

Supplemental Table 1. System-Based Chronic and Late-Onset Medical Event Severity Grading in the St. Jude Lifetime Cohort Study

Organ/System	Grading Source	Grading Rubric
Auditory-Hearing		
Cerumen impaction	CTCAEv4.03 Ear and labyrinth disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Cholesteatoma	CTCAEv4.03 Ear and labyrinth disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Hearing loss (Includes: sensorineural, conductive and mixed hearing loss)	New grading source Modified Chang Ototoxicity Grading Scale Chang KW, Chinosornvatana N. Practical grading system for evaluating cisplatin ototoxicity in children. J Clin Oncol 2010;28(10):1788-95.	1: ≥ 40 dB at any frequency 6-12 kHz (Chang 1a); > 20 and < 40 dB at 4kHz (Chang 1b) 2: ≥ 40 dB at 4 kHz and above (Chang 2a); > 20 and < 40 dB at any frequency < 4kHz (Chang 2b) 3: ≥ 40 dB at 2 or 3 kHz and above 4: ≥ 40 dB at 1 kHz and above 5: Not applicable
Tinnitus	CTCAEv4.03 Ear and labyrinth disorders: Tinnitus	1: Mild symptoms; intervention not Indicated 2: Moderate symptoms; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL 4: Not applicable 5: Not applicable
Vertigo (Includes: Meniere's)	CTCAEv4.03 Ear and labyrinth disorders: Vertigo	1: Mild symptoms; intervention not Indicated 2: Moderate symptoms; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric
Cardiovascular		
Aortic root aneurysm	Modified CTCAE v4.03 Cardiac Disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated (aortic root >= 3.5 cm to < 4 cm) 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL (aortic root > = 4 cm) 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Arteriovenous malformation	CTCAE v4.03 Cardiac Disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Atrioventricular heart block (Includes: 1 st degree (PR> 200msec), 2 nd degree, Mobitz I, 2 nd degree, Mobitz II, 3 rd degree (complete) Bundle branch block, QRS > 120ms, Stokes-Adams Syndrome)	CTCAE v4.03 Cardiac Disorders: AV Block first degree (grades 1&2); AV block complete; Mobitz (type) II AV block; Mobitz type I (grades 3&4)	1: Asymptomatic; intervention not indicated 2: Symptomatic; non-urgent medical intervention indicated 3: Symptomatic and incompletely controlled medically, or controlled with device (e.g., pacemaker) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Bradycardia, sinus	Modified (definition HR < 50/minute) CTCAE v4.03 Cardiac Disorders: Sinus bradycardia	1: Asymptomatic; intervention not indicated 2: Symptomatic; medical intervention indicated 3: Severe; medically significant, medical intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Conduction abnormalities (Includes: Sick Sinus Syndrome, Wolff-Parkinson-White syndrome)	Modified CTCAE v4.03 Cardiac Disorders: Conduction disorder	1: Asymptomatic or mild symptoms; intervention not indicated 2: Moderate symptoms; non-urgent intervention indicated 3: Severe symptoms; intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Congestive heart failure	Modified CTCAE v4.03 Cardiac Disorders: Heart failure	1: Asymptomatic with laboratory (e.g., BNP) or cardiac imaging abnormalities (NYHA I) 2: Symptoms with mild to moderate activity or exertion (NYHA II) 3: Severe with symptoms at rest or with minimal activity or exertion; intervention indicated (NYHA III) 4: Life-threatening consequences; urgent intervention indicated (e.g., continuous IV therapy or mechanical hemodynamic support (NYHA IV) 5: Death

Organ/System	Grading Source	Grading Rubric
Coronary artery disease (Includes myocardial infarction)	Modified CTCAE v4.03 Cardiac Disorders: Myocardial infarction	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Mild symptoms and cardiac enzymes minimally abnormal and no evidence of ischemic ECG changes 3: Severe symptoms; cardiac enzymes abnormal; hemodynamically stable; ECG changes consistent with infarction (Q waves) 4: Life-threatening consequences; hemodynamically unstable (CABG or angioplasty) 5: Death
Cor pulmonale (right heart failure)	CTCAE v4.03 Cardiac Disorders: Right ventricular dysfunction	1: Asymptomatic with laboratory (e.g., BNP) or cardiac imaging abnormalities 2: Symptoms with mild to moderate activity or exertion 3: Severe symptoms, associated with hypoxia, right heart failure; oxygen indicated 4: Life-threatening consequences; urgent intervention indicated (e.g., ventricular assist device); heart transplant indicated 5: Death
Dysrhythmia (Includes: atrial fibrillation, atrial flutter, SVA, SVT, PAT; ventricular arrhythmia, and lethal arrhythmia requiring defibrillation)	CTCAE v4.03 Cardiac Disorders: Atrial fibrillation	1: Asymptomatic, intervention not indicated 2: Non-urgent medical intervention indicated 3: Symptomatic and incompletely controlled medically, or controlled with device (e.g., pacemaker), or ablation 4: Life-threatening consequences; urgent intervention indicated 5: Death
Heart valve disorder	Modified CTCAE v4.03 Cardiac Disorders: Aortic valve disease; mitral valve disease; pulmonary valve disease; tricuspid valve disease	1: Asymptomatic valvular thickening/ calcifications with or without mild valvular regurgitation or stenosis by imaging 2: Asymptomatic; moderate regurgitation or stenosis by imaging 3: Symptomatic; severe regurgitation or stenosis by imaging; symptoms controlled with medical intervention 4: Life-threatening consequences; urgent intervention indicated (e.g., valve replacement, valvuloplasty) 5: Death
High total cholesterol	Modified CTCAE v4.03 Investigations: Cholesterol high	1: >200 mg/dL - 300 mg/dL 2: >300 - 400 mg/dL; treatment with one lipid lowering agent 3: >400 - 500 mg/dL; treatment with >=2 lipid lowering agent 4: >500 mg/dL 5: Not applicable

Organ/System	Grading Source	Grading Rubric	
Hypertension (from resting blood pressure)	<p>Modified CTCAE v4.03 Vascular Disorders: Hypertension</p> <p>National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. Pediatrics. 2004;114(2 Suppl 4th Report):555.</p>	<p>Adult</p> <p>1: Prehypertension (systolic BP 120 - 139 mm Hg or diastolic BP 80 - 89 mm Hg)</p>	<p>Pediatrics</p> <p>1: Prehypertension (systolic and/or diastolic BP \geq 90th percentile but $<$ 95th percentile for gender, age and height, or if in adolescents BP exceeds 120/80 mmHg even if $<$90th percentile)</p>
		<p>2: Stage 1 hypertension (systolic BP 140 - 159 mm Hg or diastolic BP 90 - 99 mm Hg); medical intervention indicated or initiated; recurrent or persistent (\geq24 hrs); symptomatic increase by $>$20 mm Hg (diastolic) or to $>$140/90 mm Hg if previously WNL; monotherapy indicated or initiated</p>	<p>2: Stage 1 hypertension (systolic and/or diastolic BP between the 95th percentile and 5 mmHg above the 99th percentile for gender, age and height, or if in adolescents the BP exceeds 140/90 mmHg even $<$95th percentile); monotherapy indicated or initiated</p>
		<p>3: Stage 2 hypertension (systolic BP \geq160 mm Hg or diastolic BP \geq100 mm Hg); medical intervention indicated; more than one drug or more intensive therapy than previously used indicated or initiated</p>	<p>3: Stage 2 hypertension (systolic and/or diastolic BP \geq99th percentile plus 5 mmHg for gender, age, and height); more than one drug or more intensive therapy than previously used indicated or initiated</p>
		<p>4: Life-threatening consequences (e.g., malignant hypertension, transient or permanent neurologic deficit, hypertensive crisis); urgent intervention indicated</p>	<p>4: Life-threatening consequences (e.g., malignant hypertension, transient or permanent neurologic deficit, hypertensive crisis); urgent intervention indicated</p>
		<p>5: Death</p>	<p>5: Death</p>
Hypertriglyceridemia	<p>Modified CTCAE v4.03 Metabolism and Nutrition Disorders: Hypertriglyceridemia</p>	<p>1: 150 mg/dL - 300 mg/dL 2: $>$300 mg/dL - 500 mg/dL; treatment with one lipid lowering agent 3: $>$500 mg/dL - 1000 mg/dL; treatment with \geq2 lipid lowering agents 4: $>$1000 mg/dL; life-threatening consequences 5: Death</p>	
Left ventricular systolic dysfunction (Includes cardiomyopathy)	<p>Modified CTCAE v4.03 Investigations: Ejection fraction decreased (grades 2&3) Left ventricular systolic dysfunction (grade 4)</p>	<p>1: Not applicable 2: Resting EF $<$ 50-40%; 10 - 19% absolute drop from baseline 3: Resting EF 39-20%; $>$20% absolute drop from baseline; medication indicated or initiated 4: Resting EF$<$20%; refractory or poorly controlled heart failure due to drop in ejection fraction; on medical management; intervention such as ventricular assist device, intravenous vasopressor support, or heart transplant indicated 5: Death</p>	
Pericarditis	<p>Modified CTCAE v4.03 Cardiac Disorders: Pericarditis</p>	<p>1: Asymptomatic, ECG or physical findings (e.g., rub) consistent with pericarditis 2: Symptomatic pericarditis (e.g., chest pain) 3: Pericarditis with physiologic consequences (e.g., pericardial constriction) 4: Life-threatening consequences; urgent intervention indicated (e.g., cardiac tamponade) 5: Death</p>	

