Center Outcomes Forum November 2021

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Center Outcomes Forum 2021 Agenda

- Goals of Center Outcomes Forum 2021 and Overview
- Summary of Center-Specific Analysis 2021
- Center-Specific Analysis 2022
  - Data Available for Use
  - Proposed Analysis Plan
  - Limitations of Analysis Plan
- Communication Plans
- Next Steps/Wrap Up

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My sincere appreciation

- Center-Specific Analysis “Core” Team:
  - Michael Heim, Andrew St. Martin, Waleska Perez, Sue Logan, Jenni Bloomquist, Steve Spellman, Janet Brunner Grady, Brent Logan, Kwang Ahn
- Carol Doleysh – Program Manager, SCTOD
- Alicia Halfmann and Carol – Center Outcomes Forum
- Panelists:
  - John Wingard, Miguel Perales, Marcie Riches, Bill Wood, Navneet Majhail, Jeff Auletta, Christopher Dandoy, Brent Logan, Michael Heim, Andrew St. Martin

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Why all the attention to the COVID pandemic on HCT outcomes?

- The premise of risk adjustment is that different centers have different case mixes and these dramatically affect outcomes.
- If such differences are not adjusted, one can not determine if a center's survival rate is driven by its case mix or the skills and performance of the center's team and its practices.
- CIBMTR risk-adjusted outcomes analysis relies on the assumption is that outcomes are a reflection of center quality
- This assumption is threatened by uncontrollable forces in which much of the quality measures put in place by centers to promote quality may be disrupted

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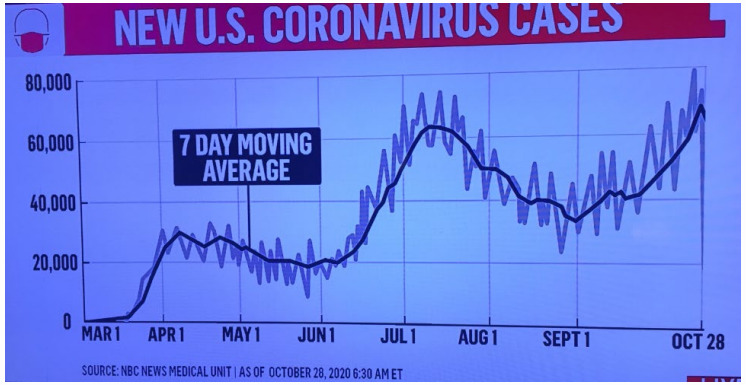
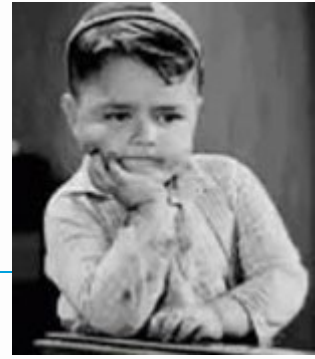
What COVID-19 data should be put into the analysis (1)



- **Did COVID-19 affect center mortality rate?**
  - Is the effect significant?
  - Can we define a “dose dependent” effect?
  - Is it transient or persistent?
- **What is the best marker of COVID-19 burden?**
  - Infection? Hospitalizations? Deaths?
  - Should we measure COVID-19 burden at the center or in the community where the patient lives
- **What is the best way to account for location?**
  - Should COVID-19 activity be broken down by region, state, a smaller geographical unit?
  - Should we also consider burden in the patient’s local community, where it differs from transplant center
- **What is the best proxy for the indirect effects of COVID-19 burden on a center?**
  - This is difficult to measure
    - is it even possible to measure?
  - ? Would a decrease in transplant volume at the center be a surrogate?
  - ? Will the center’s responses in the COVID-19 impact reports provide a gauge of the impact

What other data should be put into analysis (2)



- **What additional data do we need to collect in our CRDFs?**
  - COVID-19: date, outcome
  - GVHD & IS: date of GVHD onset, GVHD severity, date IS stopped
  - Center: zip code & its relationship to whatever COVID-19 unit of location we select
- ✓ **CIBMTR developed COVID-19 impact supplemental data reports (to be used in the 2021 report)**
  - Early on, data was incomplete
    - This was at a time when center data staff was mostly working remote; ability to collect the data was suboptimal & varied by center
    - As of Oct 2020: 57% not yet completed, 30% no impact, 12% impacted

COF COVID-19 Adjustment Recommendations

1. CIBMTR should expedite data collection efforts for allogeneic HCT recipients from 2019 to facilitate preliminary modeling to understand the impact of the COVID-19 pandemic on outcomes.

2. Develop a modeling approach to test the impact of COVID-19 on outcomes for 2019 and implement that approach in early 2021.
   - Communicate with center directors and escalate relevant data collection efforts with centers to support earlier timelines for data submission to support these analyses
   - The preliminary modeling approach is likely to employ Cox modeling to handle time-dependent covariates

COF COVID-19 Adjustment Recommendations

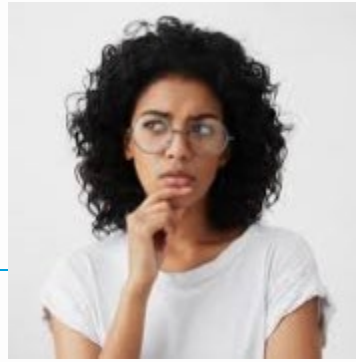
3. Use the results of the preliminary modeling for impact of COVID-19 to design, if possible, a modified pseudo-value modeling approach for the Center-Specific Survival Analysis for the cohort of patients transplanted in 2017-2019.
   - Use a consistent Center-Specific Survival Analysis model, if possible, to achieve results that are consistent with previous years to allow year-over-year comparisons and maintain confidence in the modeling process.
   - Outline the methodology and limitations of the risk adjustment for COVID-19 pandemic in the Center-Specific Survival Analysis report.

COF COVID-19 Adjustment Recommendations

4. Develop communications for use across all relevant stakeholder groups regarding plans for Center-Specific Survival Analysis in 2021 and subsequent years to address COVID-19.

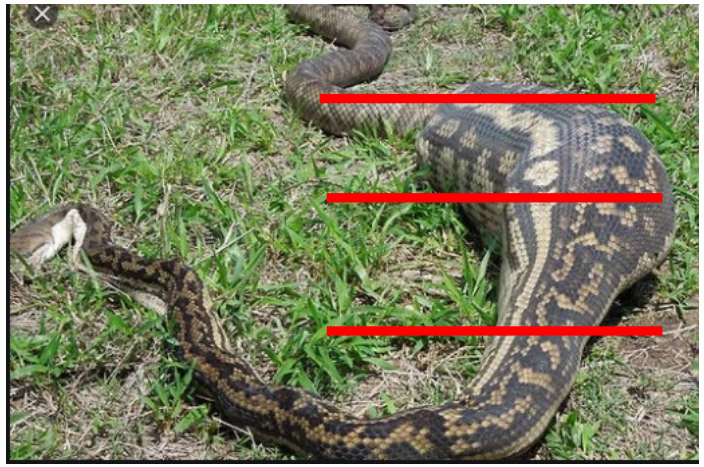
5. Continue to collaborate with SRTR and other organizations involved in public outcomes reporting to explore if other organizations are making assessments of the impact of COVID-19 on general acute care for geographic areas to inform this effort

How to think about assessing the possible impact of COVID-19 on rolling 3-year HCT time periods



Report	Pre- & Peri-HCT care	Post-HCT care	What HCT phase was impacted & for what years?
2020 (2016-2018)	No	No	none
2021 (2017-2019)	No	Yes	2019 post only
2022 (2018-2020)	Yes	Yes	2019 post; 2020 Pre/peri/post
2023 (2019-2021)	Yes	Yes	2019 post; 2020 Pre/peri/post; 2021 post yes;?pre/peri

Ask this snake if he has a bellyache



Does this hurt?

