>1.12</td>
<td>0.952</td>
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<tr>
<td>45 to 50 K</td>
<td>2754</td>
<td>1.03</td>
<td>0.91</td>
<td>1.16</td>
<td>0.639</td>
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<td>≥ 50 K</td>
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<td>0.97</td>
<td>0.79</td>
<td>1.19</td>
<td>0.754</td>
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<table>
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<tr>
<th>Distance from transplant center (Form 2000 or Legacy Form only)</th>
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<th>Odds ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>p value</th>
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<td>1.23</td>
<td>1.07</td>
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<td>1.17</td>
<td>0.91</td>
<td>1.51</td>
<td>0.229</td>
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</table>
Center Outcomes Cycle and Timeline

Continuous Data Collection, CPI, Data confirmation by centers

Data File preparation
• January - April

Analysis and Review
• May - August

Draft Report Submitted
• September 1

HRSA review and approval
• November

Publication - Centers and Website
• Dec - January

Slides to delete
Reporting Results

• Results of risk adjustment model:
  – Odds ratios (95% CI’s) for one year survival (>1 means better survival)
• For each center, we include a table with
  – Number of tx
  – Case mix score
  – Observed survival
  – Predicted survival
  – 95% prediction interval
  – An indicator of whether the center is underperforming, performing comparably to, or overperforming the entire network
• Graphical representations can also be helpful
### Reporting Results

#### Table 4. Center-Specific Results

<table>
<thead>
<tr>
<th>Center</th>
<th>n Range</th>
<th>Case Mix Score</th>
<th>Actual (%)</th>
<th>Predicted (%)</th>
<th>Lower (%)</th>
<th>Upper (%)</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
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<td>1</td>
<td>&gt;230</td>
<td>5</td>
<td>50.83</td>
<td>53.38</td>
<td>48.54</td>
<td>58.42</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>2</td>
<td>47.96</td>
<td>73.87</td>
<td>53.48</td>
<td>93.35</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
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<td>3</td>
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<td>2</td>
<td>67.43</td>
<td>66.68</td>
<td>62.81</td>
<td>70.96</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>4</td>
<td>36-70</td>
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<td>53.73</td>
<td>59.32</td>
<td>48.57</td>
<td>70.23</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>36-55</td>
<td>5</td>
<td>51.16</td>
<td>57.62</td>
<td>43.17</td>
<td>71.31</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>6</td>
<td>&gt;20-70</td>
<td>4</td>
<td>24.44</td>
<td>9.100</td>
<td>48.18</td>
<td>74.14</td>
<td>U</td>
<td>U</td>
<td>U</td>
<td>U</td>
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<td>U</td>
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<td>7</td>
<td>21-35</td>
<td>4</td>
<td>56.67</td>
<td>62.97</td>
<td>46.38</td>
<td>78.52</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>&gt;230</td>
<td>5</td>
<td>59.17</td>
<td>59.11</td>
<td>54.44</td>
<td>64.14</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td>9</td>
<td>71-89</td>
<td>5</td>
<td>44.63</td>
<td>60.18</td>
<td>50.62</td>
<td>70.26</td>
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<td>0</td>
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<td>-1</td>
<td>-1</td>
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</table>

#### Predicted and Actual Survival Rates for Transplant Centers with 11–20 Transplants

![Graph showing predicted and actual survival rates](chart)
Reporting Results - Public

• Results are posted online and accessible through
  – HRSA website
  – Be the Match
  – CIBMTR

• Format may change in next year or two

What is on the Website?

• http://marrow.org/Patient/Transplant_Planning/Choosing_a_Transplant_Center/U_S__Transplant_Centers.aspx
• Demographics of program
• Estimated search and HCT costs
• Transplant experience
• Center specific analysis
• Actual (not KM) survival by disease and age strata
Reporting Results

Center-Specific Analysis
This analysis is based on transplants performed from Jan. 1, 2007 through Dec. 31, 2009 using unrelated donors and transplants performed from Jan. 1, 2008 through Dec. 31, 2009 using related donors. It only includes patients who underwent their first allogeneic transplant within these respective time periods and who had at least 100-day follow-up.

1. This center reported survival status data for 89 patients.
2. The actual one-year survival of these patients was 70%.
3. The predicted one-year survival was 62% (with a 95% confidence limit that the predicted survival was between 58% and 77%).
4. This center’s actual results are similar to the predicted range for this center.

For help with understanding these statistics, please see How to Understand Transplant Center Statistics.
What’s new from 2010 to 2012

• Completeness of follow-up criteria now 90% or higher
  – No center excluded by this criteria 2012
• Combined data for Related and Unrelated HCT in statistical model
  – Complete data (all 3 years) for related and unrelated HCT
• Three year window for analysis

What’s new from 2010 to 2012

• Test new variables for inclusion
• Modifications of risk adjustment model
  – Full set of HCT-CI data now available vs. Yes/No previously
  – Finer resolution of upper age categories
  – Breakdown of nonmalignant disease types
  – For Discussion at this meeting
• More information in reports to center directors
What have we tested in last 2 years?