Organ/System	Grading Source	Grading Rubric
Prolonged QTcorrected (QTc) interval	Modified CTCAE v4.03 Investigations: Prolonged QTc interval	1: QTc 460 - 480 ms (men); 470-480 ms (women) 2: QTc 481 - 500 ms 3: QTc >= 501 ms on >= two separate ECGs 4: QTc >= 501 or >60 ms change from baseline and Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia 5: Not applicable
Pulmonary hypertension	CTCAE v4.03 Respiratory, thoracic, and mediastinal disorders: Pulmonary hypertension	1: Minimal dyspnea; findings on physical exam or other evaluation 2: Moderate dyspnea, cough; requiring evaluation by cardiac catheterization and medical intervention 3: Severe symptoms, associated with hypoxemia, right heart failure; oxygen indicated 4: Life-threatening airway consequences; urgent intervention indicated (e.g., tracheotomy or intubation) 5: Death
Raynaud phenomenon	CTCAE v4.03 Vascular Disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Right ventricular systolic dysfunction	Modified CTCAE v4.03 Cardiac Disorders: Right ventricular dysfunction	1: Asymptomatic cardiac imaging abnormalities 2: Symptoms with mild to moderate activity or exertion 3: Severe symptoms, associated with hypoxia, right heart failure; oxygen indicated 4: Life-threatening consequences; urgent intervention indicated (e.g., ventricular assist device); heart transplant indicated 5: Death
Tachycardia, sinus	Modified (definition HR >110/minute) CTCAE v4.03 Cardiac Disorders: Sinus tachycardia	1: Asymptomatic, intervention not indicated 2: Symptomatic; non-urgent medical intervention indicated 3: Urgent medical intervention indicated 4: Not applicable 5: Not applicable
Thrombus	CTCAE v4.03 Vascular Disorders: Thromboembolic event	1: Venous thrombosis (e.g., superficial thrombosis) 2: Venous thrombosis (e.g., uncomplicated deep vein thrombosis), medical intervention indicated 3: Thrombosis (e.g., non-embolic cardiac mural [arterial] thrombus), medical intervention indicated 4: Life-threatening (e.g., cerebrovascular event, arterial insufficiency); hemodynamic or neurologic instability; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Vascular disease (Stenosis/occlusion of vessel other than coronary or cerebral vessels, e.g., carotid, subclavian)	CTCAE v4.03 Vascular Disorders Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Endocrine		
Abnormal glucose metabolism (Includes: impaired fasting glucose, insulin resistance with impaired glucose tolerance, diabetes mellitus)	Modified CTCAE v4.03 Metabolism and nutrition disorders: Glucose intolerance	1: Asymptomatic; clinical or diagnostic observations only; pharmacologic intervention not indicated or initiated (e.g. dietary modification) 2: Symptomatic; oral agent indicated or initiated 3: Severe symptoms; insulin indicated or initiated 4: Life threatening consequences, urgent intervention indicated or initiated 5: Death
Adrenal insufficiency	Modified CTCAE v4.03 Endocrine disorders: Adrenal insufficiency	1: Asymptomatic; clinical or diagnostic observations only; intervention indicated during periods of stress 2: Moderate symptoms; daily maintenance indicated (i.e. am cortisol < 5 mcg/dL) or initiated 3: Severe symptoms; hospitalization indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Adult growth hormone deficiency	Modified CTCAE v4.03 Investigations: Growth hormone abnormal	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated (IGF-1 z-score < -2 in isolation or abnormal dynamic test with decision not to pursue treatment) 2: Symptomatic; medical intervention indicated; limiting instrumental ADL 3: Not applicable 4: Not applicable 5: Not applicable
Childhood growth hormone deficiency (Based on dynamic testing in survivors who have not completed growth)	Modified CTCAE v4.03 Investigations: Growth hormone abnormal	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated (abnormal dynamic test with decision not to pursue treatment) 2: Symptomatic; medical intervention indicated; limiting instrumental ADL 3: Not applicable 4: Not applicable 5: Not applicable
Diabetes insipidus	CTCAE v4.03 Endocrine disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric	
Growth hormone excess	CTCAE v4.03 Endocrine disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL 3: Death Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Hyperparathyroidism	Modified CTCAE v4.03 Endocrine disorders: Hyperparathyroidism	1: Mild symptoms; intervention not indicated 2: Moderate symptoms; medical intervention indicated or initiated 3: Not applicable 4: Not applicable 5: Not applicable	
Hyperprolactinemia	CTCAE v4.03 Endocrine disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL 3: Death Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Hyperthyroidism	Modified CTCAE v4.03 Endocrine disorders: Hyperthyroidism	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; thyroid suppression indicated or initiated ; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL; hospitalization indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Hypoparathyroidism	Modified CTCAE v4.03 Endocrine disorders: Hypoparathyroidism	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; medical intervention indicated or initiated 3: Severe symptoms; medical intervention or hospitalization indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Hypothyroidism (Includes compensated hypothyroidism)	Modified CTCAE v4.03 Endocrine disorders: Hypothyroidism	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated (compensated hypothyroidism) 2: Symptomatic; thyroid replacement indicated or initiated ; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL; hospitalization indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Overweight/Obesity	New grading source for < 20 years Criteria per Centers for Disease Control and Prevention guidelines	For age ≥ 20 years 1: Not applicable 2: BMI 25 - 29.9 kg/m ² 3: BMI 30 - 39.9 kg/m ² 4: BMI ≥ 40 kg/m ² 5: Not applicable	For age 2 - <20 years 1: Not applicable 2: BMI $\geq 85^{\text{th}}$ile <95thile 3: BMI $\geq 95^{\text{th}}$ile 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric	
Syndrome of inappropriate antidiuretic hormone secretion	CTCAE v4.03 Endocrine disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL 3: Death Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Underweight	New category and grading source Criteria per Centers for Disease Control and Prevention guidelines	For age >= 20 years 1: Not applicable 2: BMI < 18.5 kg/m2 3: Not applicable 4: Not applicable 5: Not applicable	For age 2 -< 20 years 1: Not applicable 2: BMI < 5th %ile 3: Not applicable 4: Not applicable 5: Not applicable
Gastrointestinal			
Bowel perforation	CTCAEv4.03 Gastrointestinal disorders: Small intestinal perforation	1: Not applicable 2: Symptomatic; medical intervention indicated 3: Severe symptoms; elective operative intervention indicated 4: Life-threatening consequences; urgent operative intervention indicated 5: Death	
Celiac disease	CTCAEv4.03 Gastrointestinal disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Dysphagia	CTCAEv4.03 Gastrointestinal disorders: Dysphagia	1: Symptomatic, able to eat regular diet 2: Symptomatic and altered eating or swallowing 3: Severely altered eating or swallowing; tube feeding or TPN or hospitalization indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Enterocolitis (Includes: ileitis, typhlitis, colitis, enterocolitis, diverticulitis, Crohn's disease, ulcerative colitis)	CTCAEv4.03 Gastrointestinal disorders: Enterocolitis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Abdominal pain; mucus or blood in stool 3: Severe or persistent abdominal pain; fever; ileus; peritoneal signs 4: Life-threatening consequences; urgent intervention indicated 5: Death	
Esophageal varices	CTCAEv4.03 Gastrointestinal disorders: Esophageal varices	1: Not applicable 2: Self-limited; intervention not indicated 3: Transfusion, radiologic, endoscopic, or elective operative intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death	

Organ/System	Grading Source	Grading Rubric
Esophagitis	CTCAEv4.03 Gastrointestinal disorders: Esophagitis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; altered eating/swallowing; oral supplements indicated 3: Severely altered eating/swallowing; tube feeding, TPN or hospitalization indicated 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Fecal incontinence	CTCAEv4.03 Gastrointestinal disorders: Fecal incontinence	1: Occasional use of pads required 2: Daily use of pads required 3: Severe symptoms; elective operative intervention indicated 4: Not applicable 5: Not applicable
Gastritis/duodenitis	CTCAEv4.03 Gastrointestinal disorders: Gastritis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; altered GI function; medical intervention indicated 3: Severely altered eating or gastric function; TPN or hospitalization indicated 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Gastroesophageal reflux disease	CTCAEv4.03 Gastrointestinal disorders: Gastroesophageal reflux disease	1: Mild symptoms; intervention not indicated 2: Moderate symptoms; medical intervention indicated 3: Severe symptoms; surgical intervention indicated 4: Not applicable 5: Not applicable
Gastrointestinal fistulas	CTCAEv4.03 Gastrointestinal disorders: Gastrointestinal fistula	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; altered GI function 3: Severely altered GI function; tube feeding, TPN or hospitalization indicated; elective operative intervention indicated 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Gastrointestinal hemorrhage	Modified CTCAEv4.03 Gastrointestinal disorders: Upper/Lower gastrointestinal hemorrhage	1: Mild; intervention not indicated 2: Moderate symptoms; medical intervention or minor cauterization indicated 3: Transfusion; invasive intervention indicated (e.g. radiologic, endoscopic, or elective operative interventions) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Gastrointestinal necrosis	CTCAEv4.03 Gastrointestinal disorders: Gastric necrosis	1: Not applicable 2: Not applicable 3: Inability to aliment adequately by GI tract; radiologic, endoscopic, or operative intervention indicated 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Gastrointestinal obstruction	CTCAEv4.03 Gastrointestinal disorders: Small intestinal obstruction	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; altered GI function; limiting instrumental ADL 3: Hospitalization indicated; elective operative intervention indicated; limiting self -are ADL; disabling 4: Life-threatening consequences; urgent operative intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Gastrointestinal strictures	CTCAEv4.03 Gastrointestinal disorders: Esophageal stenosis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; altered GI function 3: Severely altered GI function; tube feeding; hospitalization indicated; elective operative intervention indicated 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Gastrointestinal ulcer	Modified CTCAEv4.03 Gastrointestinal disorders: Gastric ulcer	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; altered GI function; medical intervention indicated; limiting instrumental ADLs 3: Severely altered GI function; TPN indicated; invasive intervention indicated (e.g. elective operative or endoscopic intervention); limiting self-care ADL; disabling 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Gastroparesis syndrome	CTCAEv4.03 Gastrointestinal disorders: Gastroparesis	1: Mild nausea, early satiety and bloating, able to maintain caloric intake on regular diet 2: Moderate symptoms; able to maintain nutrition with dietary and lifestyle modifications; may need pharmacologic intervention 3: Weight loss; refractory to medical intervention; unable to maintain nutrition orally 4: Not applicable 5: Not applicable
Malabsorption syndrome	CTCAEv4.03 Gastrointestinal disorders: Malabsorption	1: Not applicable 2: Altered diet; oral intervention Indicated 3: Inability to aliment adequately; TPN indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Pancreatic insufficiency	CTCAEv4.03 Investigations: Pancreatic enzymes decreased	1: <LLN and asymptomatic 2: Increase in stool frequency, bulk, or odor; steatorrhea 3: Sequelae of absorption deficiency 4: Not applicable 5: Not applicable
Pancreatitis	CTCAEv4.03 Gastrointestinal disorders: Pancreatitis	1: Not applicable 2: Enzyme elevation or radiologic findings only 3: Severe pain; vomiting; medical intervention indicated (e.g., analgesia, nutritional support) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Proctitis	CTCAEv4.03 Gastrointestinal disorders: Proctitis	1: Rectal discomfort, intervention not indicated 2: Symptoms (e.g., rectal discomfort, passing blood or mucus); medical intervention indicated; limiting instrumental ADL 3: Severe symptoms; fecal urgency or stool incontinence; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Sialoadenitis	CTCAEv4.03 Gastrointestinal disorders: Salivary duct inflammation	1: Slightly thickened saliva; slightly altered taste (e.g., metallic) 2: Thick, ropy, sticky saliva; markedly altered taste; alteration in diet indicated; secretion-induced symptoms; limiting instrumental ADL 3: Acute salivary gland necrosis; severe secretion-induced symptoms (e.g., thick saliva/oral secretions or gagging); tube feeding or TPN indicated; limiting self-care ADL; disabling 4: Life-threatening consequences; urgent intervention indicated 5: Death
Hepatobiliary		
Cholecystitis Cholelithiasis	Modified CTCAEv4.03 Hepatobiliary disorders: Cholecystitis	1: Not applicable 2: Symptomatic; medical intervention indicated 3: Severe symptoms; invasive intervention indicated (e.g radiologic, endoscopic or elective operative intervention) 4: Life-threatening consequences; urgent operative intervention indicated 5: Death
Constipation	Modified CTCAEv4.03 Gastrointestinal disorders: Constipation	1: Not applicable 2: Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL 3: Obstipation with manual evacuation indicated; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Fibrosis/Cirrhosis (Includes patients with Hepatitis B and Hepatitis C induced cirrhosis)	New category and grading source Multidisciplinary team consensus	1: Not applicable 2: Not applicable 3: Compensated biopsy proven fibrosis/cirrhosis (e.g. asymptomatic varices or asymptomatic thrombocytopenia) 4: Decompensated biopsy proven fibrosis/cirrhosis (e.g., coagulopathy, encephalopathy, coma, variceal hemorrhage) 5: Death
Hepatic failure	Modified CTCAEv4.03 Gastrointestinal disorders: Hepatic failure	1: Not applicable 2: Not applicable 3: Asterixis; mild encephalopathy; limiting self-care ADL 4: Moderate to severe encephalopathy; coma; life threatening consequences; requiring liver transplantation 5: Death
Hepatopathy	CTCAEv4.03 Investigations: Alanine and aspartate aminotransferase Increased	1: >ULN - 3.0 x ULN 2: >3.0 - 5.0 x ULN 3: >5.0 - 20.0 x ULN 4: >20.0 x ULN 5: Not applicable
Portal hypertension	CTCAEv4.03 Gastrointestinal disorders: Portal hypertension	1: Not applicable 2: Decreased portal vein flow 3: Reversal/retrograde portal vein flow; associated with varices and/or ascites 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Veno-occlusive disease of liver (Sinusoidal obstructive syndrome)	CTCAEv4.03 Hepatobiliary disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Hematologic		
Anemia	Modified CTCAEv4.03 Blood and lymphatic disorders: Anemia	1: Hgb <LLN by sex/age-appropriate standards but >=10.0 g/dL 2: Hgb <10.0 - 8.0 g/dL 3: Hgb <8.0 g/dL; transfusion indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Coagulopathy (Includes: disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, acquired von Willebrand disease, etc.)	Modified CTCAEv4.03 Blood and lymphatic disorders: Disseminated intravascular Coagulation	1: Not applicable 2: Not applicable 3: Laboratory findings and bleeding 4: Life-threatening consequences; urgent intervention indicated 5: Death
Iron overload	New category and grading source Multidisciplinary team consensus	1: Tissue iron overload confirmed by imaging (e.g., T2*) or biopsy; intervention not indicated 2: Tissue iron overload confirmed by imaging (e.g., T2*) or biopsy; phlebotomy or oral chelation therapy indicated or initiated 3: Tissue iron overload confirmed by imaging (e.g., T2*) or biopsy; intravenous or subcutaneous chelation therapy indicated or initiated 4: Life-threatening consequences; urgent intervention indicated or initiated; liver transplantation indicated or completed 5: Death
Neutropenia	Modified CTCAEv4.03 Investigations: Neutrophil count decreased	1: <1500 - 1000/mm³ 2: <1000 - 500/mm³ 3: <500/mm³ 4: Not applicable 5: Not applicable
Polycythemia	Modified CTCAEv4.03 Investigations: Hemoglobin increased	1: Increase in >0 - 2 g/dL above ULN or above baseline if baseline is above ULN 2: Increase in >2 - 4 g/dL above ULN or above baseline if baseline is above ULN; requiring phlebotomy or other medical intervention. 3: Increase in >4 g/dL above ULN or above baseline if baseline is above ULN 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric
Thrombocytopenia	CTCAEv4.03 Investigations: Platelet count decreased	1: Platelets <LLN - 75,000/mm ³ 2: <75,000 - 50,000/mm ³ 3: <50,000 - 25,000/mm ³ 4: <25,000/mm ³ 5: Not applicable
Thrombocytosis	CTCAEv4.03 Blood and lymphatic disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Immunologic		
Autoimmune disorders (Includes: sarcoidosis, collagen vascular diseases -- rheumatoid arthritis, systemic lupus erythematosus, scleroderma, dermatomyositis, polyarteritis nodosa)	CTCAEv4.03 Immune system disorders: Autoimmune disorder	1: Asymptomatic; serologic or other evidence of autoimmune reaction, with normal organ function; intervention not indicated 2: Evidence of autoimmune reaction involving a nonessential organ or function (e.g., hypothyroidism) 3: Autoimmune reactions involving major organ (e.g., colitis, anemia, myocarditis, kidney) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Graft-versus-host disease	Modified CTCAEv4.03 Immune system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated or initiated 2: Moderate; minimal, local or non-invasive intervention indicated or initiated ; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Immunodeficiency (Includes: hypogammaglobulinemia IgA deficiency, immunodeficiency NOT due to HIV or other infectious/neoplastic processes)	Modified CTCAEv4.03 Immune system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated or initiated 2: Moderate; minimal, local or non-invasive intervention indicated (e.g. IVIG) or initiated ; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Infectious Bronchial/lung infections, chronic/recurrent (defined as 3 infections in 6 months)	Modified CTCAEv4.03 Infections and infestations: Lung infection	1: Not applicable 2: Moderate symptoms; oral intervention indicated or initiated (e.g., antibiotic, antifungal, antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic, endoscopic, or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Endocarditis	Modified CTCAEv4.03 Infections and infestations: Endocarditis infective	1: Not applicable 2: Not applicable 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention) 3: Life-threatening consequences; urgent intervention indicated 4: Death
Gastrointestinal infection (Includes: appendicitis diverticulitis, typhlitis, esophagitis, gastritis, and enterocolitis)	Modified CTCAEv4.03 Infections and infestations: Small intestine infection	1: Not applicable 2: Moderate symptoms; oral intervention indicated or initiated (e.g., antibiotic, antifungal, antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic, endoscopic, or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Genitourinary infection	Modified CTCAEv4.03 Infections and infestations: Urinary tract infection	1: Not applicable 2: Oral intervention indicated or initiated (e.g., oral or topical antibiotic, antifungal, antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic, endoscopic, or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Hepatitis B, chronic	Modified CTCAEv4.03 Infections and infestations: Hepatitis viral	1: Asymptomatic 2: Asymptomatic but treated with antiviral therapy 3: Symptomatic liver dysfunction; fibrosis by biopsy; compensated cirrhosis; hospitalization or prolongation of existing hospitalization indicated 4: Decompensated liver function (e.g., coagulopathy, encephalopathy, coma, variceal hemorrhage) 5: Death
Hepatitis C, chronic	Modified CTCAEv4.03 Infections and infestations: Hepatitis viral	1: Asymptomatic 2: Asymptomatic but treated with antiviral therapy 3: Symptomatic liver dysfunction; fibrosis by biopsy; compensated cirrhosis; hospitalization or prolongation of existing hospitalization indicated 4: Decompensated liver function (e.g., coagulopathy, encephalopathy, coma, variceal hemorrhage) 5: Death

