



# Comprehensive Characterization of COVID-19 Patients with Repeatedly Positive SARS-CoV-2 Tests Using a Large U.S. Electronic Health Record Database

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ABSTRACT In the absence of genome sequencing, two positive molecular tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) separated by negative tests, prolonged time, and symptom resolution remain the best surrogate measure of possible reinfection. Using a large electronic health record database, we characterized clinical and testing data for 23 patients with repeatedly positive SARS-CoV-2 PCR test results  $\geq$ 60 days apart, separated by  $\geq$ 2 consecutive negative test results. The prevalence of chronic medical conditions, symptoms, and severe outcomes related to coronavirus disease 19 (COVID-19) illness were ascertained. The median age of patients was 64.5 years, 40% were Black, and 39% were female. A total of 83% smoked within the prior year, 61% were overweight/obese, 83% had immunocompromising conditions, and 96% had  $\geq$ 2 comorbidities. The median interval between the two positive tests was 77 days. Among the 19 patients with 60 to 89 days between positive tests, 17 (89%) exhibited symptoms or clinical manifestations consistent with COVID-19 at the time of the second positive test and 14 (74%) were hospitalized at the second positive test. Of the four patients with  $\geq$  90 days between two positive tests (patient 2 [PT2], PT8, PT14, and PT19), two had mild or no symptoms at the second positive test and one, an immunocompromised patient, had a brief hospitalization at the first diagnosis, followed by intensive care unit (ICU) admission at the second diagnosis 3 months later. Our study demonstrated a high prevalence of compromised immune systems, comorbidities, obesity, and smoking among patients with repeatedly positive SARS-CoV-2 tests. Despite limitations, including a lack of semiquantitative estimates of viral load, these data may help prioritize suspected cases of reinfection for investigation and continued surveillance.

**IMPORTANCE** The comprehensive characterization of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing and clinical data for patients with repeatedly positive SARS-CoV-2 tests can help prioritize suspected cases of reinfection for investigation in the absence of genome sequencing data and for continued surveillance of the potential long-term health consequences of SARS-CoV-2 infection.

**KEYWORDS** COVID-19, EHR, reinfection

A sof 9 August 2021, there have been more than 202 million confirmed cases of coronavirus disease 19 (COVID-19) globally, including 35 million in the United States. A reverse transcriptase PCR (RT-PCR) test is considered the gold standard for detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in upper and lower respiratory specimens and for diagnosis of COVID-19. While neutralizing antibodies are detectable for several months following recovery from SARS-CoV-2 infection (1, 2), it **Citation** Dong X, Zhou Y, Shu X-O, Bernstam EV, Stern R, Aronoff DM, Xu H, Lipworth L. 2021. Comprehensive characterization of COVID-19 patients with repeatedly positive SARS-CoV-2 tests using a large U.S. electronic health record database. Microbiol Spectr 9:e00327-21. https://doi.org/10.1128/Spectrum.00327-21.

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Large EHR study shows high prevalence of immune compromise and other comorbidities among patients with repeatedly positive SARS-CoV-2 tests. May help prioritize suspected reinfections for investigation or surveillance @VUMCepi @VUMD\_ID @UTHealth\_SBMI

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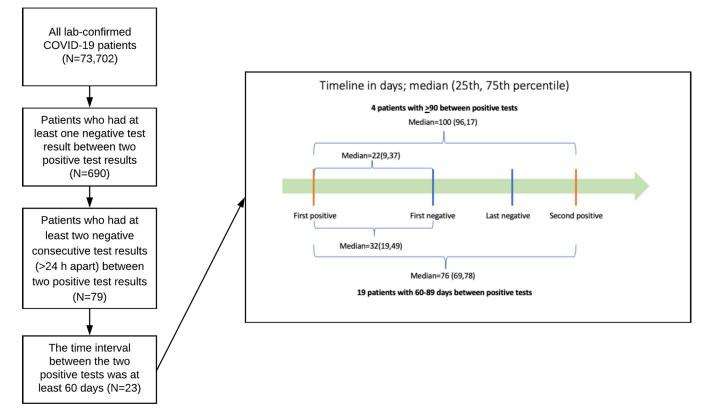


FIG 1 Study flow chart and SARS-CoV-2 PCR testing timeline (days) for 23 repeatedly positive patients.

