

## Online Supplemental Tables

Supplemental Table 1: Summary of cost-identification studies of hematopoietic cell transplantation in the United States after 2000

Reference	Data Source	Population Characteristics	Methods	Costs	Conclusions/Remarks
Lee et al. (2000) <sup>22</sup>	Single institution; 1994 - 1997	N=236 Auto =55, Allo MRD=103, Allo URD=78  Multiple diagnoses  Inpatient only  Adult patients	<i>Time horizon:</i> Hospital admission for conditioning until hospital discharge <i>Cost data:</i> Charges from accounting dept and medical chart review; charges converted to costs using cost-to-charge ratios; costs reported as 1997 US \$ <i>Method notes:</i> Excluded costs incurred before admission (e.g., costs of mobilization chemo, procurement, central venous access placement); non-medical costs not included*	Median costs: Auto=\$55,500 Allo=\$105,300  Median costs for allo patients with no complications: \$90,100  Median costs for allo patients with complications: \$153,500	- Overall costs were significantly higher for allo than auto HCT - Higher costs driven by occurrence of major complications (acute GVHD, VOD, infection or death) - Use of mismatched donors among allo recipients was a significant pre-HCT predictor of costs
Saito et al. (2007) <sup>20</sup>	Single institution; 2000-2003	N=275  Allo MA=185, Allo RIC=90  Multiple diagnoses  Inpatient and outpatient costs  Adult patients	<i>Time horizon:</i> Graft infusion through 1 year post-HCT <i>Cost data:</i> Cost information from accounting dept and medical chart review; costs estimated using RVU methods; costs reported as 2004 US \$ <i>Method notes:</i> Excluded search and procurement costs; non-medical costs not included	Median costs: Allo MA=\$128,253 Allo RIC=\$80,499  Adjusting for patient factors, RIC HCT had 16 fewer hospital days and cost \$53,030 less than MA HCT	- For 1-year after allo HCT, RIC HCT less expensive than MA HCT with comparable clinical outcomes - Costs for unrelated donor HCT significantly higher than related donor HCT - HCT for patients with advanced disease more costly than those with less advanced disease
Saito et al. (2008) <sup>21</sup>	Single institution; 2000-2004	N=315  Allo MRD=158, Allo MUD=157  Multiple diagnoses  Inpatient only  Adult patients	<i>Time horizon:</i> Admission to 1 year post HCT <i>Cost data:</i> Data from hospital accounting system; costs estimated using RVU methods; costs reported as 2004 US \$ <i>Method notes:</i> Donor identification and graft procurement costs were excluded; non-medical costs not	Median total cost over first 100 days: \$102,574  Median total cost over first year: \$128,800  Average costs if no complications	- Room costs, pharmacy and blood bank were largest contributors to total costs in first 100 days - Pre-transplant predictors of higher costs included use of unrelated donors and advanced disease status at HCT - Pre- and post- transplant, complications (grade II to IV acute GVHD, late neutrophil recovery or