2022 & 23: yeah, a lot

2021: yeah, a little

2020: not really

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Task Force Recommendations for COVID-19 Adjustments for Future Years' Analyses

- Using results from the analysis conducted in 2021, begin to develop an approach to subsequent analyses that address all relevant COVID-19 impacts for HCTs performed in 2020.
- Many more factors may impact outcomes for HCT performed in 2020 and the approach will need to re-analyze factors tested this year, and others, to develop appropriate methods.

Center-Specific Survival Analysis 2021 Update

Center Outcomes Forum–2021

November 12, 2021

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Agenda for Center Outcomes Forum - 2020

- Center-Specific Survival Analysis 2020 – brief summary
  - Activities related to the Center Outcomes Forum 2018
- Is Minimal Residual Disease for acute leukemia ready for use as a risk adjustment factor in the center-specific analysis?
- Are there new approaches to account for social determinants of health beyond those currently assessed in risk adjustment model?
- Can CIBMTR adequately adjust for the impact of the COVID-19 pandemic in the center specific analysis and if so, how?
- Center-Specific Analysis research project proposals
- Update on consequences of public reporting

CSA Data for COVID Preliminary Analysis

- COVID case and death counts from NY Times public database (https://github.com/nytimes/covid-19-data)
- Use Census Bureau population estimates to derive 2-week average case and death rates (per 100,000) for each patient's transplant center county
- Post-HCT follow-up period is broken into windowed 2-week average case and death rates for each patient centered around transplant date

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CSA Preliminary Analyses for COVID - 1

- Potential Impact of COVID-19 pandemic care related factors on HCT outcomes first year post HCT
  - NOT COVID infection itself
- Cox Hazards modeling to account for time-varying factors
- All variables from CSA 2020 included in the analysis
- Patients are unit of analysis – not centers
- Includes first alloHCT recipients 1/1/2017 – 12/31/2019
- Patients who developed COVID infection censored on infection date
- Multiple comparisons – p value of significance <0.01

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CSA Preliminary Analyses for COVID - 2

- Primarily testing 3 time-varying COVID affects – tested categorically and continuously (linear and quadratic):
  - **Calendar time period** (pre-COVID (pre 1/21/2020), vs. early in the COVID pandemic (1/21/2020 to 6/21/2020), vs. later in the COVID pandemic (6/21/2020 to 12/31/2020))
  - **Average COVID infection rates** (per 100,000 population) over the preceding 2 weeks **based on the zip code of the transplant center** where the patient received their transplant (0 vs. >0 to 6.5 vs. >6.5), where 6.5 was approximately the median of the non-zero values in the dataset.
  - **Average COVID death rates** over the preceding 2 weeks based on the **zip code of the transplant center** where the patient received their transplant (0 vs. >0 to 0.15 vs. >0.15), where 0.15 = the median of the non-zero values in the dataset.

CSA Preliminary Analyses for COVID - 3

- Explicitly examined interaction with COVID effect modifiers of interest (each time varying):
  - Time period post-HCT (first 100d, 100d-6 mos, 6 mos-1 year)
  - History of acute GVHD grades II-IV
  - History of chronic GVHD

- No interaction found between these time-varying effect modifiers and the COVID effects

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CSA Preliminary Analyses for COVID - Results

Variable	Level	HR	Lower	Upper	p-value
Calendar time	Pre 1/21/2020	1.00			0.327
	1/21/2020-6/20/2020	0.98	0.89	1.08	0.724
	6/21/2020-12/31/2020	0.86	0.70	1.05	0.139
COVID infection rates	0	1.00			0.118
	>0 to 6.5	1.00	0.88	1.15	0.950
	>6.5	0.85	0.72	0.99	0.040
COVID death rates	0	1.00			0.113
	>0 to 0.15	1.03	0.88	1.22	0.697
	>0.15	0.85	0.73	1.00	0.044

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CSA Preliminary Analyses for COVID - Interpretation

- After censoring for COVID infection in the first year after HCT, there does not appear to be an effect of geographic or calendar-driven COVID incidence/mortality rates or differences in surveillance/follow-up practices associated with survival
- For those patients who did not develop COVID infection, the risk of mortality at one year is not clearly affected by the pandemic, broadly speaking. In other words, there is no evidence to support a differential impact of the pandemic on survival after HCT across the US after we censor for COVID infection in patients themselves, so the pandemic impact on centers should also not be differential.

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Plans for Final Analysis CSA 2021

- We have not demonstrated an independent effect of the COVID pandemic and potential impacts on care delivery, after censoring for COVID infection itself in HCT recipients, upon the survival outcomes by one year post HCT.
- We performed the existing logistic regression modeling approach for the Center-Specific Analysis in 2021, including HCT recipients between 1/1/2017 and 12/31/2019, with censoring of patients who developed COVID infection at their infection date in the first year after HCT.

Center Outcomes Reporting for HCT Status Update 2021

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Center Outcomes Report

Final study population - 2021

- Center outcomes report 2021 includes 3 full years of data:
  - Unrelated and Related HCT 2017 – 2019
- Multivariate analysis adjusts for ‘risk factors’
  - Adult and Pediatric BMI introduced 2020
- Centers must have >90% overall f/u at 1 year
  - 4 centers closed or became inactive,
- 173 US centers; 25,167 patients first allogeneic HCT
  - 7 centers (~609 pts) removed because of quality concerns in audits
- Primary outcome: One-year survival
  - Overall: 75.6% (77.9% REL, 73.7% UNR) – 2020: 74.1, 76.4, 72.2

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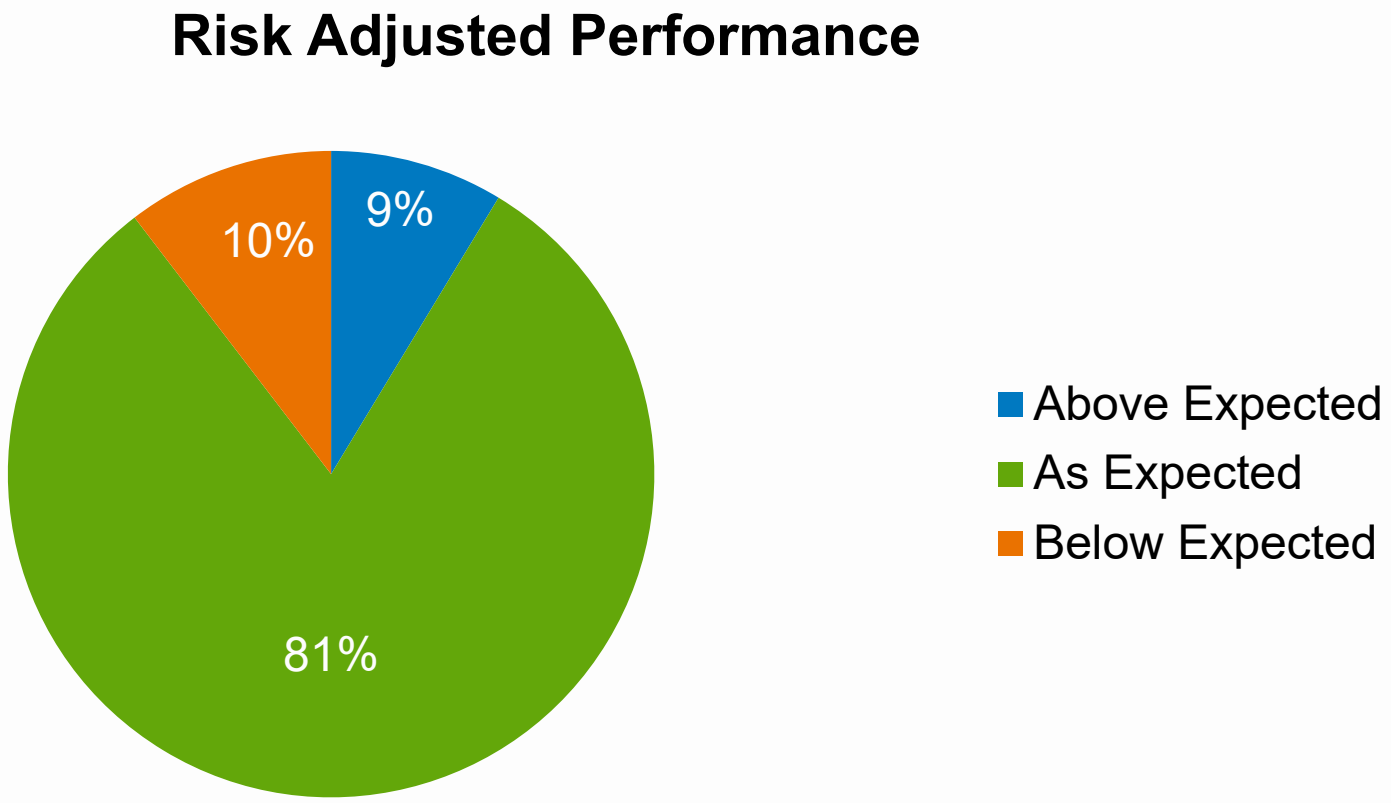
How are US centers doing? 2021



