APPENDIX

Table 1. Possible CCSR code lists, based on prior Cox Proportional Hazard Model

Select CCSR codes and exponentiated hazard ratio, p values collected from the Health Verity analyses. CCSR were selected across the adult/child inpatient/outpatient subgroups based on p-value significance, hazard ratio quantification and clinical significance. The "ind" column indicates CCSR groups that have different importance factor in comparison across methods. Red indicates the elevated HR and has clinical association with COVID-19. Yellow indicates an elevated HR but clinically may not be associated with COVID-19 indicating need for a nuanced evaluation. Green indicates a minorly increased, or decreased HR and clinical relevance is unknown, but additional analyses could provide interesting insight.

For the pilot study 2 CCSRs will be selected from each indicator level. Selected CCSRs should be relevant across the adult/child inpatient/outpatient stratifications.

Example set: 1 (CIR013, CIR005), 2 (NEO059, NEO064), 3 (MBD003, MBD005)

Further evaluation is still required.

NOTE: This table is from unpublished work and should only be used for CCSR selection for the current study. It should not be used in any external reference documents.

adult	inpat	CCSR	CCSR Category Description	category	exp_coef	p	ind
1	1	RSP005	Acute bronchitis	RSP	1.7954623	1.6E-144	1
0	1	CIR013	Acute pulmonary embolism	CIR	7.0497964	2.69E-15	1
0	0	CIR013	Acute pulmonary embolism	CIR	4.3488606	1.08E-08	1
1	1	CIR013	Acute pulmonary embolism	CIR	3.0790954	0	1
1	0	CIR013	Acute pulmonary embolism	CIR	2.1448295	1.7E-299	1
0	1	MBD005	Anxiety and fear-related disorders	MBD	0.7757884	2.19E-08	3
1	0	BLD003	Aplastic anemia	BLD	1.3215618	0	2
0	1	RSP010	Aspiration pneumonitis	RSP	3.5179492	1.71E-07	1
0	0	NEO073	Benign neoplasms	NEO	1.2020316	7.47E-31	2
1	0	NEO073	Benign neoplasms	NEO	1.0632487	1.07E-59	2
0	0	MBD003	Bipolar and related disorders	MBD	1.1311011	3.25E-05	3
1	1	EYE010	Blindness and vision defects	EYE	1.241318	1.01E-23	3
1	0	MBD019	Cannabis-related disorders	MBD	0.9477187	7.7E-08	3
0	0	CIR001	Chronic rheumatic heart disease	CIR	2.067478	3.33E-18	1
0	1	NVS014	CNS abscess	NVS	7.5098899	6.24E-07	1
0	0	MBD002	Depressive disorders	MBD	1.2238261	3.7E-93	2
0	1	MBD002	Depressive disorders	MBD	0.5974941	1.84E-27	3
1	1	END004	Diabetes mellitus, Type 1	END	1.6746768	3.51E-52	2
1	1	END005	Diabetes mellitus, Type 2	END	2.42595	0	2
1	1	FAC007	Encounter for mental health conditions	FAC	1.1653911	2.75E-16	3