Organ/System	Grading Source	Grading Rubric
HIV infection	Modified CTCAEv4.03 Infections and infestations: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only 2: Moderate; minimal, local or noninvasive intervention indicated or initiated (e.g., HAART therapy) ; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening, including sequelae of opportunistic infection ; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Lymphatic infection	Modified CTCAEv4.03 Infections and infestations: Lymph gland infection	1: Not applicable 2: Localized; local intervention indicated or initiated (e.g., topical antibiotic, antifungal, or antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Meningoencephalitis	Modified CTCAEv4.03 Infections and infestations: Meningitis	1: Not applicable 2: Not applicable 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention); focal neurologic deficit 4: Life-threatening consequences; urgent intervention indicated 5: Death
Osteomyelitis	Modified CTCAEv4.03 Infections and infestations: Bone infection	1: Not applicable 2: Not applicable 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Otitis media, chronic/recurrent (defined as 3 infections in 6 months)	Modified CTCAEv4.03 Infections and infestations: Otitis media	1: Not applicable 2: Localized; local intervention indicated or initiated (e.g., topical antibiotic, antifungal, or antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Pelvic inflammatory disease	Modified CTCAEv4.03 Infections and infestations: Pelvic infection	1: Not applicable 2: Moderate symptoms; oral intervention indicated or initiated (e.g., antibiotic, antifungal, antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Pharyngitis/tonsillitis, chronic/recurrent (defined as 3 infections in 6 months)	Modified CTCAEv4.03 Infections and infestations: Pharyngitis	1: Not applicable 2: Localized; local intervention indicated or initiated (e.g., topical antibiotic, antifungal, or antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic, endoscopic, or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Sinusitis, chronic/recurrent (defined as 3 infections in 6 months)	Modified CTCAEv4.03 Infections and infestations: Sinusitis	1: Not applicable 2: Localized; local intervention indicated or initiated (e.g., topical antibiotic, antifungal, or antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic, endoscopic, or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Soft tissue infection	Modified CTCAEv4.03 Infections and infestations: Soft tissue infection	1: Not applicable 2: Moderate symptoms ; oral intervention indicated or initiated (e.g., antibiotic, antifungal, antiviral) 3: IV antibiotic, antifungal, or antiviral intervention indicated or initiated; invasive intervention indicated (e.g., radiologic or operative intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Musculoskeletal		
Amputation	New category and grading source ICD-9-CM Diagnosis and Procedure Codes: Abbreviated and Full Code Titles. Centers for Medicare & Medicaid Services < https://www.cms.gov/medicare/coding/ICD9providerdiagnosticcodes/codes.html# >.	1: Partial ostectomy or other bone repair 2: Amputation below ankle or below elbow; revision of amputation 3: Total ostectomy; upper extremity amputation above elbow or higher; lower extremity amputation above ankle or higher 4: Not applicable 5: Not applicable
Arthralgia	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Arthralgia	1: Mild pain 2: Moderate pain; limiting instrumental ADL 3: Severe pain; limiting self-care ADL 4: Not applicable 5: Not applicable
Arthritis	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Arthritis	1: Mild pain with inflammation, erythema, or joint swelling 2: Moderate pain associated with signs of inflammation, erythema, or joint swelling; limiting instrumental ADL 3: Severe pain associated with signs of inflammation, erythema, or joint swelling; irreversible joint damage; disabling; limiting self-care ADL 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric	
Bone mineral density deficit	<p>Modified CTCAEv4.03 Musculoskeletal & connective tissue disorders: Osteoporosis</p> <p>-and-</p> <p>New grading source (Pediatric) International Society of Clinical Densitometry</p>	<p>Adults</p> <p>1: Radiologic evidence of osteoporosis or Bone Mineral Density (BMD) t-score -1 to -2.5 (osteopenia); no loss of height or intervention indicated;</p> <p>2: BMD t-score <-2.5; loss of height <2 cm; anti-osteoporotic therapy indicated or initiated; therapy to improve BMD indicated or initiated; limiting instrumental ADL;</p> <p>3: Loss of height >=2 cm; hospitalization indicated; limiting self-care ADL</p> <p>4: Not applicable</p> <p>5: Not applicable</p>	<p>Pediatric</p> <p>1: Radiologic evidence of low BMD with z score of ≤-2.0 and no history of significant fractures</p> <p>2: Low BMD (z-score ≤-2.0) and significant fracture history (defined as a long bone fracture of the lower extremity, vertebral compression, 2 or more long bone fracture of the upper extremities); therapy to improve BMD indicated or initiated</p> <p>3: Limiting self-care ADL</p> <p>4: Not applicable</p> <p>5: Not applicable</p>
Dental maldevelopment (Includes: adontia, hypodontia, microdontia, root stunting, enamel demineralization/ decalcification, etc.)	CTCAEv4.03 Gastrointestinal disorders: Tooth development disorder	<p>1: Asymptomatic; hypoplasia of tooth or enamel</p> <p>2: Impairment correctable with oral surgery</p> <p>3: Maldevelopment with impairment not surgically correctable; disabling</p> <p>4: Not applicable</p> <p>5: Not applicable</p>	
Hernia (Includes: abdominal, umbilical, ventral, inguinal, femoral, etc.)	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	<p>1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated</p> <p>2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL</p> <p>3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL</p> <p>4: Life-threatening consequences; urgent intervention indicated</p> <p>5: Death</p>	
Intervertebral disc disorder (Includes: disc degeneration, disc herniation)	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	<p>1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated</p> <p>2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL</p> <p>3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL</p> <p>4: Life-threatening consequences; urgent intervention indicated</p> <p>5: Death</p>	
Kyphosis	<p>Modified CTCAEv4.03 Musculoskeletal & connective tissue disorders: Kyphosis</p>	<p>1: Not applicable</p> <p>2: Moderate accentuation; limiting instrumental ADL</p> <p>3: Severe accentuation; operative intervention indicated; limiting self-care ADL</p> <p>4: Not applicable</p> <p>5: Not applicable</p>	

