Appendix J: Reporting Comorbidities

CIBMTR collects comorbidities data based on criteria from the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), which was developed and validated by investigators at the Fred Hutchinson Cancer Research Center in Seattle, Washington. The HCT-CI was developed to identify comorbidities relevant to transplant and act as a tool for risk assessment before allogeneic hematopoietic stem cell transplantation. While the criteria were originally developed for use in the adult, allogeneic population, there is utility in collecting these data for all transplant populations, and, used in conjunction with other relevant risk factors, these data are useful in determining risk for transplant for the purposes of predicting expected outcomes.

What to Report

Report a comorbidity in all of the following areas if any of the specified criteria are met.

Comorbidity	Definition and/or criteria
Arrhythmia	Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmias.
Cardiac	The presence of one or more of the following: • Any history of coronary artery disease (one or more vessels requiring medical treatment, stent, or bypass), • Any history of myocardial infarction, or • Any history of congestive heart failure (regardless of an LVEF >50% at the start of preparative regimen), or • LVEF ≤ 50% (or a shortening fraction (SF) of < 26% for pediatric cases) on most recent evaluation prior to the start of the preparative regimen
Cerebrovascular disease	Any history of: • Transient ischemic attack • Cerebrovascular accident/stroke • Subarachnoid, subdural, epidural, or intraparenchymal hemorrhage
Diabetes	Current (within 4 weeks prior to HCT) history of diabetes or steroid-induced hyperglycemia requiring insulin or oral hypoglycemics, not controlled by diet alone.
Heart valve disease	The presence of one or more of the following, found on the most recent heart evaluation by an echocardiogram: • At least a moderate or severe degree of valve stenosis or insufficiency as determined by echo, whether the valve is mitral, aortic, tricuspid or pulmonary; • Prosthetic mitral or aortic valve; • Symptomatic mitral valve prolapse
Hepatic, mild	Any of the following:

	• Chronic hepatitis • Any history of Hepatitis B or Hepatitis C • Bilirubin >ULN to 1.5 x ULN* • AST or ALT >ULN to 2.5 x ULN*
Hepatic, moderate/ severe	Any of the following: • Liver cirrhosis • Bilirubin > 1.5 x ULN* • AST or ALT > 2.5 x ULN*
Infection	The presence of one or more of the following requiring continuation of therapeutic antimicrobial / antifungal / antiviral treatment after Day 0: • Documented infection, • Fever of unknown origin, • Pulmonary nodules suspicious for fungal pneumonia • A positive PPD test requiring prophylaxis against TB
Inflammatory bowel disease	Any history of: • Crohn's disease or • Ulcerative colitis requiring treatment
Obesity	Body mass index (BMI) > 35.00 kg/m2 or BMI-for-age ≥ 95% (pediatric recipients only) during pre-transplant work-up period. For pediatric recipients, if only the BMI is known, refer to the following link to determine the BMI-for-age: https://www.cdc.gov/growthcharts/.
Peptic ulcer	Any history of peptic ulcer (gastric or duodenal) confirmed by endoscopy or radiologic diagnosis and the patient has or is receiving treatment.
Psychiatric disturbance	Any psychiatric illness requiring continuous psychiatric treatment within four weeks prior to the pre-transplant work-up period. Examples include depression, anxiety, Attention-Deficit Disorder (ADD), Attention-Deficit Hyperactivity Disorder (ADHD), schizophrenia, or bipolar disorder.
Pulmonary, moderate	Any of the following at the time of pre-transplant evaluation: • Adjusted DLCO 66-80% • FEV1 66-80%** • Dyspnea on slight activity attributed to pulmonary disease and not anemia
Pulmonary, severe	Any of the following at the time of pre-transplant evaluation: • Adjusted DLCO ≤ 65% • FEV1 ≤ 65%** • Dyspnea at rest attributed to pulmonary disease and not anemia • Requires intermediate or continuous supplemental oxygen
Renal, moderate/ severe	Any of the following: • Serum creatinine > 2 mg/dL or 177 µmol/L • On dialysis in pre-transplant evaluation period • Prior renal transplantation

Rheumatologic	Any history of rheumatologic disease requiring treatment including: • Systemic lupus erythematosus • Rheumatoid arthritis • Sjogren' • Polymyositis • Dermatomyositis • Mixed connective tissue disease • Polymyalgia rheumatic • Polychondritis • Sarcoidosis • Vasculitis syndromes
Prior malignancy	Any solid tumor(s), hematologic malignancy(ies), and / or skin malignancy(ies) that have been treated at any time point in the patient's past history. A history of any benign tumor(s) should not be reported.