0	0	NVS009	Epilepsy; convulsions	NVS	1.2275328	2.91E-18	2
1	1	GEN014	Erectile dysfunction	GEN	1.1198235	0.000491	3
1	0	CIR007	Essential hypertension	CIR	1.2763791	0	1
0	0	MBD010	Feeding and eating disorders	MBD	1.1899123	1.41E-08	2
0	0	MUS033	Gout	MUS	2.8517775	3.08E-05	1
0	0	CIR019	Heart failure	CIR	2.3703313	1.65E-16	1
1	1	BLD002	Hemolytic anemia	BLD	1.7272069	3.11E-20	2
1	0	DIG014	Hemorrhoids	DIG	1.0827375	5.7E-43	2
1	1	RSP003	Influenza	RSP	1.7905031	1.94E-26	1
0	1	NEO059	Leukemia - acute lymphoblastic leukemia (ALL)	NEO	3.2288179	4.06E-07	2
0	0	NEO059	Leukemia - acute lymphoblastic leukemia (ALL)	NEO	2.340359	8.49E-06	2
1	0	NEO059	Leukemia - acute lymphoblastic leukemia (ALL)	NEO	1.5945705	0.000128	2
1	0	NEO060	Leukemia - acute myeloid leukemia (AML)	NEO	1.5985418	1.62E-05	2
0	1	NEO064	Leukemia - all other types	NEO	6.292654	6.81E-09	2
0	0	NEO064	Leukemia - all other types	NEO	2.0589724	9.73E-05	2
1	0	NEO064	Leukemia - all other types	NEO	1.3208777	3.2E-05	2
1	1	NEO061	Leukemia - chronic lymphocytic leukemia (CLL)	NEO	1.9189025	2.57E-05	2
1	1	NEO063	Leukemia - hairy cell	NEO	3.2833748	0.011287	2
1	0	FAC020	Lifestyle/life management factors	FAC	1.0673707	7.37E-25	2
1	0	SYM007	Malaise and fatigue	SYM	1.6209277	0	1
1	1	NEO071	Malignant neoplasm, unspecified	NEO	0.5018848	4.49E-31	3
0	0	NVS001	Meningitis	NVS	2.748152	6.51E-07	1
1	0	MBD026	Mental and substance use disorders in remission	MBD	0.9456827	3.81E-08	3
1	0	NEO068	Myelodysplastic syndrome (MDS)	NEO	1.4718427	1.46E-06	2
0	1	CIR005	Myocarditis and cardiomyopathy	CIR	10.536773	7.16E-60	1
0	0	CIR005	Myocarditis and cardiomyopathy	CIR	2.2794526	5.44E-26	1
0	1	NVS018	Myopathies	NVS	7.6245425	1.36E-11	1
1	1	NVS018	Myopathies	NVS	5.9103924	0	1
0	0	NEO072	Neoplasms of unspecified nature or uncertain behavior	NEO	1.2809227	4.32E-21	2
0	0	BLD001	Nutritional anemia	BLD	1.275163	2.59E-28	2
1	1	END009	Obesity	END	2.138089	0	2
0	1	CIR015	Other and ill-defined heart disease	CIR	7.0696459	1.82E-65	1

0	0	NVS006	Other nervous system disorders (often hereditary or degenerative)	NVS	1.1990588	5.42E-07	2
0	0	END015	Other specified and unspecified endocrine disorders	END	1.1572825	2.08E-12	2
1	1	RSP016	Other specified and unspecified lower respiratory disease	RSP	3.1448903	0	1
1	0	MBD025	Other specified substance-related disorders	MBD	0.945129	7.95E-06	3
1	0	CIR026	Peripheral and visceral vascular disease	CIR	1.2869823	2.3E-160	1
1	1	RSP002	Pneumonia (except that caused by tuberculosis)	RSP	6.0755698	0	1
1	0	RSP002	Pneumonia (except that caused by tuberculosis)	RSP	2.4796018	0	1
1	1	RSP014	Pneumothorax	RSP	2.6576532	2.8E-176	1
1	1	RSP017	Postprocedural or postoperative respiratory system complication	RSP	2.7657928	3.6E-164	1
0	1	SKN003	Pressure ulcer of skin	SKN	3.6670158	1.3E-08	2
1	1	NEO022	Respiratory cancers	NEO	0.4670023	4.65E-29	3
1	1	RSP012	Respiratory failure; insufficiency; arrest	RSP	6.1026716	0	1
1	0	RSP012	Respiratory failure; insufficiency; arrest	RSP	1.7652003	0	1
1	1	SYM013	Respiratory signs and symptoms	SYM	2.6949782	0	1
0	1	INF002	Septicemia	INF	4.3015319	2.21E-33	2
0	0	SYM003	Shock	SYM	2.8751147	6.64E-22	1
0	0	EYE007	Strabismus	EYE	1.1077043	8.32E-07	3
0	1	MBD012	Suicidal ideation/attempt/intentional self-harm	MBD	0.6443465	6.14E-11	3
0	1	MUS024	Systemic lupus erythematosus and connective tissue disorders	MUS	13.721766	3.86E-80	2
1	0	MBD024	Tobacco-related disorders	MBD	0.9132662	2.47E-64	3
0	1	CIR037	Vasculitis	CIR	11.05839	1.19E-46	1
0	0	CIR037	Vasculitis	CIR	2.3523214	1.14E-22	1
1	1	INF008	Viral infection	INF	3.1707846	0	1

Table 2: Expanded Analytic Protocol Based on Prior Premier PCC Analysis. (Variation in the primary analyses will still follow this generalized structure)