Organ/System	Grading Source	Grading Rubric
Limb length discrepancy	Modified CTCAEv4.03 Musculoskeletal & connective tissue disorders: Unequal limb length	1: Not applicable 2: Moderate length discrepancy 2-5 cm; shoe lift indicated; limiting instrumental ADL 3: Severe length discrepancy >5 cm; limiting self-care ADL; disabling; operative intervention indicated 4: Not applicable 5: Not applicable
Osteonecrosis	Modified CTCAEv4.03 Musculoskeletal & connective tissue disorders: Avascular necrosis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; medical intervention indicated (e.g., analgesics, anti-inflammatory); limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL; elective operative intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Palatal defects, acquired	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Prosthetic malfunction (Includes: dislodgement, fracture, loosening)	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Scoliosis	Modified CTCAEv4.03 Musculoskeletal & connective tissue disorders: Scoliosis	1: > 8 and <15 degrees ; clinically undetectable 2: >=15 - 30 degrees ; visible by forward flexion; limiting instrumental ADL 3: >=30 degrees ; scapular prominence in forward flexion; operative intervention indicated; limiting self-care ADL; disabling 4: Not applicable 5: Not applicable
Skeletal spine disorder (Includes: spondylitis, spondylolisthesis, spondylomalacia, spondylosis)	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Slipped capital femoral epiphysis	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Temporomandibular joint disorder	CTCAEv4.03 Musculoskeletal & connective tissue disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Neurologic		
Autonomic dysfunction (Includes Horner's syndrome)	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Cavernoma	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Cerebellar dysfunction (Includes: demyelization, drug-induced, hereditary, nutritional, surgical, trauma, tumors, or vascular causes)	CTCAEv4.03 Nervous system disorders: Ataxia	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL; mechanical assistance indicated 4: Not applicable 5: Not applicable
Cerebral necrosis	CTCAEv4.03 Nervous system disorders: Central nervous system necrosis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; corticosteroids indicated 3: Severe symptoms; medical intervention indicated (e.g., HBO) 4: Life-threatening consequences; urgent/surgical intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Cerebrovascular accident (Includes: lacunes, hemorrhagic stroke, Ischemic stroke)	CTCAEv4.03 Nervous system disorders: Stroke	1: Asymptomatic or mild neurologic deficit; radiographic findings only 2: Moderate neurologic deficit 3: Severe neurologic deficit 4: Life-threatening consequences; urgent intervention indicated 5: Death
Cerebrovascular disease (Includes: stenotic or occlusive large vessel disease, moyamoya)	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Cranial nerve disorder	Modified CTCAEv4.03 Nervous system disorders: Trigeminal, oculomotor, etc... cranial nerve disorder	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL (e.g., surgical intervention indicated) 4: Not applicable 5: Not applicable
Dysarthria	Modified CTCAEv4.03 Nervous system disorders: Dysarthria	1: Mild slurred speech (easily understood) 2: Moderate impairment of articulation or slurred speech (some need for repetition to be understood) 3: Severe impairment of articulation or slurred speech (unintelligible speech) 4: Not applicable 5: Not applicable
Headaches, chronic/ recurrent (Includes: migraines) Chronic headaches defined as headaches 15 days in a month for 3 consecutive months Recurrent headaches defined as at least 5 headaches over lifetime	Modified CTCAEv4.03 Nervous system disorders: Headaches	1: Mild pain 2: Moderate pain requiring prescriptive abortive medication ; limiting instrumental ADL 3: Severe pain requiring prophylactic medication ; limiting self-care ADL 4: Not applicable 5: Not applicable
Hydrocephalus	CTCAEv4.03 Nervous system disorders: Hydrocephalus	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; intervention not indicated 3: Severe symptoms or neurological deficit; intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Hydrosyringomyelia (Includes: syrinx, syringohydromyelia, syringomyelia)	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Intracranial hemorrhage (Includes: subdural, subarachnoid, intraventricular)	Modified CTCAEv4.03 Nervous system disorders: Intracranial hemorrhage	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated (MRI evidence of microhemorrhage, e.g. hemosiderin) 2: Moderate symptoms; medical intervention indicated 3: Ventriculostomy, ICP monitoring, intraventricular thrombolysis, or operative intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Movement disorders (Includes: athetosis, ballism, chorea, dystonia, myoclonus, opsoclonus/ myoclonus, Parkinsonism, restless legs, tic tremor, torticollis)	Modified CTCAEv4.03 Nervous system disorders: Movements involuntary	1: Mild involuntary movements 2: Moderate involuntary movements ; limiting instrumental ADL 3: Severe involuntary movements ; limiting self-care ADL 4: Not applicable 5: Not applicable
Multiple sclerosis	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Narcolepsy	Modified CTCAEv4.03 Nervous system disorders: Hypersomnia	1: Not applicable 2: Documentation of narcolepsy without need for therapy ; moderate increased need for sleep 3: Documentation of narcolepsy with need for therapy ; severe increased need for sleep 4: Not applicable 5: Not applicable
Nerve root disorder (Includes: radiculopathy, plexopathy, cauda equina syndrome)	CTCAEv4.03 Nervous system disorders: Radiculitis	1: Mild symptoms 2: Moderate symptoms; limiting instrumental ADL; medical intervention indicated 3: Severe symptoms; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Neurogenic bladder	Modified CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated (medical management e.g., oxybutynin); limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; surgical intervention indicated (e.g. ileal-anal pouch) ; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Neurogenic bowel	Modified CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated (e.g. stool softener); limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; surgical intervention indicated (e.g. MACE) ; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Neuromuscular disorders (Includes: dermatomyositis, myotonia, neuromuscular disorder, polymyositis, rhabdomyolysis, steroid myopathy, critical illness myopathy/neuropathy)	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Paralytic disorder (Includes: hemiparesis/ plegia, quadriplegia/ plegia, paraparesis/ plegia, flaccid paralysis, spastic paralysis)	Modified CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms (e.g., facial paraparesis); clinical or diagnostic observations only; intervention not indicated 2: Moderate (e.g., paraparesis); minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe weakness or sensory loss (e.g., paraplegia requiring wheelchair); limiting self-care ADL 4: Life-threatening consequences (e.g., quadriplegia); urgent intervention indicated 5: Death
Peripheral motor neuropathy (Includes: inflammatory demyelinating polyneuropathy disorder - Guillain-Barre syndrome)	CTCAEv4.03 Nervous system disorders: Peripheral motor neuropathy	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL; assistive device indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Peripheral sensory neuropathy	CTCAEv4.03 Nervous system disorders: Peripheral sensory neuropathy	1: Asymptomatic; loss of deep tendon reflexes or paresthesia 2: Moderate symptoms; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Pseudomeningocele	CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Pseudotumor cerebri	Modified CTCAEv4.03 Nervous system disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical management or diagnostic observations only (e.g., weight control) 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL; medical intervention indicated or initiated (e.g., acetazolamide) 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL; surgical intervention indicated or initiated (e.g., lumbar puncture) 4: Life-threatening consequences; urgent intervention indicated (e.g., severe visual impairment) 5: Death
Seizures	New grading source Multidisciplinary team consensus	1: Seizures not requiring medication 2: Seizures requiring one non-prn medication 3: Seizures requiring two or more non-prn medications; poorly controlled seizures with prescribed medications 4: Seizures requiring evaluation for surgical intervention 5: Death
Shunt malfunction	CTCAEv4.03 Nervous system disorders: Hydrocephalus	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Moderate symptoms; intervention not indicated 3: Severe symptoms or neurological deficit; intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Ocular/Visual		
Cataract	Modified CTCAEv4.03 Eye disorders: Cataracts	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated (20/30 or better) 2: Symptomatic; moderate decrease in visual acuity (20/40 or better) 3: Symptomatic with marked decrease in visual acuity (worse than 20/40 but better than 20/200); operative intervention indicated (e.g., cataract surgery) 4: Blindness (20/200 or worse)in the affected eye 5: Not applicable
Diplopia	Modified CTCAEv4.03 Eye disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately sight threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Not applicable 5: Not applicable
Dry eye syndrome (Includes: Keratitis sicca, xerophthalmia, kerato-conjunctivitis sicca, Sjogren's syndrome, lacrimal duct atrophy, limbal stem cell deficiency)	CTCAEv4.03 Eye disorders: Dry eye	1: Asymptomatic; clinical or diagnostic observations only; mild symptoms relieved by lubricants 2: Symptomatic; multiple agents indicated; limiting instrumental ADL 3: Decrease in visual acuity (<20/40); limiting self-care ADL 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric
Eyelid function disorder (Includes: entropion, ectropion, lagophthalmos, ptosis)	CTCAEv4.03 Eye disorders: Eyelid function	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; non-operative intervention indicated; limiting instrumental ADL 3: Limiting self-care ADL; operative intervention indicated 4: Not applicable 5: Not applicable
Glaucoma	CTCAEv4.03 Eye disorders: Glaucoma	1: Elevated intraocular pressure (EIOP) with single topical agent for intervention; no visual field deficit 2: EIOP causing early visual field deficits; multiple topical or oral agents indicated; limiting instrumental ADL 3: EIOP causing marked visual field deficits (e.g., involving both superior and inferior visual fields); operative intervention indicated; limiting self-care ADL 4: Blindness (20/200 or worse) in the affected eye 5: Not applicable
Ocular disease, noninfectious (Includes: chorioretinitis, uveitis, iritis, scleritis)	CTCAEv4.03 Eye disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately sight threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Sight-threatening consequences; urgent intervention indicated; blindness (20/200 or worse) in the affected eye 5: Not applicable
Ocular surface disease (Includes: conjunctivitis, chronic, keratitis, keratoconjunctivitis, keratopathy)	CTCAEv4.03 Eye disorders: Keratitis	1: Not applicable 2: Symptomatic; medical intervention indicated (e.g., topical agents); limiting instrumental ADL 3: Decline in vision (worse than 20/40 but better than 20/200); limiting self-care ADL 4: Perforation or blindness (20/200 or worse) in the affected eye 5: Not applicable
Orbital prosthetic complications (Includes: displacement, exposure, giant papillary conjunctivitis)	Modified CTCAEv4.03 Eye disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Not applicable 5: Not applicable
Photophobia	CTCAEv4.03 Eye disorders: Photophobia	1: Symptomatic but not limiting ADL 2: Limiting instrumental ADL 3: Limiting self-care ADL 4: Not applicable 5: Not applicable
Phthisis bulbi (Defined as blind, painful eye)	CTCAEv4.03 Eye disorders: Eye pain	1: Mild pain 2: Moderate pain; limiting instrumental ADL 3: Severe pain; limiting self-care ADL 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric
Retinal detachment	Modified CTCAEv4.03 Eye disorders: Retinal detachment	1: Asymptomatic 2: Rhegmatogenous or exudative and visual acuity 20/40 or better 3: Rhegmatogenous or exudative detachment; operative intervention indicated; decline in vision (worse than 20/40 but better than 20/200) 4: Blindness (20/200 or worse) in the affected eye 5: Not applicable
Retinopathy	CTCAEv4.03 Eye disorders: Retinopathy	1: Asymptomatic; clinical or diagnostic observations only 2: Symptomatic with moderate decrease in visual acuity (20/40 or better); limiting instrumental ADL 3: Symptomatic with marked decrease in visual acuity (worse than 20/40); disabling; limiting self-care ADL 4: Blindness (20/200 or worse) in the affected eye 5: Not applicable
Strabismus (Includes: esotropia, exotropia, hypertropia, Parinaud's syndrome, Internuclear ophthalmoplegia)	CTCAEv4.03 Eye disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately sight threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Sight-threatening consequences; urgent intervention indicated; blindness (20/200 or worse) in the affected eye 5: Not applicable
Visual acuity, reduced (OD)	Modified CTCAEv4.03 Eye disorders: Optic nerve disorder	1: Asymptomatic; clinical or diagnostic observations only (reduced visual acuity corrected to 20/40 or better) 2: Limiting vision of the affected eye (reduced visual acuity corrected to less than 20/40 but better than 20/60) 3: Limiting vision in the affected eye (reduced visual acuity corrected to 20/60 but better than 20/200) 4: Blindness (corrected to 20/200 or worse, includes count fingers, hand motion, light perception only) in the affected eye (cortical blindness, enucleation) 5: Not applicable
Visual acuity, reduced (OS)	Modified CTCAEv4.03 Eye disorders: Optic nerve disorder	1: Asymptomatic; clinical or diagnostic observations only (reduced visual acuity corrected to 20/40 or better) 2: Limiting vision of the affected eye (reduced visual acuity corrected to less than 20/40 but better than 20/60) 3: Limiting vision in the affected eye (reduced visual acuity corrected to 20/60 but better than 20/200) 4: Blindness (corrected to 20/200 or worse, includes count fingers, hand motion, light perception only) in the affected eye (cortical blindness, enucleation) 5: Not applicable