- Factors associated with related and unrelated HCT essentially same
  - Single combined model pools sample size
  - Combined model nearly same predicted accuracy as separate models

Predicted probabilities of combined vs. separate models

Brier Score: Combined $R^2=10.1\%$; Sep $R^2=10.6\%$
What have we tested in the last 2 years?

- Median household income from zipcode
- Distance from HCT center
- Cytogenetics risk category AML

<table>
<thead>
<tr>
<th>HCT-CI</th>
<th>n</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
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<td>0</td>
<td>8861</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2654</td>
<td>0.85</td>
<td>(0.77-0.93)</td>
<td>0.001</td>
</tr>
<tr>
<td>2</td>
<td>2097</td>
<td>0.85</td>
<td>(0.76-0.95)</td>
<td>0.003</td>
</tr>
<tr>
<td>3</td>
<td>2321</td>
<td>0.77</td>
<td>(0.70-0.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>1318</td>
<td>0.65</td>
<td>(0.57-0.74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5</td>
<td>1343</td>
<td>0.54</td>
<td>(0.48-0.62)</td>
<td>&lt;0.001</td>
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<tr>
<td>Unknown, No other coexisting disease reported</td>
<td>169</td>
<td>1.40</td>
<td>(0.96-2.08)</td>
<td>0.080</td>
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<tr>
<td>Unknown, Other coexisting disease reported</td>
<td>184</td>
<td>0.80</td>
<td>(0.58-1.11)</td>
<td>0.181</td>
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### Nonmalignant diseases

Previously only SAA vs. Other nonmalignant disease

<table>
<thead>
<tr>
<th>Type</th>
<th>N</th>
<th>OR</th>
<th>Lower</th>
<th>Upper</th>
<th>P-value</th>
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<td>Inherited Erythrocyte Abnormalities</td>
<td>315</td>
<td>1.00</td>
<td>0.18</td>
<td>0.66</td>
<td>0.001</td>
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<td>Fanconi Anemia</td>
<td>99</td>
<td>0.35</td>
<td>0.18</td>
<td>0.66</td>
<td>0.001</td>
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<td>Severe Aplastic Anemia</td>
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<td>Inherited Immune System Disorders</td>
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<td>0.35</td>
<td>0.99</td>
<td>0.047</td>
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<td>Inherited Metabolism Disorders</td>
<td>192</td>
<td>0.44</td>
<td>0.25</td>
<td>0.77</td>
<td>0.004</td>
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<td>Histiocytic disorders</td>
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<td>0.32</td>
<td>0.18</td>
<td>0.55</td>
<td>&lt;0.001</td>
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<td>Other</td>
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<td>0.40</td>
<td>0.21</td>
<td>0.78</td>
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### Recipient Age

Previously > 60 category

<table>
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<th>Recipient age</th>
<th>n</th>
<th>OR</th>
<th>(95% CI)</th>
<th>p-value</th>
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<td>1.00</td>
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<td>10 to 19</td>
<td>1639</td>
<td>0.84</td>
<td>(0.70-1.00)</td>
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<td>(0.68-0.98)</td>
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<td>30 to 39</td>
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<td>0.82</td>
<td>(0.68-1.00)</td>
<td>0.046</td>
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<td>40 to 49</td>
<td>3066</td>
<td>0.66</td>
<td>(0.55-0.79)</td>
<td>&lt;0.001</td>
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<td>50 to 59</td>
<td>4791</td>
<td>0.56</td>
<td>(0.47-0.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>60 to 64</td>
<td>2191</td>
<td>0.49</td>
<td>(0.40-0.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>65 to 69</td>
<td>1250</td>
<td>0.42</td>
<td>(0.34-0.52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>70 or more</td>
<td>299</td>
<td>0.42</td>
<td>(0.31-0.57)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

60 to 64 vs. 65 to 69: p=0.047
60 to 64 vs. >=70: p=0.289
Where do we go from here?

Pediatrics as distinct centers

- Concern that large adult centers are “masking” substandard small pediatrics programs within the combined center
- Special analysis of combined centers 2011 Report
- 35 of 156 (22%) combined centers with at least 10 adult and pediatric
- If analyzed separately, what would results have been?
### Pediatrics as distinct centers

- 20 of 35 (57%) no change
- 6 underperforming combined centers
  - 3 (-) adult with ‘as predicted’ peds
  - 3 (-) peds with ‘as predicted’ adult
- 6 ‘as predicted’ combined
  - 2 with (-) adult, 1 with (+) adult
  - 3 with (+) peds
- 3 (+) combined
  - 2 (+) adult with as expected peds
  - 1 (+) peds with as predicted adult

### Cautions re ‘Peds only’ distinction

- Small subgroups with less power
- Greater number of centers may increase risk of Type I error incorrectly identifying center as over or under performing
  - Like having 70 more centers in analysis
- Distinctions based upon age cutoff which may be artificial.