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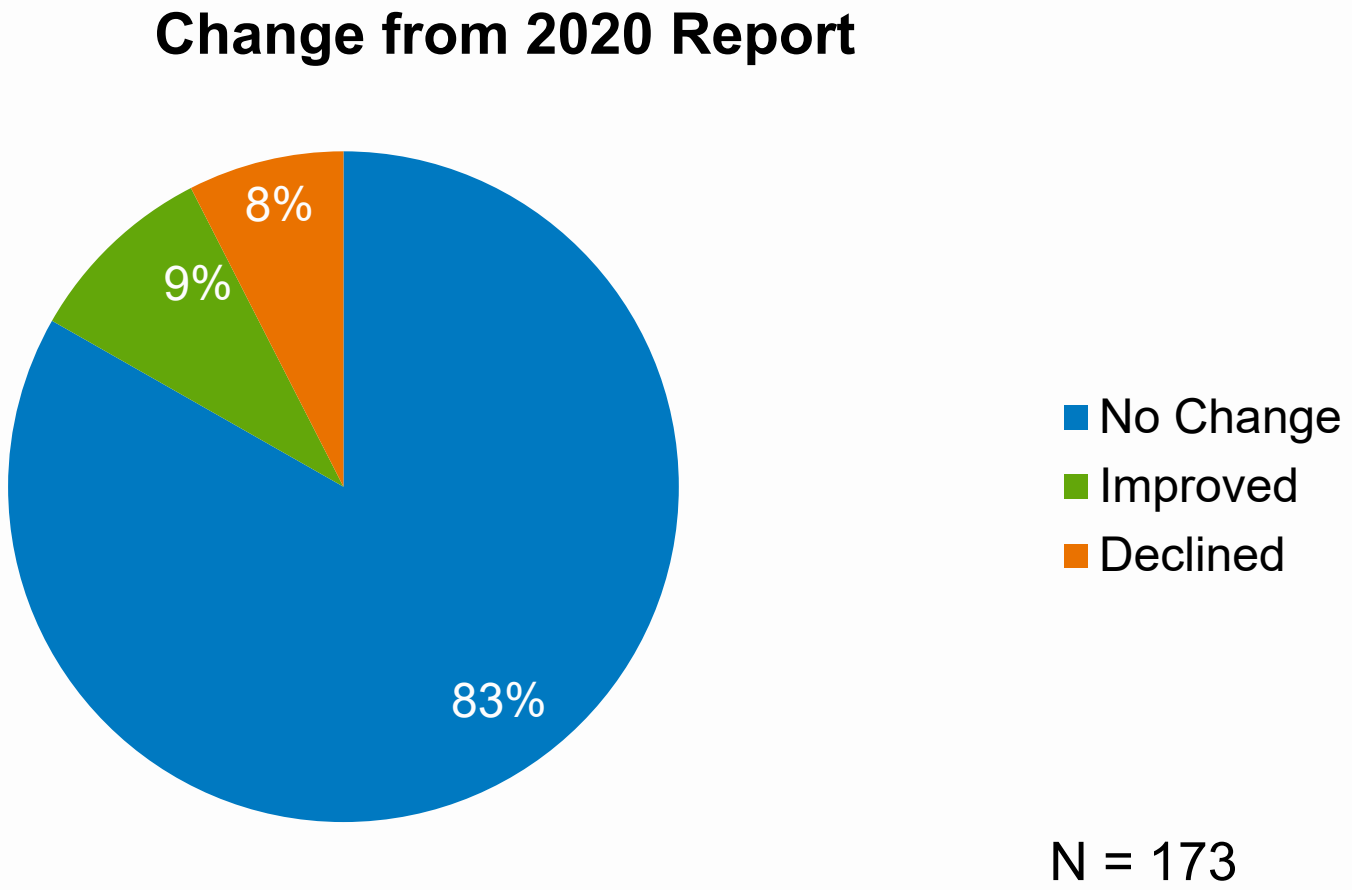
N = 173

Changes in Performance: 2020 → 2021



N = 173

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Changes in 2021 Report

- Censoring for COVID-19 infection at date of reported infection
  - 121 patients in first year after HCT
- Time varying COVID effects were NOT significant
- Therapy-related MDS not significant this year
- Therapy-related AML, MM ISS stage at dx were significant

- Individual Centers' data available on CIBMTR portal
  - Includes of the intercept term for analysis (since 2017)
  - Allows centers to develop tools

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Center Outcomes Forum COVID-19 Adjustment Recommendations

- Using results from the analysis conducted in 2021, begin to develop an approach to subsequent analyses that address all relevant COVID-19 impacts for recipients of HCT in 2020.
- Many more factors may impact outcomes for HCT performed in 2020 and the approach will need to re-analyze factors tested this year, and others to develop appropriate methods.

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Available COVID Data in CIBMTR

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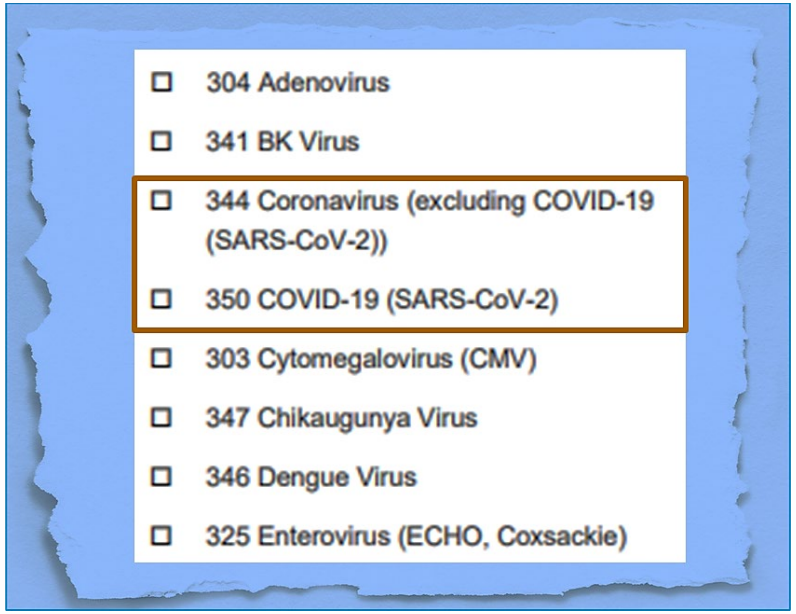
CRFs (2100, 2149, 2900)

- Started collecting information as an infection 3/27/2020
- F2149R1

  Collects detailed infection information for SARS-CoV-2
  - Diagnostic information
  - Symptoms to assess severity
  - Treatment information
  - Outcome of infection
- Added to 2900 for COD information



TED Forms (2400, 2450)

- Collection started May 2020 on 2400R7 and 2450R5
  - Pre-HCT COVID-19 infection, and related hospitalization or ventilation (no dates) (pre-TED)
  - Development of COVID-19 since last report and date (post-TED)
- Current version (2400R9, 2450R6) 10/29/2021
  - Includes information on hospitalization and mechanical ventilation needs
  - Includes information on vaccination status
- COVID as primary or contributing COD – as of May 2020
  - Post-TED and Death Form (2900)

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COVID Approach Variables -

- Was the HCT impacted for a reason related to the COVID-19 pandemic?
  - Y or N
- Is the HCT date different than the originally intended date?
  - Provide intended date
- Is the donor different than the originally intended donor?
  - Provide intended donor
- Was the product thawed from a cryopreserved state before infusion?
- Is the product type different than originally intended?
  - Provide original product type
- Did the preparative regimen change from the original plan?
  - Y or N
- Did the GVHD prophylaxis change from the original plan?
  - Y or N

These variables were collected on a supplemental data form beginning August 2020 for patients whose HCT was after March 1, 2020

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Completeness of COVID approach data collection

Completeness of data collected for HCT in 2020 for COVID approach: Was the HCT impacted for a reason related to the pandemic?