Organ/System	Grading Source	Grading Rubric
Visual field deficit	Modified CTCAEv4.03 Eye disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL (can't drive) 3: Severe or medically significant but not immediately sight threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL (can't ambulate/navigate) 4: Not applicable 5: Not applicable
Pulmonary		
Asthma (Based on physician diagnosis by appropriate clinical signs and symptoms, <u>reversible</u> airway obstruction)	Modified CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Bronchospasm	1: Mild symptoms; intervention not Indicated 2: Symptomatic; medical intervention indicated; limiting instrumental ADL; intermittent asthma requiring short-acting beta agonists as needed 3: Limiting self-care ADL; oxygen saturation decreased; persistent asthma requiring daily controller medication (oral or inhaled) 4: Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated 5: Death
Chronic obstructive pulmonary disease (COPD) (Based on physician diagnosis by appropriate clinical signs and symptoms, <u>irreversible</u> airway obstruction; includes emphysema, chronic bronchitis, and mixed chronic obstructive asthma/COPD syndrome)	Modified CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated or initiated (inhaled medications); limiting age-appropriate instrumental ADL 3: Severe or medically significant but not immediately life-threatening (e.g., requiring supplementation of oxygen, systemic corticosteroids, BIPAP, or CPAP); hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Epistaxis, chronic/recurrent (Defined as 3 events in last 6 months)	CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Epistaxis	1: Mild symptoms; intervention not Indicated 2: Moderate symptoms; medical intervention indicated (e.g., nasal packing, cauterization; topical vasoconstrictors) 3: Transfusion, radiologic, endoscopic, or operative intervention indicated (e.g., hemostasis of bleeding site) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Obstructive sleep apnea	New category and grading source Multidisciplinary team consensus	1: Documentation of apnea; no need for medication 2: Documentation of mild apnea; behavioral intervention initiated or indicated 3: Documentation of moderate apnea; CPAP initiated or indicated 4: Documentation of severe apnea with secondary complications (CHF, HTN, headache) 5: Not applicable

Organ/System	Grading Source	Grading Rubric
<p>Obstructive ventilatory defect</p> <p>(Defined by FEV1 < 80% predicted and <LLN. Disorders associated with this pattern and reduced FEV1/FVC ratio (obstructive ventilatory defect) include: asthma, COPD, tracheobronchomalacia, obliterative bronchiolitis and bronchiectasis. Disorders associated with this pattern and normal or increased FEV1/FVC (possible restrictive ventilatory defect, confirm with TLC) include pulmonary fibrosis, other interstitial lung diseases, chest wall disorders)</p>	<p>New grading source</p> <p>Pellegrino et al, Interpretative strategies for lung function tests. Eur Resp J 2005;26:948-968. Table 6</p>	<p>1: FEV1 (percentages of observed FEV1 related to its predicted value): 79-70% predicted 2: FEV1: 69-50% predicted 3: FEV1: 49-35% predicted 4: FEV1: <35% predicted 5: Not applicable</p>
<p>Pleural space disorders</p> <p>(Includes: pleural effusions, chylothorax, hemothorax)</p>	<p>Modified CTCAEv4.03 Respiratory, thoracic and mediastinal disorders Pneumothorax</p>	<p>1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate to severe symptoms and non-operative intervention indicated (e.g., tube placement without sclerosis) 3: Sclerosis and/or operative intervention indicated; hospitalization indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death</p>
<p>Pneumonitis</p>	<p>Modified CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Pneumonitis</p>	<p>1: Not applicable 2: Symptomatic; medical intervention indicated; limiting instrumental ADL 3: Severe symptoms; limiting self-care ADL; oxygen indicated 4: Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheotomy or intubation) 5: Death</p>
<p>Pulmonary diffusion defect</p> <p>(Defined by DLCOcorr < 75% predicted and <LLN. Includes: pneumonitis, pulmonary fibrosis, other interstitial lung diseases, pulmonary vascular disorders and emphysema)</p>	<p>New grading source</p> <p>Pellegrino et al, Interpretative strategies for lung function tests. Eur Resp J 2005;26:948-968. Table 14</p>	<p>1: DLCO: 74-60% predicted 2: DLCO: <60%-40% predicted 3: DLCO: <40% predicted 4: Not applicable 5: Not applicable</p>
<p>Pulmonary embolism</p>	<p>Modified CTCAEv4.03 Vascular disorders: Thromboembolic event</p>	<p>1: Not applicable 2: Not applicable 3: Urgent medical intervention indicated 4: Life-threatening with hemodynamic or neurologic instability 5: Death</p>

Organ/System	Grading Source	Grading Rubric
Respiratory tract hemorrhage	CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Bronchopulmonary hemorrhage	1: Mild symptoms; intervention not Indicated 2: Moderate symptoms; medical intervention indicated 3: Transfusion, radiologic, endoscopic, or operative intervention indicated (e.g., hemostasis of bleeding site) 4: Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated 5: Death
Restrictive ventilatory defect (Defined by TLC < 75% predicted and <LLN. Includes: pulmonary fibrosis and other interstitial lung disease, pneumonitis, chest wall disorders)	New grading source American Thoracic Society, Lung Function Testing: Selection of Reference Values and Interpretative Strategies. Am Rev Respir Dis 1991;144:1202-1218. Table 13	1: TLC: 74 -70% 2: TLC: 69 - 60% predicted; limiting instrumental ADL 3: TLC: <60% predicted; limiting self-care ADL 4: Not applicable 5: Not applicable
Tracheal aspiration	CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Aspiration	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Altered eating habits; coughing or choking episodes after eating or swallowing; medical intervention indicated (e.g., suction or oxygen) 3: Dyspnea and pneumonia symptoms (e.g., aspiration pneumonia); hospitalization indicated; unable to aliment orally 4: Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated 5: Death
Tracheal stenosis	CTCAEv4.03 Respiratory, thoracic and mediastinal disorders: Tracheal stenosis	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic (e.g., noisy airway breathing), but causing no respiratory distress; medical management indicated (e.g., steroids) 3: Stridor or respiratory distress limiting self-care ADL; endoscopic intervention indicated (e.g., stent, laser) 4: Life-threatening airway compromise; urgent intervention indicated (e.g., tracheotomy or intubation) 5: Death
Renal/Urinary Tract		
Acute kidney injury	Modified CTCAEv4.03 Renal and urinary disorders: Acute kidney injury	1: Creatinine 1.5-2.0 x above age-specific ULN 2: Creatinine 2 - 3 x above age-specific ULN 3: Creatinine >3 x age-specific ULN or >4.0 mg/dL; hospitalization indicated 4: Life-threatening consequences; dialysis indicated 5: Death
Chronic hematuria Defined as > 5 RBCs/hpf documented on more than one urinalysis	Modified CTCAEv4.03 Renal and urinary disorders: Hematuria	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; urinary catheter or bladder irrigation indicated; limiting instrumental ADL 3: Gross hematuria; transfusion, IV medications or hospitalization indicated; elective invasive intervention indicated ; limiting self-care ADL 4: Life-threatening consequences; urgent invasive intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Chronic kidney disease Includes CKD requiring dialysis/transplant	Modified CTCAEv4.03 Renal and urinary disorders: Chronic kidney disease eGFR estimated used in the KDIGO estimating equations: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf	1: eGFR (estimated Glomerular Filtration Rate) or CrCl (creatinine clearance) <LLN – 60 ml/min/1.73 m ² AND proteinuria 1+ present; urine protein/creatinine >0.5 2: eGFR or CrCl 59-30 ml/min/1.73 m ² ; medication (e.g., electrolytes, ACE inhibition, etc....) indicated or initiated 3: eGFR or CrCl 29-15 ml/min/1.73 m ² 4: eGFR or CrCl <15 ml/min/1.73 m ² ; dialysis or renal transplant indicated or initiated/performed 5: Death
Incontinence	CTCAEv4.03 Renal and urinary disorders: Urinary incontinence	1: Occasional (e.g., with coughing, sneezing, etc.), pads not indicated 2: Spontaneous; pads indicated; limiting instrumental ADL 3: Intervention indicated (e.g., clamp, collagen injections); operative intervention indicated; limiting self-care ADL 4: Not applicable 5: Not applicable
Obstructive uropathy (Includes: urinary tract stenosis; urinary tract stricture)	Modified CTCAEv4.03 Renal and urinary disorders: Urinary tract obstruction	1: Asymptomatic; clinical or diagnostic observations only 2: Symptomatic but no hydronephrosis, sepsis or renal dysfunction; urethral dilation, urinary or suprapubic catheter indicated 3: Symptomatic and altered organ function (e.g., hydronephrosis, or renal dysfunction); elective invasive intervention indicated 4: Life-threatening consequences; urgent invasive intervention indicated 5: Death
Urinary bladder dysfunction (Includes: dysfunctional voiding, hypertonic bladder, urinary frequency, urinary hesitancy)	Modified CTCAEv4.03 Renal and urinary disorders: Urinary frequency Urinary urgency	1: Present 2: Limiting instrumental ADL; medical management indicated or initiated 3: Surgical management indicated or initiated (e.g., trans-electrical nerve stimulation, sacral neural modulation) 4: Not applicable 5: Not applicable
Urinary tract calculi (Includes: renal calculi, bladder stone/calculi, ureteral calculi)	Modified CTCAEv4.03 Renal and urinary disorders: Renal calculi	1: Asymptomatic or mild symptoms; occasional use of nonprescription analgesics indicated 2: Symptomatic; oral antiemetics indicated; around the clock nonprescription analgesics or any oral narcotic analgesics indicated 3: Hospitalization indicated; IV intervention (e.g., analgesics, antiemetics); elective invasive intervention indicated 4: Life-threatening consequences; urgent invasive intervention indicated 5: Death
Vesicoureteral reflux, acquired	CTCAEv4.03 Renal and urinary disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate, local or noninvasive intervention indicated; limiting instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Reproductive/Genital		
Abnormal sperm concentration (Includes: oligospermia, azoospermia)	Modified Reproductive system and breast disorders: Oligospermia Azoospermia	1: Not applicable 2: Sperm concentration > 0 but < 15 million spermatozoa/mL 3: Absence of sperm in ejaculate 4: Not applicable 5: Not applicable
Cervical dysplasia	Modified CTCAE v4.03 Reproductive system and breast disorder: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age appropriate instrumental ADL (e.g., colposcopy) 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL (e.g., conization for carcinoma-in-situ) 4: Not applicable 5: Not applicable
Dysfunctional uterine bleeding	CTCAE v4.03 Reproductive system and breast disorders Menorrhagia	1: Mild; iron supplements indicated 2: Moderate symptoms; medical intervention indicated (e.g., hormones) 3: Severe; transfusion indicated; surgical intervention indicated (e.g., hysterectomy) 4: Life-threatening consequences; urgent intervention indicated 5: Death
Dyspareunia	CTCAE v4.03 Reproductive system and breast disorders: Dyspareunia	1: Mild discomfort or pain associated with vaginal penetration; discomfort relieved with use of vaginal lubricants or estrogen 2: Moderate discomfort or pain associated with vaginal penetration; discomfort or pain partially relieved with use of vaginal lubricants or estrogen 3: Severe discomfort or pain associated with vaginal penetration; discomfort or pain unrelieved by vaginal lubricants or estrogen 4: Not applicable 5: Not applicable
Endometriosis	Modified CTCAE v4.03 Reproductive system and breast disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL (e.g., medical management) 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL (e.g., surgical intervention) 4: Life-threatening consequences; urgent intervention indicated 5: Death