remains unknown whether and for how long these antibody responses protect patients from reinfection. There have been many case reports of patients with a second positive PCR test after their PCR results turned negative and symptoms resolved (3). Most of these reports are suspected cases of reinfection based on limited clinical or testing data; in a minority of suspected cases of reinfection, the viral genome sequences were analyzed and shown to be distinct, strongly supporting a reinfection rather than failure to clear an initial infection (4). In the absence of genomic evaluations, the presence of two positive molecular tests separated by negative tests, prolonged time, and clinical resolution of symptoms remain the best surrogate measure of possible reinfection. Using the Centers for Disease Control and Prevention Common Investigation Protocol for Investigating Suspected SARS-CoV-2 Reinfection (4) as a guide, we conducted a comprehensive evaluation of patients who had repeated positive SARS-CoV-2 PCR tests in a large U.S. COVID-19 electronic health record (EHR) database. We characterized their demographic and clinical characteristics, including their SARS-CoV-2 testing journey, symptoms, medication use, and COVID-19-related complications.

## RESULTS

For the 4 patients with at least 90 days between positive tests, the median interval between the 2 positive tests, separated by 2 or more consecutive negative tests >24 h apart, was 100 days (25th, 75th percentile of 96, 107), and the median interval between the first positive and first negative test was 22 days (9, 37) (Fig. 1). For the 19 patients with 60 to 89 days between positive tests, the corresponding intervals were 76 days (69, 78) and 32 days (19, 49), respectively (Fig. 1).

The median age of the 23 repeatedly positive patients at the index date was 64.5 years (25th, 75th percentile of 53.5, 69.8). Seventeen patients were diagnosed in the Northeast, 5 in the Midwest, and 1 in the South; 40% of patients were Black, 40% white, and 20% other/unknown race; 83% had non-Hispanic ethnicity; and 39% were

female. Almost 83% of patients smoked within the prior year, and 61% were overweight or obese.

Comorbidity diagnoses and symptom prevalence for the 23 individual patients at the time of each positive test are presented in Table 1, and their PCR test and clinical journeys are shown in Fig. 2. Chronic disease prevalence was high, including hypertension (70%), CVD, atrial fibrillation or CKD (each 26%), and insulin-dependent type 2 diabetes or history of venous thromboembolism/long-term anticoagulation (each 22%). Overall, 96% of patients had  $\geq$ 2 comorbidities. Most notably, 19 of the patients (83%) had immunocompromising conditions, including 2 of the 4 patients with  $\geq$ 90 days between positive tests (patient 14 [PT14] and PT19).

For individuals with 45 to 89 days between positive SARS-CoV-2 tests, CDC investigative criteria included having "a symptomatic second episode and no obvious alternate etiology for COVID-19–like symptoms OR close contact with a person known to have laboratory-confirmed COVID-19." Among the 19 patients in our study with 60 to 89 days between positive tests, 17 (89%) exhibited symptoms or clinical manifestations consistent with COVID-19 at the time of the second positive test, including 9 (47%) with acute respiratory failure, 8 (42%) with acute kidney failure, 6 (32%) with shortness of breath, 5 (26%) with fever, and 3 (16%) with acute embolism and thrombosis. Fourteen of the 19 (74%) patients were hospitalized at the second positive test, of whom all but 4 were also hospitalized at the first positive SARS-CoV-2 test. One patient was treated with tocilizumab (PT7, at the time of first positive test and during an extended hospitalization) and 4 were treated with dexamethasone after the first diagnosis of COVID-19.

As shown in Fig. 2 and Table 1, four of the patients (PT5, PT7, PT12, and PT17) with immunocompromising conditions had severe symptoms and lengthy hospitalizations (including ICU and mechanical ventilation for PT12 and PT17) beginning at the first positive COVID-19 test and numerous negative tests, often with their second positive test in close proximity to one or multiple negative tests. Additionally, PT10 had no COVID-19-like symptoms or related treatments at the second positive test, and PT18 had esophageal cancer and no COVID-19-like symptoms at the time of either positive test. Neither PT5 nor PT10 was assigned an ICD-10 code for COVID-19 (ICD10 U07.1) at the time of the second positive SARS-CoV-2 test. The clinical journeys of these six repeatedly positive patients cast doubt about the accuracy of categorizing them as true reinfections.