			included	(n=15): \$79,222	non-engraftment, VOD, alveolar hemorrhage, severe neurological toxicity, and in-hospital death) were associated with higher costs
Majhail et al. (2009) <sup>19</sup>	Single Institution; 2004- 2006	N=294 Allo: MRD & UCB  MA MRD=67, MA UCB=63, RIC MRD=54, RIC UCB=110  Multiple diagnoses  Inpatient and outpatient  Adult patients	<u>Time horizon:</u> From 30 days before until day 100 post-HCT <u>Cost data:</u> Cost information from institutional accounting dept <u>Method notes:</u> Costs included inpatient and outpatient clinic visits; excluded graft acquisition, physician services, outpatient prescription drug and home-infusion costs; non-medical costs not included	Median costs: MA: \$137,112 RIC: \$84,824  UCB: \$137,564 MRD: \$83,583  Median cost per day survived: MRD-MA: \$1,016 MRD-RIC: \$612 UCB-MA: \$2,082 UCB-RIC: \$1156	- Room and board and pharmacy services were major contributors to total costs - UCB HCT more expensive than MRD HCT and MA HCT more expensive than RIC HCT - Costs for both graft sources primarily driven by severe post-transplant complications (graft failure, dialysis, and mechanical ventilation) and prolonged inpatient stay
Majhail et al. (2010) <sup>27</sup>	Single Institution; 2004-2006	N=146 Allo MRD=27, Allo MUD=28, UCB=91  Multiple diagnoses  Inpatient and outpatient  Pediatric patients	<u>Time horizon:</u> From 30 days before until day 100 post-HCT <u>Cost data:</u> Cost information from institutional accounting dept <u>Method notes:</u> Costs included inpatient and outpatient clinic visits; excluded graft acquisition, physician services, outpatient prescription drug and home-infusion costs; non-medical costs not included	Mean cost per day survived: MRD: \$3,446 MUD: \$4,050 UCB: \$4,522	- Costs of MUD and UCB similar while MRD HCT less costly - Room and board and pharmacy services were major contributors to total costs - Independent predictors of higher costs: Lansky score at transplant, graft failure post-transplant, need for dialysis, need for mechanical ventilation and VOD
Jones et al. (2008) <sup>23</sup>	Secondary database analysis (HCUP NIS); 2000-2001	N=8,891 Auto  Multiple myeloma and lymphoma  Inpatient only	<u>Time horizon:</u> Admission to discharge for a single hospitalization associated with HCT procedure <u>Cost data:</u> NIS charges converted to costs using Medicare cost-to-charge ratios for urban centers; costs reported as 2003 US \$ <u>Method notes:</u> Patients identified	Mean costs: \$51,312	- Complications (bacteremia, infections, parenteral nutrition and death) increased hospital costs - TBI associated with longer hospital stay and hospital costs

		Adult patients	by ICD-9-CM diagnosis and procedure codes; could account for costs associated with the hospitalization for HCT only; non-medical costs not included		
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HCUP NIS – Healthcare Cost and Utilization Project Nationwide Inpatient Sample; HCT – hematopoietic cell transplantation; Allo – allogeneic; Auto – autologous; MRD – matched related donor; MUD – matched unrelated donor; UCB – umbilical cord blood; PB – peripheral blood stem cells; BM – bone marrow; MA – myeloablative regimen; RIC – reduced intensity conditioning regimen; RVU – relative value unit; GVHD – graft-versus-host disease; VOD – hepatic veno-occlusive disease; TBI – total body irradiation

\* Non-medical costs include patient out-of-pocket costs, transportation, lodging, caregiver time

Supplemental Table 2: Summary of cost identification studies of hematopoietic cell transplantation from countries other than the United States after 2000

Reference	Data Source	Population Characteristics	Methods	Costs	Conclusions/Remarks
Ngamkiatphaisan et al. (2007) <sup>26</sup>	Single Institution (Thailand) 1994-2005	N=67 Allo PB=47; Allo BM=4; Auto PB=16  AML  Inpatient and outpatient  Pediatric and Adult patients	<u>Time horizon:</u> One year post-HCT <u>Cost data:</u> Costs were calculated from research and reports of annual cost analysis and utilization review of medical records; costs reported as 2006 US \$ <u>Methods notes:</u> Costs included direct medical costs, including personnel costs and outpatient visits; donor costs and non-medical costs were excluded	Total costs of HCT Auto: \$24,171 Allo: \$22,593	- Drug costs were cost driver for allo HCT - Routine service costs (labor, material, capital costs and indirect costs) were cost driver of auto HCT
Svahn et al. (2006) <sup>24</sup>	Single institution (Sweden) 1998-1999	N=93 Allo: MRD=35, MUD=43; Mismatched UD=14  Multiple diagnoses  Inpatient and outpatient  Pediatric and adult patients	<u>Time horizon:</u> 1 <sup>st</sup> day of admission through 5 years after HCT <u>Cost data:</u> Costs were calculated using a "cost per patient" system, where the total cost can be determined for each inpatient day for each patient, and reimbursement system of Stockholm; costs reported as 2005 € <u>Methods notes:</u> Costs of finding a donor were not included; non-medical costs not included	Median total costs: MRD: €129,133 MUD: €160,658	- Total costs in patients with acute leukemia were higher than those with all other diagnoses - Complications associated with higher costs: bacteremia, VOD, and acute GVHD - Costs highest during first year of transplant - Similar total costs during 5-year period for MUD and MRD; cost drivers included hospitalization and complications
Mishra et al. (2001). <sup>30</sup>	Single Institution (Norway) 1999-2000	N=17 Allo: MRD & MUC, PB & BM  AML, ALL, CML, MDS	<u>Time horizon</u> Pre-HCT phase through 1 year post-HCT <u>Cost data:</u> Costs were obtained from medical records; overhead costs were allocated by a step-down cost allocation method <u>Methods notes:</u> Costs included	Median total costs: \$69,270	- In the transplant phase, mean personnel cost was 54% of total costs - Correlation between length of stay and hospital cost