Cohort Definition

1. Scope:
    a. Study periods:
        i. General: Mar 01, 2019 to Apr 30, 2022
        ii. Retrospective period: Mar 01, 2019 – Mar 01, 2020
        iii. Inclusion period: Mar 01, 2020 – Nov 30, 2021 (index date)
        iv. PCC detection period padding: Nov 30, 2021 – Apr 30, 2022
        v. Sensitivity study periods
            1.
2. Define Index date:
    a. COVID exposure as first encounter meeting one of the following criteria in the applied inclusion period
        i. positive covid test (during Mar 01, 2020 – Nov 30, 2021)
        ii. ICD10 diagnoses of B97.29 (during Mar 01, 2020 – April 30, 2020)
        iii. ICD-10 diagnoses of U07.1 (during Apr 01, 2020 – Nov 30, 2021)
        iv. Sensitivity study periods COVID definition
    b. COVID non-exposed as encounter meeting one of the following criteria in the applied inclusion period
        i. Random negative covid test
        ii. Random covid-like encounter(?)
        iii. Random encounter
        iv. And meeting the exclusion criteria in scope:
            1. Not having history of covid treatment
            2. Not having record of positive covid test
3. Apply Inclusion Criteria:
    a. Continuous enrollment 1 year before index date
    b. Continuous enrollment 6 months after index date
4. Apply Exclusion Criteria:
    a. ICD-10 exclusion codes **(Table 3)**
    b. Unknown sex
    c. Unknown US census region
    d. Define sensitivity exclusion criteria
        i. Having CCSR in period 1 or period 2
        ii. Familial CCSR in period 3 (?)
5. Define study periods:
    a. Based on Index Dates
        i. Period 1 (historical lookback)
            1. -365 -> -7 days from index date
        ii. Period 2 (acute phase)
            1. -7 -> 31 days from index date
        iii. Period 3 (post-acute phase)

1. 31 -> 180 days from index date

6. Define Outcome definition:
    a. Identify CCSR outcomes for each patient for all CCSRs
7. Define COVID exposure status (primary predictor):
    a. Binary variable regarding COVID exposure status on index date
8. Define baseline covariates:
    a. On index date
        i. age
        ii. sex
        iii. US Census Region
        iv. Payer Type
        v. Inpatient Status (@ index date)
    b. In historical lookback
        i. Hospitalization frequency
        ii. Charlson Comorbidity Index (CCI)
    c. In acute phase
        i. Inpatient status (in period 2)
    d. Define sensitivity expanded covariate set
        i. Having CCSR in period 2
        ii. Length inpatient stay period 2
        iii. Frequency of encounter period 2/3
        iv.
9. Censoring criteria:
    a. Loss to follow-up
    b. Death
    c. New COVID exposure (?)

Analyses:

1. Conduct exploratory analyses of the cohort
    a. Table 1
2. Incidence of CCSRs in period 1, period 2, period 3
3. Fit Cox Proportional Hazard Models for the analytic set of CCSRs individually controlled for COVID exposure, age, sex, CCI, prior hospitalization, US Census Region
    a. Sensitivity expanded covariate set, variant time frames, data sources
4. Bayesian Additive Regression Trees Models for the analytic set of CCSRs individually controlled for COVID exposure, age, sex, CCI, prior hospitalization, US Census Region
    a. Sensitivity expanded covariate set, variant time frames, data sources
5. Make comparative inferences on the model outcomes

Table 3. Exclusion Criteria

ICD	NDC	CPT	Medication Names
"U071",	"61755004202",	"Q0240",	"casirivimab",
"U072",	"61755004502",	"Q0243",	"imdevimab",
"U099",	"61755003502",	"Q0244",	"etesevimab",
"B342",	"61755003608",	"M0240",	"bamlanivimab",
"B9721",	"61755003705",	"M0241",	"sotrovimab",
"B9729",	"61755003805",	"M0243",	"bebtelovimab",
"J1281",	"61755003901",	"M0244",	"paxlovid",
"J1282",	"61755002501",	"Q0245",	"molnupiravir",
"M3581",	"61755002701",	"M0245",	"remdesivir",
"Z8616",	"00002791001",	"M0246",	
"B948",	"00002795001",	"Q0247",	
"B949",	"00002791001",	"M0247",	
	"00002795001",	"M0248",	
	"00173090186",	"Q0222",	
	"00002758901",	"M0222",	
	"00069108530",	"M0223",	
	"00069108506",	"J0248",	
	"00006505506",		
	"00006505507",		
	"61958290202",		
	"61968290101",		