Organ/System	Grading Source	Grading Rubric
Erectile dysfunction	CTCAE v4.03 Reproductive system and breast disorders: Erectile dysfunction	1: Decrease in erectile function (frequency or rigidity of erections) but intervention not indicated (e.g., medication or use of mechanical device, penile pump) 2: Decrease in erectile function (frequency/ rigidity of erections), erectile intervention indicated, (e.g., medication or mechanical devices such as penile pump) 3: Decrease in erectile function (frequency/ rigidity of erections) but erectile intervention not helpful (e.g., medication or mechanical devices such as penile pump); placement of a permanent penile prosthesis indicated (not previously present) 4: Not applicable 5: Not applicable
Genitourinary adhesions	CTCAE v4.03 Reproductive system and breast disorders: Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL 4: Life-threatening consequences; urgent intervention indicated 5: Death
Hypogonadism, central (hypogonadotropic)	Modified CTCAE v4.03 Investigations: Blood gonadotropin abnormal	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; medical intervention indicated or initiated ; limiting instrumental ADL 3: Severe symptoms; medical intervention indicated or initiated ; limiting self-care ADL 4: Not applicable 5: Not applicable
Leydig cell insufficiency	Modified CTCAE v4.03 Reproductive system and breast disorders: Other, specify	1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated 2: Symptomatic; medical intervention indicated or initiated ; limiting instrumental ADL 3: Severe symptoms; medical intervention indicated or initiated ; limiting self-care ADL 4: Not applicable 5: Not applicable
Polycystic ovarian syndrome	Modified CTCAE v4.03 Reproductive system and breast disorders Other, specify	1: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated (e.g., mild signs/symptoms of hyperandrogenemia) 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age appropriate instrumental ADL (e.g., more severe hirsutism, irregular menses; need for metformin or hormone replacement) 3: Severe or medically significant but not immediately life threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL (e.g., need for surgery for cyst or bleed) 4: Not applicable 5: Not applicable
Precocious puberty	Modified CTCAE v4.03 Endocrine disorders: Precocious puberty	1: Not applicable 2: Physical signs and biochemical markers of puberty for females <8 years and males <9 years 3: Not applicable 4: Not applicable 5: Not applicable

Organ/System	Grading Source	Grading Rubric
Primary ovarian failure	CTCAE v4.03 Reproductive system and breast disorders: Premature menopause	1: Not applicable 2: Not applicable 3: Present 4: Not applicable 5: Not applicable
Prostatic hypertrophy, benign	CTCAEv4.03 Reproductive system and breast disorders: Prostatic obstruction	1: Diagnostic observations only; intervention not indicated 2: Mild symptoms; elective intervention indicated 3: Severe symptoms; elective operative intervention indicated 4: Not applicable 5: Not applicable
Retrograde ejaculation	CTCAE v4.03 Reproductive system and breast disorders: Ejaculation disorder	1: Diminished ejaculation 2: Anejaculation or retrograde ejaculation 3: Not applicable 4: Not applicable 5: Not applicable
Vaginal fistula	CTCAE v4.03 Reproductive system and breast disorders: Female genital tract fistula	1: Asymptomatic clinical or diagnostic observations only; intervention not indicated 2: Symptomatic and intervention not indicated 3: Severe symptoms; elective operative intervention indicated 4: Life-threatening consequences; urgent intervention indicated 5: Death
Vaginal stenosis	Modified CTCAE v4.03 Reproductive system and breast disorders: Vaginal stricture	1: Asymptomatic; mild vaginal shortening or narrowing 2: Vaginal narrowing and/or shortening not interfering with physical examination 3: Vaginal narrowing and/or shortening interfering with the use of tampons, sexual activity or physical examination (e.g., surgical intervention indicated or performed) 4: Not applicable 5: Not applicable

Bolded font represents modified or new categories or grading criteria.

Supplemental Tables

Supplemental Table 2. Patient characteristics of HCT and conventional chemotherapy recipients

Variables	HCT (n=112)		Conventional Therapy (n=1106)		P
Sex, n (%)					0.766
Female	55	49.1	525	47.5	
Male	57	50.9	581	52.5	
Race, n (%)					< 0.001
White	90	80.4	941	85.1	
Black	10	8.9	142	12.8	
Other	12	10.7	23	2.1	
Ethnicity, n (%)					0.002
Hispanic	11	9.8	34	3.1	
Non-Hispanic	101	90.2	1072	96.9	
Age at baseline, mean (sd, range)	28.4	5.9,18.8-43.4	29.3	6.2,18.4-47.6	0.122
Time since diagnosis, mean (sd, range)	18.5	4.2,11.3-28.5	19.9	5.1,10.5-32.9	0.002
Age at diagnosis, mean (sd, range)	9.8	5.3, 0.5-18.8	9.4	5.5, 0.2-21.8	0.425
Diagnosis, n (%)					< 0.001
Leukemia	94	83.9	693	62.7	
ALL	23	20.5	649	58.7	
AML	44	39.3	42	3.8	
CML	16	14.3	0	0.0	
Other Leukemia	1	0.9	2	0.2	
Myelodysplastic Syndrome	10	8.9	0	0.0	
Lymphoma	18	16.1	413	37.3	
Hodgkin lymphoma	8	7.1	259	23.4	
Non-Hodgkin lymphoma	10	8.9	154	13.9	
Income, n (%)					0.554
< \$20,000	62	59.0	567	54.0	
\$20,000-39,000	22	21.0	240	23.0	
\$40,000-59,000	9	8.6	134	12.8	
> \$60,000	12	11.4	107	10.2	
Education, n (%)					0.250
Less than high school	6	5.7	109	10.2	
High school graduate	26	24.5	283	26.6	
Some college	27	25.5	303	28.4	
College	36	33.9	269	25.2	
Post-graduate level	11	10.4	102	9.6	
Independent Living, n (%)					0.002
Radiation n (%)					

TBI	82	73.2	0	0.0	< 0.001
Cranial	9	8.0	278	25.1	< 0.001
Chest	5	4.5	43	3.9	0.797
Spine	7	6.3	42	3.8	0.206
Neck	6	5.4	33	3.0	0.163
Chemotherapy, mean (sd, range)					
Anthracyclines, mg/m ² *	169	100, 41-596	140	94, 23-619	0.007
Alkylators, mg/m ² †	8692	8800, 1200-47788	7577	3970, 300-51367	0.196
Epipodophyllotoxins ‡					
Teniposide, mg/m ²	2808	2116, 459-7801	4012	2332, 150-21771	0.058
Etoposide, mg/m ²	2607	3585, 17-17481	7974	5410, 211-23251	< 0.001
Steroid exposure, mean (sd, range) §					
Prednisone, mg/m ²	4753	5047, 98-17520	4947	4209, 560-25414	0.765
Dexamethasone, mg/m ²	889	929, 22-2295	1592	491, 2-3400	< 0.001
Transplant characteristics					
Stem cell source n (%)					
Autologous	33	29.5			
Allogeneic, sibling	41	36.6			
Allogeneic, unrelated	34	30.4			
Other	4	3.6			
Age at time of HCT, mean (sd, range)	11.4	5.3, 1.4-21.3			
Time since HCT, mean (sd, range)	17.0	4.1, 10.6-28.3			
Conditioning n (%)					
TBI including	82	73.2			
Chemotherapy only	30	26.8			
Chronic GVHD n (%)					
Yes	25	31.6			

Abbreviations: HCT, Hematopoietic stem cell transplantation; ALL, Acute lymphoblastic leukemia; AML, Acute myeloid leukemia; CML, chronic myeloid leukemia; TBI, Total body irradiation.

* Includes doxorubicin, daunorubicin, idarubicin, mitoxantrone, and epirubicin doses expressed in doxorubicin equivalents.

† Includes BCNU (carmustine), busulfan, CCNU (lomustine), chlorambucil, cyclophosphamide, ifosfamide, melphalan, nitrogen mustard, procarbazine, and thiotepa expressed in cyclophosphamide equivalents.

‡ Includes teniposide and etoposide doses.

§ Includes steroid exposure as part of cancer directed therapy.

Supplemental Table 3. Prevalence of grade 1-4 chronic conditions comparing HCT and conventional chemotherapy groups

	HCT (n=112)		Conventional Therapy (n=1106)		p
	n	%	n	%	
Any grade 1-4	112	100.0	1101	99.6	1.000
Cardiovascular conditions*	101	90.2	955	86.3	0.307
Aortic root aneurysm	4	3.6	71	6.4	0.303
Arteriovenous malformation	0	0.0	2	0.2	1.000
Atrial myxoma	0	0.0	1	0.1	1.000
Atrioventricular heart block	2	1.8	8	0.7	0.233
Cardiac dysrhythmia	5	4.5	15	1.4	0.030
Cardiomyopathy	10	8.9	71	6.4	0.318
Conduction abnormality	23	20.5	276	25.0	0.357
Dyslipidemia - Hypercholesterolemia	59	52.7	412	37.3	0.002
Dyslipidemia - Hypertriglyceridemia	71	63.4	334	30.2	< 0.001
Heart valve disorder	41	36.6	398	36.0	0.918
Hypertension	64	57.1	609	55.1	0.691
Myocardial infarction	3	2.7	25	2.3	0.738
Pericarditis	0	0.0	2	0.2	1.000
Prolonged QT interval	6	5.4	57	5.2	0.825
Pulmonary hypertension	0	0.0	2	0.2	1.000
Raynaud's phenomenon	2	1.8	12	1.1	0.374
Right ventricular systolic dysfunction	0	0.0	3	0.3	1.000
Sinus bradycardia	1	0.9	23	2.1	0.718
Sinus tachycardia	10	8.9	42	3.8	0.022
Thrombus	5	4.5	33	3.0	0.387
Vascular disease	2	1.8	21	1.9	1.000
Endocrine System*	96	85.7	923	83.5	0.594
Adrenal insufficiency	8	7.1	23	2.1	0.005
Adult GHD	26	23.2	185	16.7	0.089
Childhood GHD	16	14.3	54	4.9	< 0.001
Glucose metabolism	42	37.5	307	27.8	0.037
Hyperparathyroidism	0	0.0	2	0.2	1.000
Hyperprolactinemia	1	0.9	1	0.1	0.176
Hyperthyroidism	3	2.7	19	1.7	0.447
Hypoparathyroidism	0	0.0	1	0.1	1.000
Hypothyroidism	61	54.5	244	22.1	< 0.001
Hypothyroidism compensated	1	0.9	3	0.3	0.321
Obesity	45	40.2	755	68.3	< 0.001
Thyroid cyst/nodule	15	13.4	104	9.4	0.181
Underweight	13	11.6	26	2.4	< 0.001
Gastrointestinal System*	63	56.3	426	38.5	< 0.001
Celiac (coeliac) disease	0	0.0	2	0.2	1.000

Cholecystitis	11	9.8	92	8.3	0.592
Constipation	3	2.7	16	1.4	0.409
Dysphagia	5	4.5	30	2.7	0.365
Enterocolitis	3	2.7	21	1.9	0.479
Esophageal stricture	0	0.0	20	1.8	0.247
Esophageal varices	0	0.0	4	0.4	1.000
Esophagitis	0	0.0	3	0.3	1.000
Fecal incontinence	1	0.9	4	0.4	0.383
Fibrosis Cirrhosis	7	6.3	24	2.2	0.019
Fistulas	0	0.0	3	0.3	1.000
Gastritis/Duodenitis	5	4.5	18	1.6	0.053
Gastroesophageal reflux disease	23	20.5	155	14.0	0.068
Gastrointestinal hemorrhage	1	0.9	4	0.4	0.383
Gastrointestinal obstruction	3	2.7	3	0.3	0.012
Gastrointestinal ulcer	3	2.7	5	0.5	0.030
Gastroparesis syndrome	1	0.9	1	0.1	0.176
Hepatic failure	0	0.0	3	0.3	1.000
Hepatopathy	41	36.6	216	19.5	< 0.001
Malabsorption syndrome	0	0.0	1	0.1	1.000
Pancreatic insufficiency	0	0.0	1	0.1	1.000
Pancreatitis	1	0.9	7	0.6	0.539
Portal hypertension	1	0.9	1	0.1	0.176
Proctitis	0	0.0	3	0.3	1.000
Steatohepatitis	7	6.3	16	1.4	0.003
Veno-occlusive disease of liver	1	0.9	0	0.0	0.092
Hematology Conditions*	12	10.7	92	8.3	0.375
Anemia	4	3.6	35	3.2	0.777
Coagulopathy	0	0.0	1	0.1	1.000
Hemochromatosis	1	0.9	1	0.1	0.176
Neutropenia	3	2.7	12	1.1	0.153
Polycythemia	1	0.9	0	0.0	0.092
Thrombocytopenia	3	2.7	38	3.4	1.000
Thrombocytosis	1	0.9	11	1.0	1.000
Immunology and Infectious Conditions*	21	18.8	197	17.8	0.796
Autoimmune disorders	1	0.9	8	0.7	0.582
Chronic hepatitis C	6	5.4	37	3.3	0.277
Chronic active hepatitis B (PCR+)	1	0.9	1	0.1	0.176
Endocarditis	0	0.0	1	0.1	1.000
Gastrointestinal tract infection	4	3.6	35	3.2	0.777
Genitourinary tract infection	0	0.0	10	0.9	0.612
Human immunodeficiency virus infection	1	0.9	7	0.6	0.539
Immunodeficiency	1	0.9	0	0.0	0.092
Lymphatic infection	0	0.0	18	1.6	0.399
Meningoencephalitis	1	0.9	3	0.3	0.321
Osteomyelitis	0	0.0	2	0.2	1.000