Time Period	Yes, impacted	No, not impacted	Not answered	Total
Mar, 2020 – Aug, 2020	21%	54%	25%	4449
Sept, 2020 – Dec, 2020	15%	52%	33%	3241
Mar, 2020 – Dec, 2020	18%	53%	28%	7690
Jan, 2021 – Nov, 2021	12%	46%	42%	6859

Unfortunately, completeness of reporting varies widely across US HCT centers, with some centers not reporting for any of their HCT in 2020.

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Form 2149: Diagnosis

- Collect information on tests with a positive result supporting the diagnosis
  - New testing methods became available allowing an “other, specify” field

- Tests performed 7 days before and up to 14 days after the reported date of infection
  - Provides global picture of certainty of diagnosis

Form 2149: Diagnosis

1. Date of infection diagnosis: __ __ __ __ / __ __ / __ __
   YYYY MM DD

For questions 2 - 6, report all positive testing used to determine the diagnosis of the respiratory viral infection. Testing should be obtained between 7 days prior to 14 days after the diagnosis.

2. Specify positive diagnostic tests used to determine the diagnosis of the respiratory viral infection **(check all that apply)**
   - ☐ Nasal swab/wash
   - ☐ Lung fluid from bronchoalveolar lavage (BAL)
   - ☐ Histopathology findings of viral cytopathic changes **(biopsy)**
   - ☐ Culture
   - ☐ Other → 3. Specify:_____

4. Were there any positive radiographic findings supporting the infection diagnosis? **(e.g., x-ray, CT, or MRI)**
   - ☐ Yes →
     5. Specify imaging sites **(check all that apply)**
        - ☐ Chest
        - ☐ Sinus
        - ☐ Other imaging site → 6. Specify other imaging site:_____
   - ☐ No
   - ☐ Unknown

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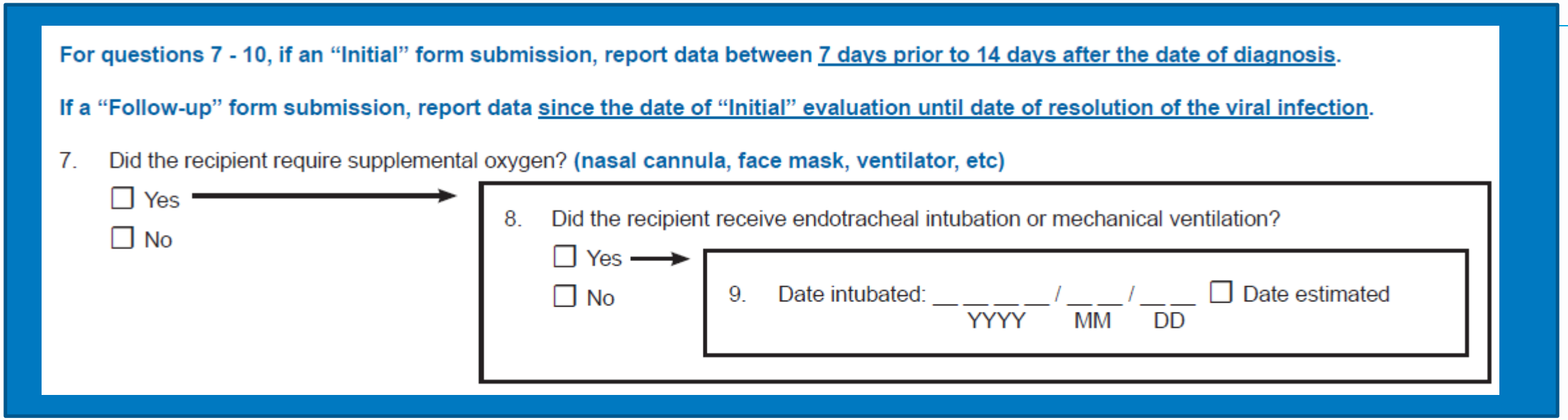
Form 2149: Clinical Factors



- Oxygen needs
  - Supplemental Oxygen
  - Ventilator support
- Steroid use
- Lab parameters
  - WBC count and differential
- Immune system parameters
  - IgG levels

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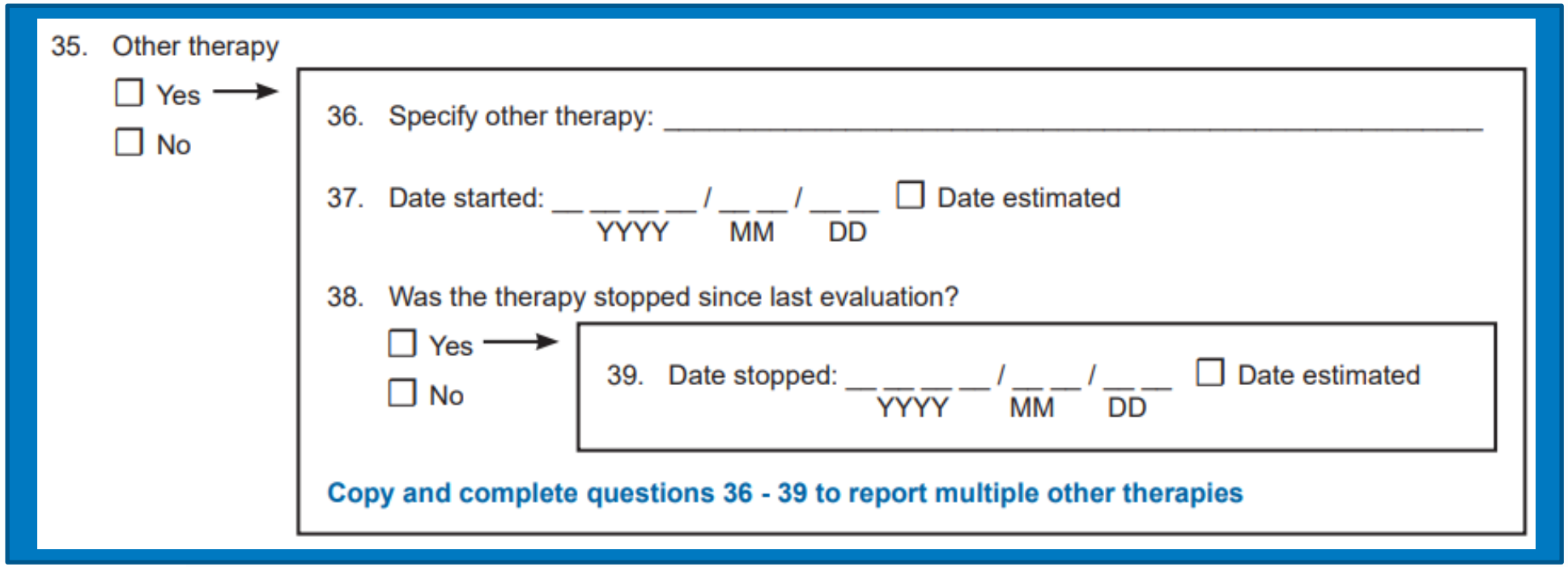
Form 2149: Therapy