Of the four patients (Fig. 2, top) who had  $\geq$ 90 days between two positive tests (PT2, PT8, PT14, and PT19), the record of one immunocompromised patient (PT14) suggests mild-to-moderate disease with few symptoms following both COVID-19 diagnoses. PT19, who was also immunocompromised, had a brief hospitalization at the first diagnosis, followed by ICU admission at the time of the second positive test 3 months later. PT2 had severe symptoms, hospitalization, and treatment with dexamethasone after the first positive test, but no symptoms or treatment at the second positive test. Notably, neither PT2 nor PT19 was assigned an ICD-10 code for COVID-19 (ICD10 U07.1) at the time of the second positive SARS-CoV-2 test. Patient 8 had a pacemaker and two hospitalizations, and the symptoms noted were shortness of breath and bradycardia at the second positive test; it is unclear why this patient was initially tested for COVID-19 in the absence of symptoms or a noted preoperative examination.

No patients had cardiac arrest, tracheostomy, amputation, or death.

### DISCUSSION

This study provides clinical and testing characterization of 23 COVID-19 patients with suspected reinfection, defined as repeatedly positive SARS-CoV-2 PCR tests separated by consecutive negative tests and prolonged time. Over one-third of patients were of Black race, and we observed a high prevalence of obesity and multiple comorbidities known to increase the risk of COVID-19 illness, including hypertension, diabetes, and CKD. Moreover, 83% of the patients with repeated positivity were current smokers, which is linked to an increased risk of severe COVID-19 (5). It is possible that