(*) ULN refers to upper limit of normal for respective laboratory study
(**) If the PFT lists both a "control" FEV1 and "post-dilator" FEV1, the "control" FEV1 should be used to determine if a pulmonary comorbidity is present.

Hepatic and Renal Comorbidities[1]
In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities
Hepatic Comorbidity: The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value. When determining the severity of the hepatic comorbidity, the value closest to the start of the preparative regimen should be used. If the liver function test values closest to the start of the preparative regimen do not meet the criteria specified above, a hepatic comorbidity should not be reported.
Renal (Moderate/Severe) Comorbidity: Serum creatinine > 2 mg/dL or > 177 µmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value. If the serum creatinine value closest to the start of the preparative regimen did not meet the criteria specified above, a renal (moderate/severe) comorbidity should not be reported.

[1] Sorror, M. L. (2013). How I assess comorbidities before hematopoietic cell transplantation. *Blood*, 121(15), 2854-2863.

Determine relevant comorbidities through careful review of the recipient medical record. Reviewed documentation should include the recipient's past medical history and objective data from the pre-transplant work-up, including pulmonary function tests, echocardiogram, body weight, and laboratory results. The

recipient medication list should be correlated with the past medical history to verify there are not any medications that do not align with the patient's medical history; if there were to be medications commonly used for a certain purpose not listed in the medical history, further clarify if a relevant comorbidity is present. However, if the medical record remains ambiguous, after careful review, as to whether a condition meets the criteria for reporting comorbidity, do not report.

Report all comorbidities meeting criteria at time of pre-transplant evaluation. This may include comorbidities secondary to the primary transplant disease or conditions resulting from prior therapy and persisting or meeting criteria for reporting at the time of transplant

> **Example 1.** A recipient with a past medical history of depression, treated with Celexa, is undergoing their pre-transplant work-up. Review of the medication list shows they also take Novolog and Lantus. Pre-transplant work-up reveals BMI 27.2 kg/m^2, EF 58%, unremarkable laboratory results, and adjusted DLCO 62%. In this case, the recipient would have psychiatric, diabetes, and severe pulmonary comorbidities, identified in the past medical history, medication list, and pre-transplant work-up data respectively.

For instances in which the pulmonary function testing report does not correct diffusing capacity of carbon monoxide for hemoglobin, use the Dinakara equation to correct.

To correct an uncorrected DLCO:
*corrected DLCO= uncorrected DLCO/(0.06965*hemoglobin)*
where hemoglobin is measured in g/dL

What not to report

Comorbidty	Do not report the following
Arrhythmia	Transient arrhythmia never requiring treatment.
Cardiac	Syncope; tachycardia; bradycardia
Cerebrovascular disease	Prior history of traumatic brain injury; syncope; concussions; seizure disorder
Diabetes	Resolved gestational diabetes; glucose intolerance
Heart valve disease	Asymptomatic mitral valve prolapse
Hepatic	Elevated liver enzymes not meeting criteria for hepatic comorbidity and without diagnosis of cirrhosis or chronic hepatitis.
Infection	History of significant infection not requiring treatment after day of transplant (Day 0)
Inflammatory bowel disease	GERD; gastric bypass surgery; irritable bowel syndrome (IBS); neutropeneic colitis

Obesity	Overweight but not meeting BMI criteria for reporting; pediatric patient in upper weight-for-age percentile not meeting criteria for reporting
Peptic ulcer	Gastritis; GERD; ulcerative colitis (ulcerative colitis would be reported as an inflammatory bowel disease comorbidity)
Psychiatric disturbance	Behavioral issues. Any mood, anxiety, or psychiatric disorder, requiring treatment but given “as needed.”
Pulmonary	Sleep apnea
Renal, moderate/ severe	Nephritis; nephrolithiasis
Rheumatologic	Osteoarthritis; osteoporosis; vasculitis

The following conditions are not relevant transplant outcomes or risk, and should not be reported under the comorbidities section.