		Inpatient only Adult patients	inpatient costs including personnel costs and costs for search and procurement; excluded outpatient costs; non-medical costs not included		
Esp�rou et al. (2004) <sup>31</sup>	Nineteen centers (France)  1998-2000	N=85  Allo: MRD PB & BM  Multiple diagnoses  Inpatient and outpatient  Pediatric and adult patients	<u>Time horizon</u> Through 24 months post-HCT <u>Cost data:</u> Costs collected from case report forms and hospital cost-accounting system; unit costs from one hospital were applied for all patients; costs reported as 2001 � <u>Methods notes:</u> Included direct medical costs including donor search and procurement, outpatient visits, emergency readmission, personnel costs; non-medical costs not included	Mean total costs: �76,237	- Major cost driver was total hospital days - Among complications, predictors of costs were GVHD, and more than two documented infections - added costs of �20,000 to �30,000
Cordonnier et al. (2005) <sup>25</sup>	Two centers (France)  1998- 2003	N=23  Allo MRD: MA=12 & RIC=11  Lymphoma  Inpatient and outpatient  Adult patients	<u>Time horizon</u> First day of hospitalization before conditioning regimen, through 12 months post-HCT or death <u>Cost data:</u> Costs collected from hospital accounting systems. Costs reported as 2001 � <u>Methods notes:</u> Costs included direct medical expenses, including donor typing and procurement, personnel, readmissions in acute care or rehabilitation facilities, outpatient visits and emergency readmissions; non-medical costs not included	Mean total costs costs: MRD-MA: �74,900 MRD-RIC: �78,700	- Major cost driver was length of stay - Mean 1-year total costs did not differ significantly between the two groups - Total costs not different during the first 6 months, but were significantly higher in the RIC group during the last 6 months
Faucher et al. (2011) <sup>32</sup>	Three centers (France)  Randomized trial of early discharge vs.	N=131  Auto PB HCT: Early discharge=66; Standard	<u>Time horizon:</u> Day of PB harvest until day 60 <u>Cost data:</u> Costs estimated by micro-costing and based on medical records; costs reported as 2005 �	Mean total cost: Early discharge: �9,777 Standard inpatient: �10,436	- Cost drivers for both arms: hospitalization and medications - Early discharge led to 20% decrease in post-auto HCT hospitalization costs