- Unknown what treatments worked but many things being tested
  - Elected not to change the previously designed treatment options
- Added Other Therapy, Specify


35. Other therapy

☐ Yes →

☐ No

36. Specify other therapy: _____

37. Date started: __ __ __ __ / __ __ / __ __ ☐ Date estimated
YYYY MM DD

38. Was the therapy stopped since last evaluation?

☐ Yes →

☐ No

39. Date stopped: __ __ __ __ / __ __ / __ __ ☐ Date estimated
YYYY MM DD

Copy and complete questions 36 - 39 to report multiple other therapies

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Therapy

Benefit Seen	No benefit	May Work	
Remdesivir	Azithromycin*	Lopinovir/ritonavir	Mesenchymal stromal cells*
Tocilizumab*	Chloroquine	Favipiravir	Ibrutinib*
Convalescent plasma	Hydroxychloroquine*	Eculizumab*	Steroids*
		Siltuximab*	Ruxolitinib*

* Have role in HCT/CT management outside of COVID-19

Patients often on other antimicrobials to minimize risk of super-infections

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Algwaiz et al, BBMT 2020; 26(12): 2181-2189

Form 2149: Infection Status and Follow-up

40. What was the status of the infection? **(If the status is captured as "Ongoing" or "Improved", an additional Respiratory Virus Post-Infusion Form (2149) will come due. The "Follow-up" form should be completed once the viral infection has resolved).**

- ☐ Death - ***Go to question 41***
- ☐ Ongoing - ***Go to question 41***
- ☐ Improved - ***Go to question 41***
- ☐ Resolved - ***Go to question 41***
- ☐ Unknown - ***Go to signature line***

41. Date of evaluation: __ __ __ __ / __ __ / __ __ ☐ Date estimated
YYYY MM DD

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Form 2149: Infection Status and Follow-up

Status	Definition	Follow-up form due
Death	Died without resolution of infection	No
Ongoing	Infection continues without significant improvement at time of evaluation	Yes
Improved	On-going treatment for infection although signs/symptoms resolved	Yes
Resolved	Signs/symptoms now absent and therapy course completed	No
Unknown	No information on status of infection	N/A

Follow-up Form: Collects data from the time of the initial report evaluation until resolution of the infection or by death

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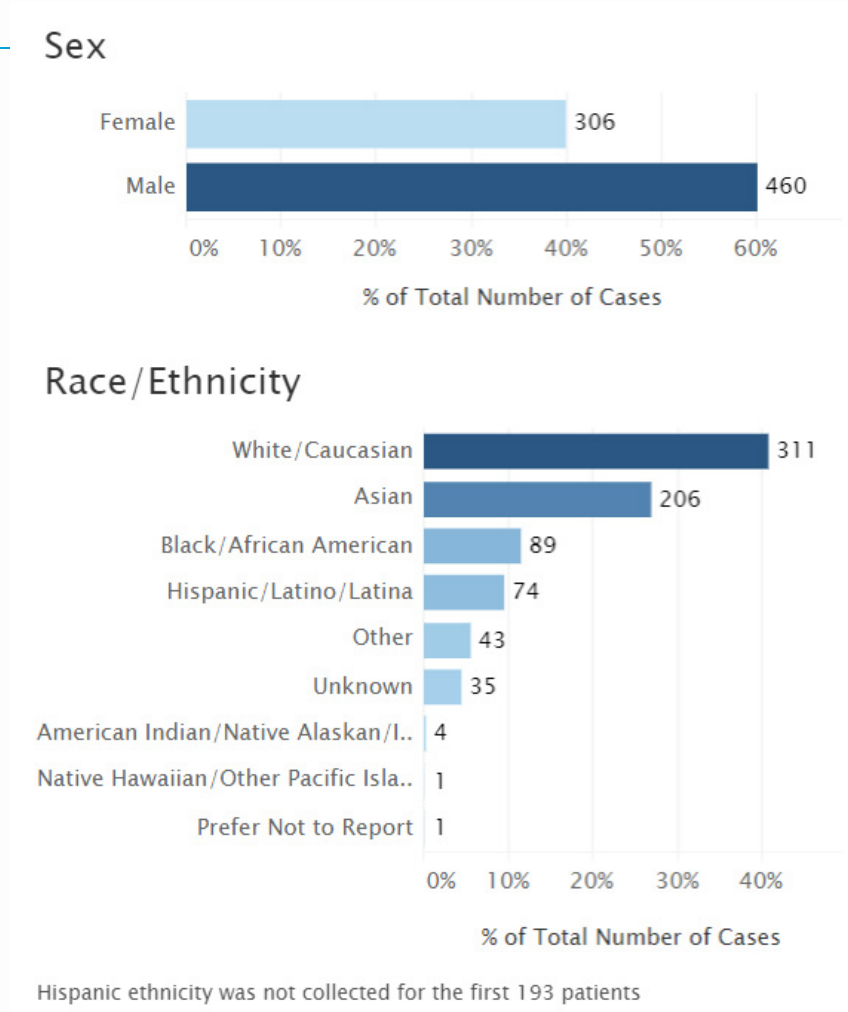
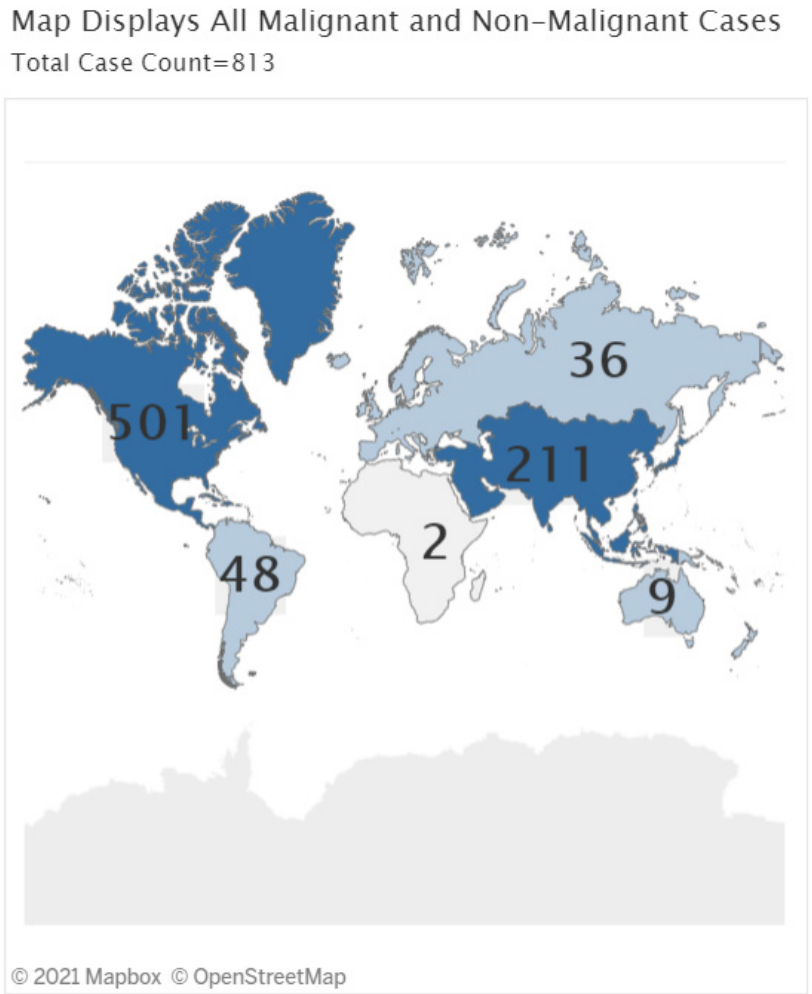
COVID-19 Cases Reported to ASH