Otitis Media	1	0.9	14	1.3	1.000
Sinopulmonary infection - Sinusitis	2	1.8	15	1.4	0.665
Sinopulmonary infection - Bronchitis	0	0.0	2	0.2	1.000
Soft tissue infection	3	2.7	25	2.3	0.738
Tonsillitis	1	0.9	43	3.9	0.176
Musculoskeletal Conditions*	88	78.6	684	61.8	< 0.001
Amputation	2	1.8	6	0.5	0.163
Arthralgia	2	1.8	14	1.3	0.653
Arthritis	1	0.9	16	1.4	1.000
BMD below expected range for age and sex	67	59.8	479	43.3	0.001
Hernia	5	4.5	50	4.5	1.000
Intervertebral disc disorder	8	7.1	99	9.0	0.603
Kyphosis	1	0.9	2	0.2	0.252
Limb length discrepancy	1	0.9	5	0.5	0.440
Osteonecrosis	23	20.5	143	12.9	0.030
Palatal defects	0	0.0	1	0.1	1.000
Prosthetic malfunction	1	0.9	4	0.4	0.383
Scoliosis	9	8.0	60	5.4	0.279
Skeletal spine disorder	4	3.6	43	3.9	1.000
Slipped capital femoral epiphysis	1	0.9	2	0.2	0.252
Temporomandibular joint disorder	2	1.8	9	0.8	0.268
Neurology Conditions*	51	45.5	560	50.6	0.322
Autonomic nervous system disorder	0	0.0	3	0.3	1.000
Cavernoma	1	0.9	16	1.4	1.000
Cerebellar dysfunction	0	0.0	5	0.5	1.000
Cerebrovascular accident	3	2.7	34	3.1	1.000
Cerebrovascular disease	2	1.8	11	1.0	0.339
Cranial nerve disorder	0	0.0	17	1.5	0.392
Dysarthria	0	0.0	1	0.1	1.000
Headaches	16	14.3	209	18.9	0.253
Intracranial hemorrhage	2	1.8	12	1.1	0.374
Movement disorders	1	0.9	12	1.1	1.000
Nerve root disorder	0	0.0	14	1.3	0.631
Neurogenic bladder	0	0.0	5	0.5	1.000
Neurogenic bowel	0	0.0	1	0.1	1.000
Paralytic disorder	2	1.8	17	1.5	0.692
Peripheral motor neuropathy	10	8.9	99	9.0	1.000
Peripheral sensory neuropathy	34	30.4	359	32.5	0.673
Pseudomeningocele	0	0.0	1	0.1	1.000
Pseudotumor cerebri	0	0.0	3	0.3	1.000
Seizure	11	9.8	90	8.1	0.588
Renal Conditions*	22	19.6	195	17.6	0.604
Acute kidney injury	4	3.6	4	0.4	0.004
Chronic hematuria	6	5.4	83	7.5	0.566
Chronic kidney disease	12	10.7	21	1.9	< 0.001

Obstructive uropathy	3	2.7	18	1.6	0.433
Urinary bladder dysfunction	1	0.9	15	1.4	1.000
Urinary incontinence	2	1.8	20	1.8	1.000
Urinary tract calculi (Urolithia)	1	0.9	63	5.7	0.025
Vesicoureteral reflux, acquired	0	0.0	1	0.1	1.000
Respiratory Conditions*	83	74.1	296	26.8	< 0.001
Asthma	16	14.3	108	9.8	0.140
Chronic obstructive pulmonary disease	0	0.0	7	0.6	1.000
Epistaxis, chronic/recurrent	0	0.0	2	0.2	1.000
Obstructive pulmonary deficit	58	51.8	123	11.1	< 0.001
Pleural space disorders	0	0.0	15	1.4	0.386
Pneumonitis	1	0.9	1	0.1	0.176
Pulmonary diffusion deficits	63	56.3	136	12.3	< 0.001
Pulmonary embolism	3	2.7	9	0.8	0.090
Restrictive pulmonary deficit	36	32.1	62	5.6	< 0.001
Tracheal stenosis	0	0.0	2	0.2	1.000
Reproductive Conditions*	59	52.7	264	23.9	< 0.001
Central hypogonadism	2	1.8	38	3.4	0.575
Cervical dysplasia (females)	5	9.1	82	15.6	0.237
Dyspareunia (females)	1	1.8	1	0.2	0.181
Endometriosis (females)	1	1.8	19	3.6	0.711
Erectile dysfunction (males)	2	3.5	18	3.1	0.697
Genitourinary adhesions (females)	0	0.0	12	2.3	0.616
Polycystic ovarian syndrome (females)	0	0.0	14	2.7	0.383
Precocious puberty	0	0.0	2	0.2	1.000
Primary hypogonadism	54	48.2	73	6.6	< 0.001
Prostatic hypertrophy (males)	0	0.0	1	0.2	1.000
Uterine bleeding (females)	4	7.3	55	10.5	0.639
Vaginal fistula (females)	0	0.0	1	0.2	1.000
Vaginal stenosis (females)	0	0.0	1	0.2	1.000
Secondary Neoplasm*	22	19.6	119	10.8	0.008
Central nervous system	3	2.7	24	2.2	0.732
Carcinoma	16	14.3	88	8.0	0.048
Hodgkin lymphoma	0	0.0	2	0.2	1.000
Leukemia	3	2.7	3	0.3	0.012
Melanoma	0	0.0	1	0.1	1.000
Non-Hodgkin's lymphoma	1	0.9	0	0.0	0.092
Sarcoma	0	0.0	5	0.5	1.000
Audiology Conditions*					
Hearing loss	21	18.8	63	5.7	< 0.001
Ocular Conditions*	78	69.6	220	19.9	< 0.001
Cataract	75	67.0	158	14.3	< 0.001
Glaucoma	5	4.5	11	1.0	0.002
Retinopathy	9	8.0	72	6.5	0.537

Abbreviations: HCT, hematopoietic stem cell transplant; GHD, growth hormone deficiency; PCR, polymerase chain reaction. * At least 1.

Supplemental Table 4. Prevalence of grade 3-4 chronic conditions comparing HCT and conventional chemotherapy groups

	HCT (n=112)		Conventional Therapy (n=1106)		p
	n	%	n	%	
Any grade 3-4	91	81.3	765	69.2	0.007
Cardiovascular conditions*	22	19.6	113	10.2	0.004
Arteriovenous malformation	0	0.0	1	0.1	1.000
Atrioventricular heart block	1	0.9	1	0.1	0.176
Cardiac dysrhythmia	1	0.9	3	0.3	0.321
Cardiomyopathy	3	2.7	25	2.3	0.738
Conduction abnormality	0	0.0	4	0.4	1.000
Dyslipidemia - Hypercholesterolemia	2	1.8	6	0.5	0.163
Dyslipidemia - Hypertriglyceridemia	9	8.0	16	1.4	< 0.001
Heart valve disorder	1	0.9	4	0.4	0.383
Hypertension	7	6.3	50	4.5	0.354
Myocardial infarction	3	2.7	24	2.2	0.732
Pericarditis	0	0.0	1	0.1	1.000
Prolonged QT interval	0	0.0	3	0.3	1.000
Thrombus	1	0.9	3	0.3	0.321
Vascular disease	1	0.9	2	0.2	0.252
Endocrine System*	29	25.9	459	41.5	0.001
Glucose metabolism	13	11.6	74	6.7	0.079
Hyperparathyroidism	0	0.0	1	0.1	1.000
Obesity	18	16.1	423	38.2	< 0.001
Gastrointestinal System*	22	19.6	131	11.8	0.024
Cholecystitis	7	6.3	72	6.5	1.000
Constipation	0	0.0	1	0.1	1.000
Dysphagia	1	0.9	7	0.6	0.539
Enterocolitis	0	0.0	3	0.3	1.000
Esophageal stricture	0	0.0	18	1.6	0.399
Esophageal varices	0	0.0	3	0.3	1.000
Esophagitis	0	0.0	2	0.2	1.000
Fecal incontinence	1	0.9	2	0.2	0.252
Fibrosis cirrhosis	7	6.3	24	2.2	0.019
Fistulas	0	0.0	3	0.3	1.000
Gastritis/Duodenitis	2	1.8	11	1.0	0.339
Gastroesophageal reflux disease	1	0.9	2	0.2	0.252
Gastrointestinal hemorrhage	1	0.9	4	0.4	0.383
Gastrointestinal obstruction	3	2.7	2	0.2	0.007
Gastrointestinal ulcer	2	1.8	3	0.3	0.070
Hepatic failure	0	0.0	3	0.3	1.000
Hepatopathy	2	1.8	2	0.2	0.045
Pancreatitis	1	0.9	7	0.6	0.539

Veno-occlusive disease of liver	1	0.9	0	0.0	0.092
Hematology Conditions*	0	0	5	0.5	1.000
Anemia	0	0.0	3	0.3	1.000
Coagulopathy	0	0.0	1	0.1	1.000
Thrombocytopenia	0	0.0	1	0.1	1.000
Immunology and Infectious Conditions*	16	14.3	160	14.5	1.000
Chronic hepatitis C	5	4.5	19	1.7	0.062
Chronic active hepatitis B (PCR+)	1	0.9	0	0.0	0.092
Endocarditis	0	0.0	1	0.1	1.000
Gastrointestinal tract infection	4	3.6	35	3.2	0.777
Genitourinary tract infection	0	0.0	5	0.5	1.000
Lymphatic infection	0	0.0	18	1.6	0.399
Meningoencephalitis	1	0.9	3	0.3	0.321
Osteomyelitis	0	0.0	2	0.2	1.000
Otitis Media	1	0.9	11	1.0	1.000
Sinopulmonary infection - Sinusitis	2	1.8	14	1.3	0.653
Sinopulmonary infection - Bronchitis	0	0.0	2	0.2	1.000
Soft tissue infection	2	1.8	20	1.8	1.000
Tonsillitis	1	0.9	43	3.9	0.176
Musculoskeletal Conditions*	14	12.5	108	9.8	0.326
Amputation	1	0.9	1	0.1	0.176
Hernia	3	2.7	49	4.4	0.621
Intervertebral disc disorder	0	0.0	20	1.8	0.247
Kyphosis	0	0.0	1	0.1	1.000
Limb length discrepancy	1	0.9	0	0.0	0.092
Osteonecrosis	8	7.1	34	3.1	0.049
Prosthetic malfunction	1	0.9	4	0.4	0.383
Scoliosis	0	0.0	3	0.3	1.000
Skeletal spine disorder	1	0.9	2	0.2	0.252
Slipped capital femoral epiphysis	1	0.9	2	0.2	0.252
Temporomandibular joint disorder	1	0.9	3	0.3	0.321
Neurology Conditions*	10	8.9	99	9.0	1.000
Cerebrovascular accident	2	1.8	19	1.7	1.000
Cerebrovascular disease	1	0.9	1	0.1	0.176
Cranial nerve disorder	0	0.0	1	0.1	1.000
Headaches	3	2.7	26	2.4	0.744
Intracranial hemorrhage	0	0.0	5	0.5	1.000
Nerve root disorder	0	0.0	3	0.3	1.000
Neurogenic bladder	0	0.0	4	0.4	1.000
Neurogenic bowel	0	0.0	1	0.1	1.000
Paralytic disorder	0	0.0	3	0.3	1.000
Peripheral motor neuropathy	0	0.0	16	1.4	0.388
Peripheral sensory neuropathy	0	0.0	17	1.5	0.392
Pseudotumor cerebri	0	0.0	2	0.2	1.000
Seizure	4	3.6	32	2.9	0.566