• Acne • Benign tumor (removed) • Bradycardia • Bulging discs • Cataracts • Concussions • Congenital alopecia • Deafness or hearing loss • Fractures • Gallbladder (stones, sludge) • Gastric bypass surgery • Glaucoma • Glomerulosclerosis (assume Cr okay) • Glucose-6-phosphate dehydrogen • Glucose intolerance • Gout • Headaches (chronic) • Hemorrhoidectomy • Hemorrhoids • Hernia • Hypercholesterolemia • Hyper-eosinophilia (if not disease related) • Hyperlipidemia • Hyperparathyroidism • Hypertension • Hypertriglyceridemia	• Kidney stones • Knee arthritis • Knee surgery • Lyme disease • Macular degeneration • Malabsorption • Malnutrition • Meniere’s disease • Menorrhagia • Microalbuminuria • Migraines • Mitral valve insufficiency (mild) • Mitral valve prolapsed (asymptomatic) • Mitral valve regurgitation (mild) • Non-alcoholic steatohepatitis (NASH) • Prior h/o necrotizing fasciitis • Neonatal jaundice • Nephritis • Nephrolithiasis • Neuropathy • Neurosyphilis • Neutropenic colitis • Osteoarthritis • Osteomyelitis • Osteopenia	• Restless leg syndrome • Rosacea • Scoliosis • Shingles • Sleep apnea • Solitary kidney • Spastic colon • Splenectomy • Syncope • Tachycardia • Thalassemia (minor or trait) • Thyroidectomy • Thyroid nodules • Tonsillectomy • Tracheoesophageal fistula • Traumatic brain injury • Tremors • Tubal ligation • Uterine fibroids • Valve regurgitation (mild) • Vasculitis • Vasectomy • Vena cava filter • Vertigo • Vision (blindness, blurred) • Vitamin deficiency (B12,

• Hysterectomy • Insomnia • Iron deficiency anemia • Iron deposition or overload	• Pancreatitis • Paraplegic • Paresthesias • Psoriasis • Raynaud's disease	D) • Vitiligo • Whipple procedure • Wisdom tooth extraction

Manual Updates:

Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

Date	Manual Section	Add/ Remove/ Modify	Description
9/9/ 2022	Appendix J: Reporting Comorbidities	Add	Update psychiatric criteria to be consistent with Pre-TED (2400) form: *Any psychiatric illness requiring continuous psychiatric treatment within four weeks prior to the pre-transplant work-up period. Examples include depression, anxiety, Attention-Deficit Disorder (ADD), Attention-Deficit Hyperactivity Disorder (ADHD), schizophrenia, or bipolar disorder.*
3/27/ 2022	Appendix J: Reporting Comorbidities	Add	Update prior malignancy criteria to be consistent with Pre-TED (2400) form: *Any solid tumor(s), ~~and / or~~ hematologic malignancy(ies), and / or skin malignancy (ies) that have been treated at any time point in the patient's past history. A history of any benign tumor(s) should not be reported.*
1/18/ 2022	Appendix J: Reporting Comorbidities	Update	Updated arrhythmia criteria to be consistent with the Pre-TED (2400) instructions: *~~Any history of • Atrial fibrillation~~* *~~• Atrial flutter~~* *~~• Sick sinus syndrome~~* *~~• Ventricular arrhythmias~~ Any history of any type of arrhythmia that has necessitated the delivery of a specific antiarrhythmic agent. Examples include, but are not limited to, atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmias.*
4/28/ 2021	Appendix J: Reporting Comorbidities	Add	Updated the table "What not to report" for psychiatric comorbidity when treatment is given "as needed."
11/ 23/ 2020	Appendix J: Reporting Comorbidities	Add	Clarification added on how to report infection comorbidity: *The presence of one or more of the following requiring continuation of therapeutic antimicrobial / antifungal /antiviral treatment after Day 0*.
10/ 14/ 2020	Appendix J: Reporting Comorbidities	Add	Clarification added on how to report a pulmonary comorbidity if both a "control" FEV1 and "post-dilator" FEV1 is available.