	standard hospital based followup  2001- 2005	inpatient=65  Multiple diagnoses  Inpatient and outpatient  Adult patients	<u>Methods notes:</u> Costs included direct medical costs, including outpatient, PB harvest and labor costs; non-medical costs not included		
van Agthoven et al. (2001) <sup>33</sup>	Six center randomized phase III trial (The Netherlands)  1994-1998	N=91  Auto: BM=29, PB=62  Lymphoma  Inpatient and outpatient  Adult patients	<u>Time horizon:</u> Start of first chemotherapy course to 3 months after hospital discharge <u>Cost data:</u> Cost analysis was based on data collected as part of trial; determined average unit costs using micro-costing; costs reported as 1997 € <u>Methods notes:</u> Costs included direct medical costs, including personnel and harvesting; non-medical costs not included*	Mean total cost of transplant phase: Auto BM: €19,000 Auto PB: €15,008  Mean total costs post-HCT to 3 month follow up: Auto BM: €3,089 Auto PB: €2,088	- Auto PB less costly than BM - Hospital days were main component of total transplant costs - Main costs during follow-up were blood components and hospital days
van Agthoven et al. (2002) <sup>34</sup>	Four centers (The Netherlands)  1994-1999	N=97  Allo: MRD-BM=47 MRD-PB=21 MUD-BM or PB=29  AML, ALL  Inpatient and outpatient  Pediatric and adult patients	<u>Time horizon</u> From patient screening up to 2 years after HCT <u>Cost data:</u> Hospital information systems and patient charts; used average unit costs; costs reported as 1998 € <u>Methods notes:</u> Costs included direct inpatient and outpatient medical costs, including donor identification costs and costs of patients who were not transplanted after they had been planned to receive a transplant; excluded hematologist costs; non-medical costs not included	Average costs: MRD BM: €98,334  MRD PB: €98,977  MUD: €151,754	- Major cost components were hospitalization and personnel - For MUD HCT, nearly one-third of total costs were spent on donor search

HCT – hematopoietic cell transplantation; Allo – allogeneic; Auto – autologous; MRD – matched related donor; MUD – matched unrelated donor; URD – unrelated donor; MA – myeloablative regimen; RIC – reduced intensity conditioning regimen; PB – peripheral blood stem cells; BM – bone marrow; GVHD – graft-versus-host disease; VOD – hepatic veno-occlusive disease \* Non-medical costs include patient out-of-pocket costs, transportation, lodging, caregiver time

Supplemental Table 3: Summary of cost-effectiveness analyses of hematopoietic cell transplantation after 2000

Reference	Data Source	Population Characteristics	Methods	Incremental Cost Effectiveness Ratio	Conclusions
Lin et al. (2010) <sup>35</sup>	Single institution (USA)  2001- 2006	N=140 (costs for 76)  Allo MUD: PB, BM  AML & ALL  Pediatric patients	<i>Time horizon:</i> Initial hospitalization to 1-year <i>Cost data:</i> Retrospective cost data from administrative records; micro-cost information from internal accounting system. Costs reported as 2008 US \$. <i>Methods notes:</i> Costs included direct medical costs, outpatient visits, emergency room visits; excluded donor costs. Indirect costs excluded.	ICER for standard-risk subgroup: -\$687,108 (favoring BM)  ICER for high risk subgroup: \$1.69 million (no clear benefit for either graft source)	-For patients with standard risk disease, BM more had lower costs and greater effectiveness than PB -For patients with high-risk disease, no clear benefit of either donor source
Kouroukis et al. (2003) <sup>36</sup>	Single institution (Canada)  1998-2000	N=52  Auto=16 Melphalan and prednisone=16  Myeloma  Adult patients	<i>Time horizon:</i> Initial therapy to not specified <i>Cost data:</i> Retrospective cost data from administrative records; micro-costing. Costs reported as 2001 Canadian \$. <i>Methods notes:</i> Costs included direct medical costs, outpatient visits. Modeling done to account for anticipated future costs in auto HCT patients. Indirect costs excluded. Used an intention-to-treat basis. Survival measured the time of initial therapy to death	ICER for base case: \$18,974  ICER for drug acquisition and clinic costs of additional treatment with pamidronate: \$25,710 (favoring transplant)	- Cost per life-year gained with transplant compares positively with other interventions. -Highest transplant costs related to hospitalization, chemotherapy, ICU admission and granulocyte-colony stimulating factor
Yu et al. (2007) <sup>11</sup>	Single Institution (Taiwan)  1994-2002	N=106  HiDAC-based therapy, allo, auto=54	<i>Time horizon:</i> Admission through "whole treatment period" (cure or mortality) <i>Cost data:</i> Costs obtained from administrative database; included direct medical costs	Treatment costs: Chemotherapy: \$7607 HiDAC: \$13,668 Allo: \$29,208 Auto: 10,037	-HiDAC is more cost effective than allo HCT in AML patients with either intermediate or unknown cytogenetic risk -Allo HCT resulted in higher