Renal Conditions*	4	3.6	57	5.2	0.649
Acute kidney injury	1	0.9	2	0.2	0.252
Chronic kidney disease	1	0.9	11	1.0	1.000
Obstructive uropathy	2	1.8	6	0.5	0.163
Urinary bladder dysfunction	0	0.0	3	0.3	1.000
Urinary incontinence	0	0.0	3	0.3	1.000
Urinary tract calculi (Urolithia)	1	0.9	34	3.1	0.246
Respiratory Conditions*	18	16.1	51	4.6	< 0.001
Asthma	1	0.9	11	2.2	0.701
Chronic obstructive pulmonary disease	0	0.0	1	0.2	1.000
Obstructive pulmonary deficit	11	9.8	21	4.1	0.013
Pleural space disorders	0	0.0	5	1.0	0.596
Pneumonitis	1	0.9	0	0.0	0.168
Pulmonary diffusion deficits	7	6.3	10	2.0	0.014
Pulmonary embolism	3	2.7	9	1.8	0.435
Restrictive pulmonary deficit	9	8.0	10	2.0	0.002
Reproductive Conditions*	36	32.1	97	8.8	< 0.001
Cervical dysplasia (females)	3	5.5	39	7.4	0.787
Dyspareunia (females)	1	1.8	1	0.2	0.181
Endometriosis (females)	1	1.8	17	3.2	1.000
Erectile dysfunction (males)	1	1.8	0	0.0	0.089
Genitourinary adhesions (females)	0	0.0	12	2.3	0.616
Primary hypogonadism	34	30.4	34	3.1	< 0.001
Uterine bleeding (females)	1	1.8	26	5.0	0.500
Vaginal fistula (females)	0	0.0	1	0.2	1.000
Secondary Neoplasm*	19	17.0	87	7.9	0.003
Central nervous system	2	1.8	19	1.7	1.000
Carcinoma	13	11.6	60	5.4	0.019
Hodgkin lymphoma	0	0.0	2	0.2	1.000
Leukemia	3	2.7	3	0.3	0.012
Melanoma	0	0.0	1	0.1	1.000
Non-Hodgkin's lymphoma	1	0.9	0	0.0	0.092
Sarcoma	0	0.0	5	0.5	1.000
Audiology Conditions*					
Hearing loss	5	4.5	19	1.7	0.046
Ocular Conditions*	24	21.4	15	1.4	< 0.001
Cataract	23	20.5	7	0.6	< 0.001
Glaucoma	1	0.9	0	0.0	0.092
Retinopathy	2	1.8	9	0.8	0.268

Abbreviations: HCT, hematopoietic stem cell transplant; PCR, polymerase chain reaction. * At least 1.

Supplemental Table 5. Association between the use of TBI and grade 3-4 chronic conditions and frail health

Outcome	OR	TBI vs non-TBI		p
		95% CI		
Frail health	6.96	0.37	130.30	0.194
Any Grade 3-4 conditions	4.07	1.52	10.92	0.005
Grade 3-4 cardiac conditions	1.69	0.54	5.29	0.368
Grade 3-4 respiratory conditions	2.83	0.68	11.73	0.152
Grade 3-4 SN	1.95	0.56	6.83	0.297

Abbreviations: TBI, total body irradiation; OR, odds ratio; CI, confidence interval; SN, second neoplasms.

Supplemental Table 6. Mean cumulative count of chronic medical conditions among HCT and conventional chemotherapy survivors at 25 years of age per 100 patients

	Grade 1 to 4		Grade 3 to 4	
	HCT	Conventional Therapy	HCT	Conventional Therapy
Cardiovascular Conditions				
Aortic root aneurysm	0	0	0	0
Arteriovenous malformation (AVM)	0	0	0	0
Atrial myxoma	0	0	0	0
Atrioventricular heart block	1	0	1	0
Cardiac dysrhythmia	3	0	2	0
Cardiomyopathy	4	2	1	1
Conduction abnormality	8	7	0	0
Dyslipidemia - Hypercholesterolemia	22	12	0	0
Dyslipidemia - Hypertriglyceridemia	27	11	1	0
Heart valve disorder	7	8	1	0
Hypertension	33	16	2	0
Myocardial infarction	1	0	1	0
Pericarditis	0	0	0	0
Prolonged QT interval	2	1	0	0
Pulmonary hypertension	0	0	0	0
Raynaud's phenomenon	2	1	0	0
Right ventricular systolic dysfunction	0	0	0	0
Sinus bradycardia	1	1	0	0
Sinus tachycardia	4	1	0	0
Thrombus	2	0	1	0
Vascular disease	2	0	2	0
Endocrine System				
Adrenal insufficiency	7	2	0	0
Adult GHD	13	6	0	0
Childhood GHD	14	5	0	0
Glucose metabolism	12	5	4	0
Hyperparathyroidism	0	0	0	0
Hyperprolactinemia	1	0	0	0
Hyperthyroidism	0	0	0	0
Hypoparathyroidism	0	0	0	0
Hypothyroidism	48	17	0	0
Hypothyroidism compensated	0	0	0	0
Obesity	10	17	5	8
Thyroid cyst/nodule	13	2	0	0
Underweight	6	1	0	0

Gastrointestinal System				
Celiac (coeliac) disease	0	0	0	0
Cholecystitis	7	3	6	2
Constipation	3	1	0	0
Dysphagia	3	1	0	0
Enterocolitis	0	1	0	0
Esophageal stricture	0	0	0	0
Esophageal varices	0	0	0	0
Esophagitis	0	0	0	0
Fecal incontinence	1	0	1	0
Fibrosis cirrhosis	4	1	4	1
Fistulas	0	0	0	0
Gastritis/Duodenitis	1	1	1	0
Gastroesophageal reflux disease	4	4	0	0
Gastrointestinal hemorrhage	1	0	1	0
Gastrointestinal obstruction	3	0	3	0
Gastrointestinal ulcer	2	0	1	0
Gastroparesis syndrome	1	0	0	0
Hepatic failure	0	0	0	0
Hepatopathy	12	4	0	0
Malabsorption syndrome	0	0	0	0
Pancreatic insufficiency	0	0	0	0
Pancreatitis	1	0	1	0
Portal hypertension	1	0	0	0
Proctitis	0	0	0	0
Steatohepatitis	1	0	0	0
Veno-occlusive disease of liver	1	0	1	0
Hematology Conditions				
Anemia	3	1	0	0
Coagulopathy	0	0	0	0
Hemochromatosis	0	0	0	0
Neutropenia	1	0	0	0
Polycythemia	0	0	0	0
Thrombocytopenia	1	2	0	0
Thrombocytosis	1	0	0	0
Immunology and Infectious Conditions				
Autoimmune disorders	0	0	0	0
Chronic hepatitis C	4	3	4	1
Chronic active hepatitis B (PCR+)	1	0	1	0
Endocarditis	0	0	0	0
Gastrointestinal tract infection	3	2	3	2
Genitourinary tract infection	0	1	0	0
Human immunodeficiency virus infection	1	0	0	0

Immunodeficiency	1	0	0	0
Lymphatic infection	0	0	0	0
Meningoencephalitis	1	0	1	0
Osteomyelitis	0	0	0	0
Otitis Media	0	1	0	1
Sinopulmonary infection - Sinusitis	2	1	1	1
Sinopulmonary infection - Bronchitis	0	0	0	0
Soft tissue infection	2	1	1	1
Tonsillitis	1	3	1	3

Musculoskeletal Conditions

Amputation	4	0	2	0
Arthralgia	0	0	0	0
Arthritis	0	0	0	0
BMD below expected range for age and sex	22	13	0	0
Hernia	1	1	0	1
Intervertebral disc disorder	4	3	0	1
Kyphosis	0	0	0	0
Limb length discrepancy	1	0	1	0
Osteonecrosis	25	19	7	6
Palatal defects	0	0	0	0
Prosthetic malfunction	0	0	0	0
Scoliosis	4	5	0	1
Skeletal spine disorder	2	1	1	0
Slipped capital femoral epiphysis	1	0	1	0
Temporomandibular joint disorder	2	0	1	0

Neurology Conditions

Autonomic nervous system disorder	0	0	0	0
Cavernoma	1	0	0	0
Cerebellar dysfunction	0	0	0	0
Cerebrovascular accident	2	1	1	0
Cerebrovascular disease	1	0	0	0
Cranial nerve disorder	0	1	0	0
Dysarthria	0	0	0	0
Headaches	10	12	2	1
Intracranial hemorrhage	0	0	0	0
Movement disorders	0	1	0	0
Nerve root disorder	0	0	0	0
Neurogenic bladder	0	0	0	0
Neurogenic bowel	0	0	0	0
Paralytic disorder	0	1	0	0
Peripheral motor neuropathy	2	1	0	0
Peripheral sensory neuropathy	5	4	0	0

Pseudomeningocele	0	0	0	0
Psuedotumor cerebri	0	0	0	0
Seizure	8	8	3	2
Renal Conditions				
Acute kidney injury	3	0	1	0
Chronic hematuria	1	2	0	0
Chronic kidney disease	3	1	1	1
Obstructive uropathy	0	0	0	0
Urinary bladder dysfunction	0	0	0	0
Urinary incontinence	0	0	0	0
Urinary tract calculi (Urolithia)	1	2	1	1
Vesicoureteral reflux, acquired	0	0	0	0
Respiratory Conditions				
Asthma	14	8	1	0
Chronic obstructive pulmonary disease	0	0	0	0
Epistaxis, chronic/recurrent	0	0	0	0
Obstructive pulmonary deficit	19	1	4	0
Pleural space disorders	0	1	0	0
Pneumonitis	0	0	0	0
Pulmonary diffusion deficits	22	2	1	0
Pulmonary embolism	1	0	1	0
Restrictive pulmonary deficit	12	1	4	0
Tracheal stenosis	0	0	0	0
Reproductive Conditions				
Central hypogonadism	1	1	0	0
Cervical dysplasia	10	13	8	6
Dyspareunia	0	0	0	0
Endometriosis	0	2	0	2
Erectile dysfunction	0	0	0	0
Genitourinary adhesions	0	0	0	0
Polycystic ovarian syndrome	0	2	0	0
Precocious puberty	0	0	0	0
Primary hypogonadism	35	3	21	1
Prostatic hypertrophy	0	0	0	0
Uterine bleeding	0	4	0	0
Vaginal fistula	0	0	0	0
Vaginal stenosis	0	0	0	0
Secondary Neoplasm				
CNS	0	1	0	1
Carcinoma	5	1	5	1
Hodgkin lymphoma	0	0	0	0
Leukemia	4	0	4	0
Melanoma	0	0	0	0

Non-Hodgkin's lymphoma	0	0	0	0
Sarcoma	0	0	0	0
Audiology Conditions				
Hearing Loss	14	4	4	1
Ocular Conditions				
Cataract	59	5	27	1
Glaucoma	3	0	0	0
Retinopathy	1	2	0	0
All conditions	609	283	148	60

SUPPLEMENTAL FIGURE