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Accessed 01/15/2021

ASH RESEARCH COLLABORATIVE
Accelerating Progress in Hematology

REGULAR ARTICLE

blood advances

Check for updates

Outcomes of patients with hematologic malignancies and COVID-19: a report from the ASH Research Collaborative Data Hub

William A. Wood,[1] Donna S. Neuberg,[2] J. Colton Thompson,[3] Martin S. Tallman,[4] Mikkael A. Sekeres,[5] Laurie H. Sehn,[6,7] Kenneth C. Anderson,[8] Aaron D. Goldberg,[4] Nathan A. Pennell,[9] Charlotte M. Niemeyer,[10] Emily Tucker,[3] Kathleen Hewitt,[3] Robert M. Plovnick,[3] and Lisa K. Hicks[11]

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Wood et al, Blood Advances 2020

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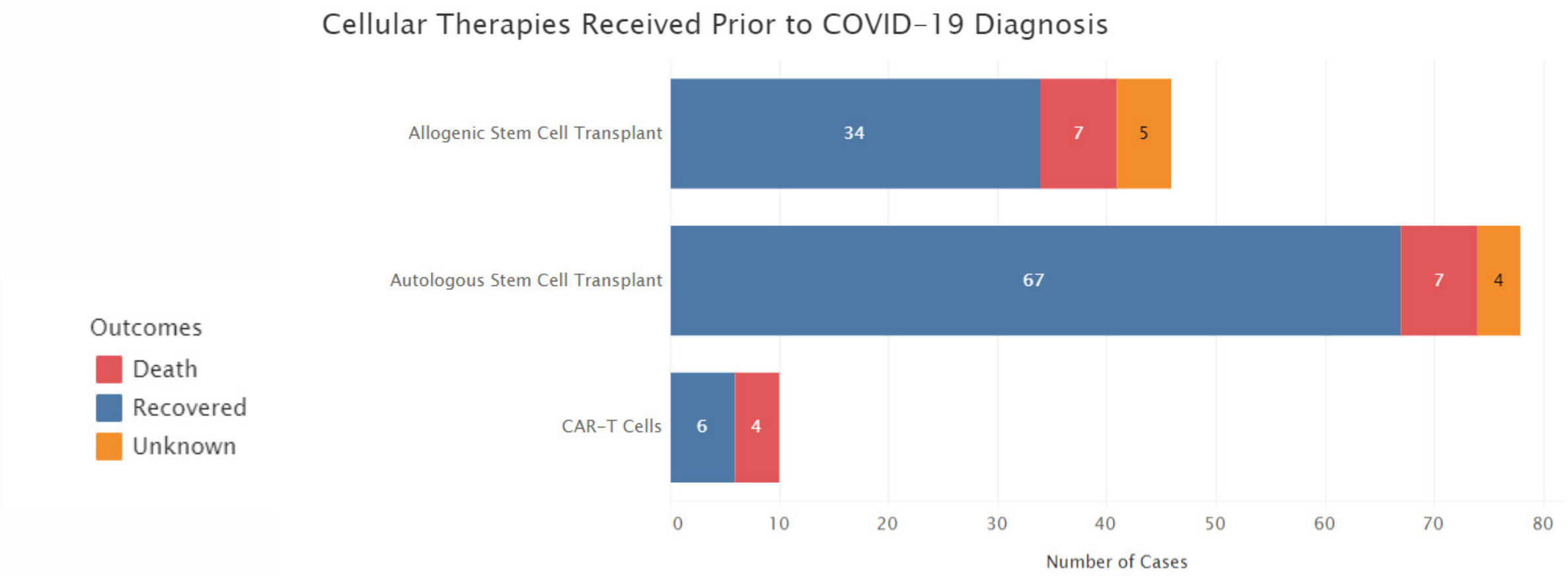
Accelerating Progress in Hematology

Cellular Therapies Received Prior to COVID-19



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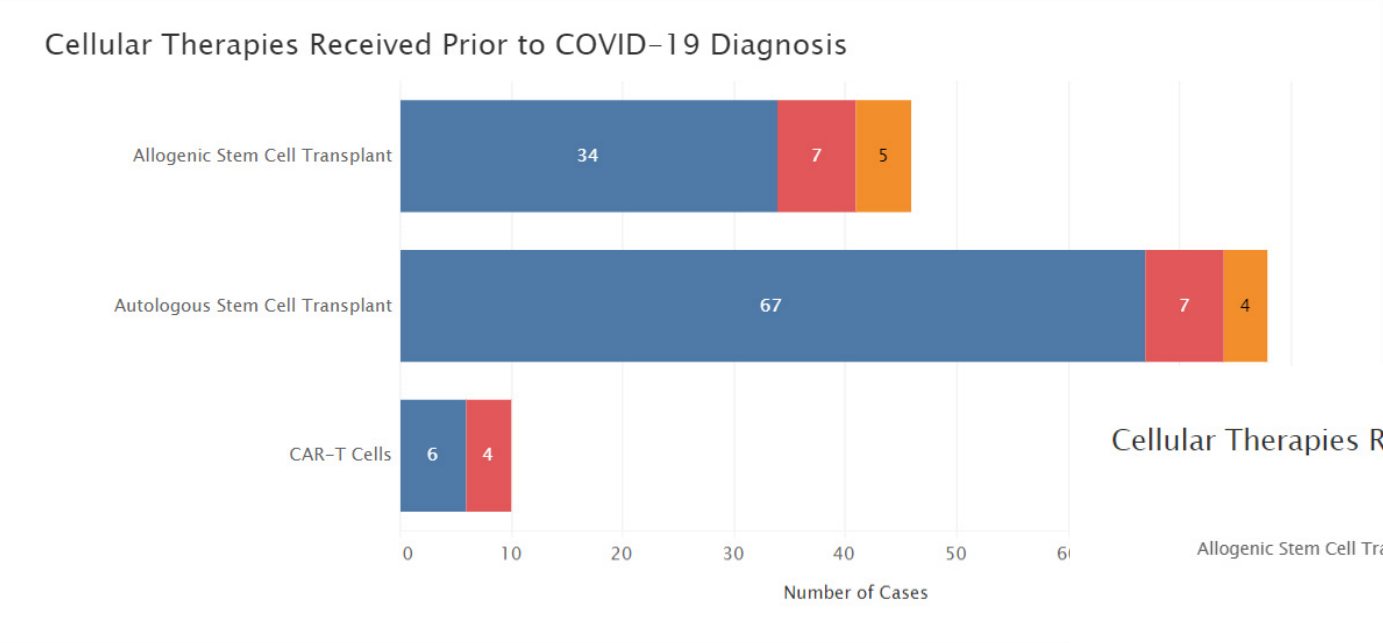