9/9/2020	Appendix J: Reporting Comorbidities	Add	Clarification added on how to report ADD and ADHD: *Psychiatric disturbance – Any psychiatric illness requiring treatment within four weeks prior to the pre-transplant work-up period. Examples include depression, anxiety, Attention-Deficit Disorder (ADD), Attention-Deficit Hyperactivity Disorder (ADHD), schizophrenia, or bipolar disorder.*
7/8/2020	Appendix J: Reporting Comorbidities	Modify	Updated the reporting instructions for prior malignancy to be consistent with the reporting instructions listed on the Pre-TED (2400) manual.
6/9/2020	Appendix J: Reporting Comorbidities	Add	Added clarification (red text) on how to report heart valve comorbidity. The presence of one or more of the following, found on the most recent heart evaluation by an echocardiogram: • At least a moderate or severe degree of valve stenosis or insufficiency as determined by echo, whether the valve is mitral, aortic, tricuspid or pulmonary; • Prosthetic mitral or aortic valve; • Symptomatic mitral valve prolapse
3/23/2020	Appendix J: Reporting Comorbidities	Add	Added link for determining pediatric BMI-for-age for obesity guidelines.
3/23/2020	Appendix J: Reporting Comorbidities	Add	Added “(regardless of an LVEF >50% at the start of preparative regimen)” after congestive heart failure bullet point.
3/6/2020	Appendix J: Reporting Comorbidities	Add	Added “mild” specification in valve regurgitation listing for table of conditions that are not relevant transplant outcomes or risk.
1/30/2020	Appendix J: Reporting Comorbidities	Remove	Removed information on reporting “Other comorbidities” as this is no longer an option on the new Pre-TED (2400) form.
4/19/19	Appendix J: Reporting Comorbidities	Add	Added (in red below) instruction for reporting a cardiac comorbidity: *The presence of one or more of the following:* • *Any history of coronary artery disease (one or more vessels requiring medical treatment, stent, or bypass),* • *Any history of myocardial infarction, or* • *Any history of congestive heart failure , or* • *LVEF ≤ 50% (or a shortening fraction (SF) of < 26% for pediatric cases) on most recent evaluation prior to the start of the preparative regimen* Also added instruction to the blue not box describing Hepatic and Renal comorbidities to clarify what to report based on laboratory values closest to the start of the preparative regimen.

10/16/17	Appendix J: Reporting Comorbidities	Modify	Updated the Hepatic and Renal Comorbidities note box to match the note box included in the Form 2400 section of the manual. ~~*For review of renal and hepatic comorbidities, criteria are met when the patient has two or more laboratory values meeting the threshold for reporting between days -24 and -10 (or the date of the last test prior to start of the preparative regimen). If the laboratory values are only assessed once in that period, extend review to between days -40 and -10.*~~ *In addition to the guidelines listed on the Pre-TED form, include the following time-specific guidelines when reporting hepatic and renal comorbidities* ***Hepatic Comorbidity:*** *The assessment of liver function tests (ALT, AST and/or Total Bilirubin) has to include at least 2 values per test on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.* ***Renal (Moderate/Severe) Comorbidity:*** *Serum creatinine > 2 mg/dL or > 177 µmol/L, as detected in at least two lab values on two different days within a period extending between day -24 and the start of the preparative regimen. If only a single value was reported in this time period, use the most recent test performed between days -40 & -25 as the second value.*
6/30/17	Appendix J: Reporting Comorbidities	Modify	Appendix M: Reporting Comorbidities has been renamed as Appendix J: Reporting Comorbidities.
7/24/15	Appendix M: Reporting Comorbities	Add	**Appendix M has been revised and combined with the former appendix U. Appendix U has been retired.**

Last modified: Sep 09, 2022