		Intensive therapy=52 AML & ALL Adult patients	including professional. Costs reported as 2003 US \$ <u>Methods notes:</u> For cost effectiveness, looked at cost per life year saved for HiDAC versus Allo HCT for patients at either intermediate or unknown cytogenetic risk. Outpatient direct medical costs, direct non-medical costs were not included.	Mean cost per life year saved: HiDAC: \$11,224 Allo: \$21,564	costs than HiDAC or auto HCT -Age, cytogenetic risk and intensive therapy were associated with higher overall survival
Costa et al. (2007) <sup>28</sup>	Multiple Centers (International)  Articles published between 2000 and 2005	N=4056 Allo: UCB=906; BM/PBSC=3150  Acute leukemia  Adult patients	<u>Time horizon:</u> Transplantation, first-year and total 10-year cumulative costs <u>Cost data:</u> Systematic Review & Markov decision analysis model with Monte Carlo simulations Discounting rate of 3% to costs and outcomes; Costs reported as 2004 US \$ <u>Methods notes:</u> Costs included direct medical costs of hospitalization, inpatient and outpatient medications, nursing and physicians' costs.	ICER: (comparing to no transplant) BM/PBSC: \$16,346 Cord blood: \$34,360	-Most costs occur early in transplant -BM/PBSC sources should be first option for unrelated donors if clinically indicated; but cord blood is a reasonable cost effective substitute
Imataki et al. (2010) <sup>12</sup>	Single institution (Japan)  2000- 2002	N=50 Allo-RIC=15; Allo-MA=35  AML or MDS  Adult patients	<u>Time horizon:</u> Admission until discharge, up to 2 years after transplant. <u>Cost data:</u> Retrospective review of patient data. Direct costs analyzed using medical service fee table and national health insurance drug price table. Discount rate of 3%. Costs reported as 2006 US \$ <u>Methods notes:</u>	Median costs: MA: \$29,630 RIC: \$29,466  ICER (MA compared to RIC): \$469/year	-Hospitalization was largest proportion of costs -Transplant-related complications in MA and late complications in RIC were associated with higher costs -Total hospitalization longer in conventional than RIC -MA and RIC comparable in regards to cost and mean

			Direct medical costs only		survival
Fagnoni, et al (2009) <sup>29</sup>	Phase III multicentre GOELAMS 072 study 1994-1999	N=197  Conventional chemotherapy (CHOP)=99; Auto PBSC =98  Aggressive NHL  Pediatric and adult patients	<u>Time horizon:</u> Costs followed from first course of chemotherapy until last CHOP course or PBSC hospitalization discharge; <u>Cost data:</u> Per day unit prices obtained from accounting system, resources used identified and collected for each patient from clinical data; unit prices for medications based on sample of centers, whole-sale price lists, and official tariffs. Discount rate of 3%. Costs reported as 2008 € <u>Methods notes:</u> Hospital institution costs, only direct medical costs, including harvesting, personnel	Average overall cost per patient: CHOP=€11,299 Auto PBSC=€46,216  ICER: €79,111 with auto PBSC  ICER for patient with high-intermediate risk according to age-adjusted IPI: €34,315 with auto PBSC	-Auto PBSC might be considered cost effective among NHL patients classified as having high-intermediate risk according to age-adjusted IPI -Long-term effectiveness data were not included -No indirect costs were included -No quality of life information was included

Allo-Allogeneic transplant; Auto-Autologous transplant; BM- Bone Marrow Transplant; MA-Myeloablative; MRD-Matched Related Donor; MUD-Matched Unrelated Donor; RIC- Reduced Intensity Conditioning Regimen; PBSC-Peripheral Blood Stem Cell Transplant; UCB-Umbilical Cord Blood; IPI- International Prognostic Index; Non-medical costs: Patient time costs, productivity costs