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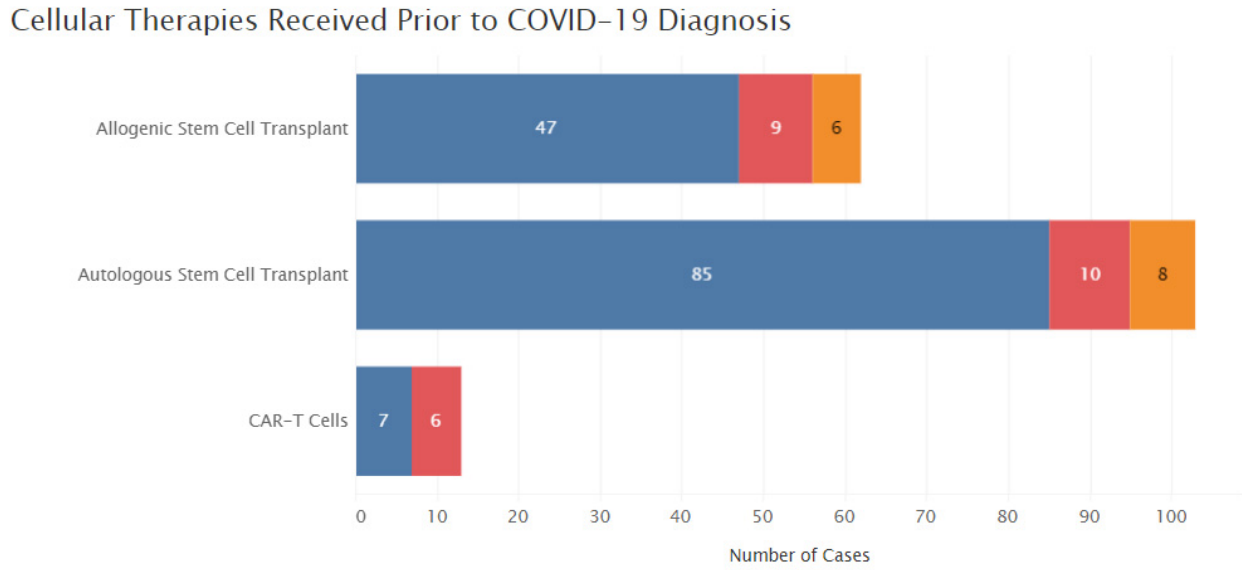

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Center Outcomes Forum 2021 Agenda

- Goals of Center Outcomes Forum 2021 and overview
- Summary of Center-Specific Analysis 2021
- Center-Specific Analysis 2022
  - Data Available for Use
  - Proposed Analysis Plan
  - Limitations of Analysis Plan
- Communication Plans
- Next steps/wrap up

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Center Outcomes Forum November 2021

Proposed Analysis Plan 2022

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CSA 2022 Overview of Analysis Plan

- Includes first alloHCT recipients 1/1/2018 – 12/31/2020
- Patients are unit of analysis – not centers
- Exploratory Analyses of Potential Impact of COVID-19 pandemic on practice changes and HCT outcomes first year post HCT
  - Broad impacts during the pandemic (and when?)
  - Differential effects across centers based on local variation reflected in COVID-19 incidence/impact
  - NOT COVID infection itself (censor pts w/COVID infections post-HCT)
  - If observed, can we account for these differential effects by adjusting for measured practice changes attributed to COVID pandemic?
- Results to guide formal approach for CSA 2022 analysis

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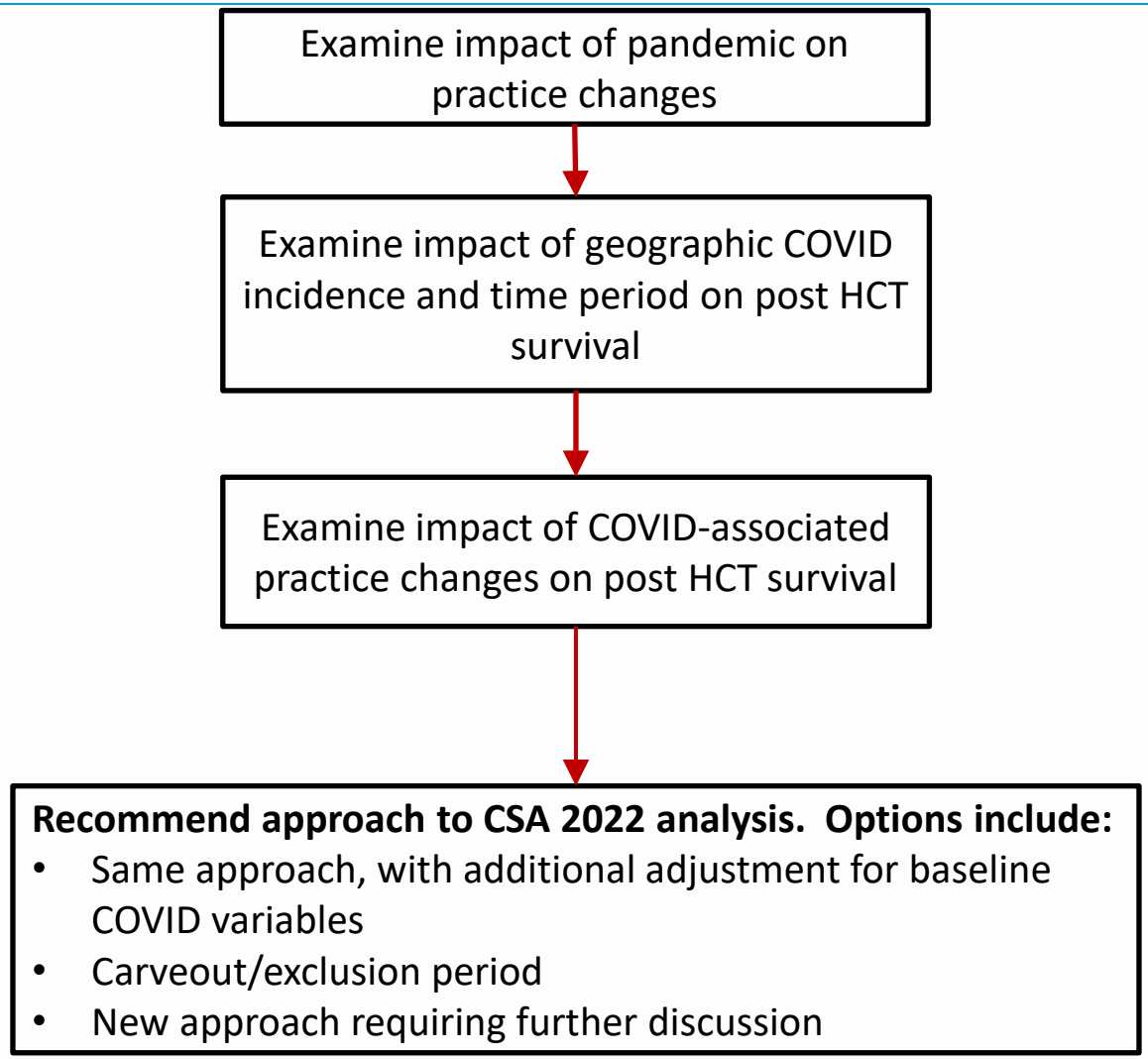
Proposed Analysis Process



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Exploratory Analyses 1: Impact of COVID-19 Pandemic on HCT Practices

- Supplemental COVID approach variables
  - Assess completeness by time period and by HCT center
  - Assess accuracy when possible: compare center reported use of cryopreservation to NMDP policy for URD HCT.
  - Describe distribution of COVID approach variables overall and by quarterly time period
  - Examine variability by center
  - Correlate reported changes in COVID approaches with geographic COVID incidence rates at HCT centers in 2 weeks prior to HCT

Exploratory Analyses 2: Impact of COVID-19 Pandemic on HCT Outcomes within 1 Year

- Prepare “Base model” using variables as in CSA 2021 analysis
- Cox regression instead of pseudovalue logistic regression model in order to handle time-varying effects of COVID-19
- Patient-level analysis
- Patients who develop a Covid-19 infection post HCT: censored

Forced into model

- Age
- Race
- KPS
- HCT-CI
- Low BMI
- CMV status
- History of mechanical ventilation
- History of invasive fungal infection
- Prior autologous transplant
- Diagnosis and disease status / stage
- AML ELN risk group
- AML transformed from MDS/MPN
- # of induction cycles to achieve CR (AML/ALL in CR)
- Time from dx to tx for AML/ALL not in CR1/PIF
- ALL cytogenetic
- MDS IPSS-R at HCT
- MDS with predisposing conditions
- Resistant disease in NHL/HL
- Year of tx
- Donor type/HLA matching
- Recipient and donor gender
- Donor age (URD BM/PBSC only)
- SES (median household income based on zip code

Tested in model

- Ethnicity
- Therapy related AML or MDS
- ALL: BCR/ABL, T-cell lineage, Ph+
- Del 17p in CLL
- NHL subtype
- MM cytogenetics
- MM ISS at dx
- URD BM/PBSC donor race/ethnicity
- BM or PBSC donor CMV serology
- BM or PBSC donor parity

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Exploratory Analyses 2: Impact of COVID-19 Pandemic on HCT Outcomes within 1 Year

- Examine COVID-19 ***time-fixed*** effects:
  - **History of Pre-HCT COVID infection**
  - **Date of HCT relative to pandemic** (pre-COVID (pre 1/21/2020), vs. early in the COVID pandemic (1/21/2020 to 6/21/2020), vs. later in the COVID pandemic (6/21/2020 to 12/31/2020))
  - **Average COVID infection rates** (per 100,000 population) over the 2 weeks preceding the HCT **based on the zip code of the transplant center** where the patient received their transplant (0 vs. >0 to 6.5 vs. >6.5),
  - **Average COVID death rates** over the 2 weeks preceding the HCT based on the **zip code of the transplant center** where the patient received their transplant (0 vs. >0 to 0.15 vs. >0.15)
- Note: cutpoints based on prior analyses: will reassess appropriate cutpoints for categories based on updated dataset
- Examine linear/quadratic relationships in addition to categories

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Exploratory Analyses 2: Impact of COVID-19 Pandemic on HCT Outcomes within 1 Year

- Examine COVID-19 ***time-varying*** effects
  - **Follow up Calendar time period** (pre 1/21/2020 vs. [1/21/2020 to 6/21/2020] vs. [6/21/2020 to 12/31/2020] vs. [1/1/2021 to 12/31/2021]
  - **Average COVID infection rates** (per 100,000 population) over the preceding 2 weeks **based on the zip code of the transplant center** where the patient received their transplant (0 vs. >0 to 6.5 vs. >6.5),
  - **Average COVID death rates** over the preceding 2 weeks based on the **zip code of the transplant center** where the patient received their transplant (0 vs. >0 to 0.15 vs. >0.15)
- Reassess cutpoints for categories based on updated dataset
- Examine linear/quadratic relationships in addition to categories

Exploratory Analyses 2: Impact of COVID-19 Pandemic on HCT Outcomes within 1 Year

- Explicitly examine interactions with COVID effect modifiers of interest (each time varying):
  - Time period post-HCT (first 100d, 100d-6 mos, 6 mos – 1 year)
  - History of acute GVHD grades II-IV
  - History of chronic GVHD
- Examine interaction between COVID incidence rates and calendar time periods
  - Is impact of variation in COVID incidence limited to certain calendar time periods (e.g. early in pandemic), which might potentially be "carved out" or excluded from CSA reporting?

Exploratory Analyses 3: Impact of COVID-19 Approach Changes on HCT Outcomes within 1 Yr

- Obtain a model which accounts for direct impact of COVID incidence and time period effects
- Examine impact of COVID approach changes on HCT outcomes, by adding COVID approach variables to this model
  - Example: Were outcomes in patients with cryopreserved grafts different than similar patients with fresh products?
- Assess whether adjusting for COVID approach variables makes the COVID incidence and other time-varying effects no longer significant

COVID Approach Variables

- Was the HCT impacted for a reason related to the COVID-19 pandemic?
  - Y or N
- Is the HCT date different than the originally intended date?
  - Provide intended date
- Is the donor different than the originally intended donor?
  - Provide intended donor
- Was the product thawed from a cryopreserved state before infusion?
- Is the product type different than originally intended?
  - Provide original product type
- Did the preparative regimen change from the original plan?
  - Y or N
- Did the GVHD prophylaxis change from the original plan?
  - Y or N

These variables were collected on a supplemental data form beginning August 2020 for patients whose HCT was after March 1, 2020

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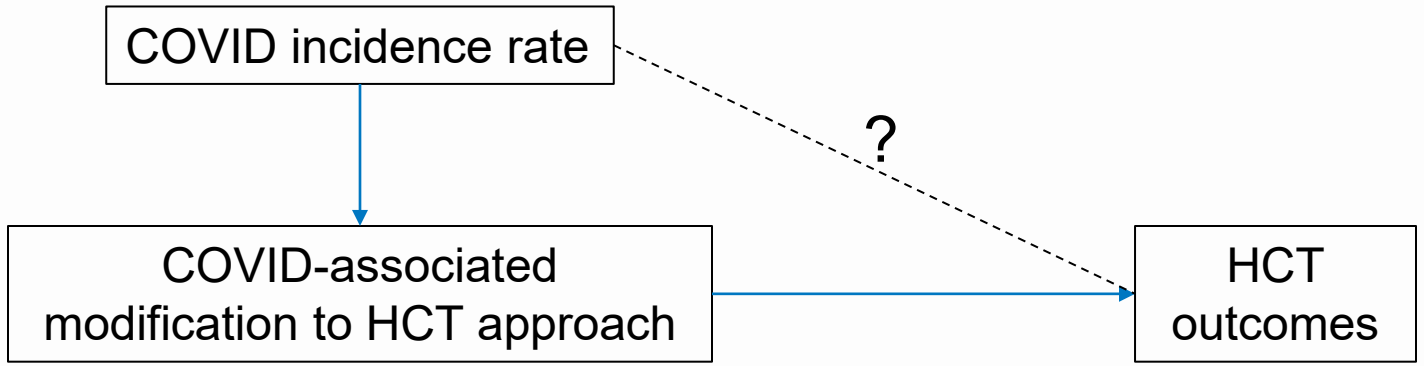
Exploratory Analyses 3: Impact of COVID-19 Approach Changes on HCT Outcomes within 1 Yr



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Potential Final Modeling Approach

- Continue to censor patients experiencing COVID within 1 year post HCT
- Approach for CSA22 dependent on findings:
  - If only baseline COVID related factors are important in the model then continue using same pseudovalue logistic regression approach as in prior reports, with additional baseline COVID variables added to the model.
  - If COVID impact seems transient (e.g. biggest or only impact during early period of pandemic) then consider carveout or exclusion period
  - If time-dependent COVID variables are needed in the model, further consideration and potential change in modeling approach/framework may be needed to account for these effects.

Limitations to Approach

- Data completeness of COVID infection, COVID approach variables
- Are reported approach changes accurate and representative across centers?
- Adjustment may not fully remove differential changes/impacts across centers or geographic regions
- New modeling framework, if necessary, would be disruptive to use of the CSA reporting and would necessitate substantial further discussions with stakeholders

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Limitations Of Analysis Plan

- COVID approach variables
  - Completeness of data submitted by centers
  - Variables may not capture complete COVID patient experience/outcomes
  - Variability across centers in reporting data on COVID approach variables
  - Accuracy and representativeness across centers
- Adjustment may not fully remove differential changes/impacts across centers or geographic regions
- New modeling framework (if needed) could lead to lower acceptance by community of analysis results

Pediatric-Specific Questions/limitations

- Was there a changes in “elective” transplants (e.g., Beta thalassemia, Fanconi Anemia)?
- What is the incidence of primary/secondary graft failure in patients with inherited marrow failure syndromes receiving cryopreserved grafts?
- What is the impact of universal mask wearing on viral/fungal infections (adult + peds)?
- Was there an increase in bacterial and fungal infections during the pandemic secondary to increased use of mismatched grafts?

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Center Outcomes Forum November 2021

Communication Plan

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Communication Plans

	Month	Center Med Dir	Center Admin	Center DM	HRSA	Payers
COF Summary and Preliminary Analysis Plan	December	√	√	√	√	√
Data and Analysis Timeline Memo	December	√	√	√		
Data Reminders	Monthly					
COVID Supplemental	Monthly		√	√		
Deficient Data	Ad hoc		√	√		
Follow-up	Monthly/Ad hoc	√	√	√		
Tandem Q&A	February	?	√			√
Preliminary Analysis Results and Final Analysis Plan	April/May	√	√	√	√	√

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Thank you

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