Patient     Concritidities     Symptom(s)     Sympto	Dave hetween nositive				
2   HTN, HLD   Coll, Could, Freer, Christ pain, preumonia, curde marker, Long CT, No VTE, Long- term AC.   Coll, Could, Freer, Christ pain, preumonia, Lond Sposia, Lind Sposia, Lind Sposia, Lind Sposia, Lind Scholl   Coll, Lond Land   Coll, Lond Land   Coll, Could   C	SARS-CoV-2 tests		Comorbidities <sup>b</sup>	Symptom(s) of COVID-19 episode 1	Symptom(s) of COVID-19 episode 2
8     Nicinia, KIN, Piccimia, KIN, Piccimia, KIN, Piccimia, KIN, Richnell, Cirrhosis, Protein-calorie     Nore     Solution     <	≥90	2	HTN, HLD	SOB, cough, fever, chest pain, pneumonia, acute respiratory failure w/hypoxia, bradycardia	None
14 Niccinic HVV alcoholic cirrhosis, protein-calorie Irily, alcohol dependence. TB Freer, presumonia, hypoxia, AIG Ferer, respira Freer, respira Freer, presumonia, hypoxia, AIG Ferer, respira Freer, respira presumbler, long OT, ho VTE, long atti- hypoxia, AIGS, after dimental status, AC, ESRD on HD, retropertoneum cancer in AL, BISTRM, paremaker, long OT, ho VTE, long term AC, ESRD on HD, retropertoneum cancer in AL, HD, HV, Aldo Net and y attivity, protein, AC, ESRD on HD, retropertoneum cancer in AL, BISTRM, paremaker, long OT, ho VTE, long term AC, ESRD on HD, retropertoneum cancer in AL, BISTRM, paremaker, long OT, ho VTE, long term protein and intrivition dependent Color Back Rain, retropertoneum attri- teres in dependent brait, wateries pain, terry status warricular rehybrardia Fere, rehybrardia   3 Kdney-heart transplant, rheumatold arthritis, protein- adore malnutrition, OSA, thyrold cancer alorie malnutrition, OSA, thyrold cancer alorie malnutrition Couph Ferer, hou addrefs, chert pain, tachybardia, cue repholoran, acture respiratory dependents. Alor enclosion, acture repholoran, acture alorie malnutrition SOB, Bear, Alor acture replicatory dependents. Alor enclosion, acture replicatory dependent. Alor enclosion, acture replicatory dependent. PMX, incortis, HTN, HD, old M, enclosion, acture respiratory failure with and remonia, acture respiratory failure with acture replicatory dependent. Alor, incortis, HTN, HD, old M, enclosion, acture respiratory failure with acture respiratory failure withypoxia, Alor. Ferer, presum acture respiratory dependent. Microsci M, enclosion, actore respiratory failure withypoxia, Alor.   3 AFIb, HTN, HLD, old M, and remonia, actore respiratory failure withypoxia, Alor. SOB, denthes, presumonia, actore respinatory dependences. Alor BHT, elegement DMZ, incortis, HTN		8	Nicotine, AFib, HTN, Pacemaker, Long QT, h/o VTE, long-	None	SOB, bradycardia
19     HTM. Actificion, accorsi dependence, IB HTM. Actificion, accorsi dependence, IB HLD. NSTEMI, pacemoleer, Jong OT, No VTE, Jong-term A.C. ESRO on HD, retropertioneum career HLD. NSTEMI, pacemoleer, Jong OT, No VTE, Jong-term A.C. ESRO on HD, retropertioneum career A.C. ESRO on HD, retropertioneum A.C. ESRO on HD, retropertioneum career A.C. ESRO on HD, retropertioneum career A.C. ESRO on HD, retropertioneum A.C. ESRO on HD, retropertioneum A.H. HLD, HU, Alcholic cirrhosis w/ascites, alcohol A.H. HLD, HU, alcoholic cirrhosis w/ascites, alcohol abues, hop pulmonyary TB A. In M. HLD, JUV, alcoholic cirrhosis w/ascites, alcohol abues, hop pulmonyary B. Freer, tardy-cardia A. Erek, radache, chert pah, tachycardia A. Brever, tardycardia A. Brever, hadache, prenomoia, acute respiratory dependence, AKI, encephalopathy, fuid overlads, intervolationey transpirat, protein- calori abues, hop pulmonyary B. Freer, A.R. encephalopathy, fuid overlads, science, phana acute enablem and thrombosis B. INH, HLD, old MI, pacemaker, long CI, long GT, long GT, long GT, long GT, long GT, long eterm AC. B. Rever, hadache premonia, acute respiratory failure whyposia, ARDS, and acute enablem and thrombosis B. HTN, HLD, cold MI, pacemaker, long GT, long eterm AC. C.C. Departementa, protein- calorie anihurtition B. HTN, HLD, cold MI, pacemaker, long GT, long eterm AC. A.B. HTN, HLD, C.G. protein- calorie Alter erabidition promotal, acute respiratory failure whyposia, ABDS, ARU B. Alfred mental status B. Alfred MI, Pacemaker, long GT, long eterm AC. A.B. HTN, HLD, C.G. protein- calorie Alter erabidition promotal, acute respiratory failure whybrosia, ABDS, ARU B. Alfred MI, Pacemaker, long GT, long eterm AC. B. Alfred MI, Pacemaker, Jong GT, long year AC. B. Alfred		14	Nicotine, HIV, alcoholic cirrhosis, protein-calorie	Low back pain	Fever
Invalidation Free, preumonia, stytosia, AN Free, preumonia, stytosia, AN Free, preumonia, AN Free, preprint Arenticular Ventricular   3 Kidney-heart transplant, theumatoid arthrits, protein 20, dhr.freas, audorid, and Ventricular <td></td> <td>(</td> <td>mainutrition, alcohol dependence, TB</td> <td>- - -</td> <td></td>		(	mainutrition, alcohol dependence, TB	- - -	
1     Insulin-dependent DN2 wCKD, COPD, Income, AFIB, HTN, HLD, NSTEM, Jacemaker, Iong CT, No VTE, Jong-term     S08, diarheas, weakness, Jong AFIB, werticular hypoxia, AFDS, atteret explanatory Hund verticular hypoxia, AFDS, atteret explanatory Hund verticular hypoxia, AFDS, atteret explanatory Hund verticular hypoxia, AFDS, atteret explanatory Hund verticular werticular reshreaded ansues hop pulmonary T8     Cough, Freex, Insedache, chest pain, activatad verticular reshreadia     Acuta resplanatory hopoxia, AFDS, atteret explanatory werticular reshreadia     Nature resplanatory bypoxia, AFDS, atteret pain, activatad verticular reshreadia     Nature resplanatory bypoxia, AFDS, atteret hypoxia, AFDS, atteret pain, activatad abolismuse hop pulmonary T8     Acuta resplanatory restructions outoget carbon about an atteret pain, activated abolism and thromonais.     Acuta resplanatory acute embolism acute embolism acute embolism acute embolism and thromonais.     Acuta resplanatory acute embolism acute ersplanatory acute embolism acute ersplanatory acute embolism acute ersplanatory acute ersplanatory		١	HTN, alconol dependence	Fever, pneumonia, nypoxia, AKI	Fever, respiratory failure w/ nypoxia, encephalopathy, AKl
HLD NSTEM, pacemaker, long QT, hod VTE, long-term   Prest mentabolic entropy failure w/   ventricular recipatory failure w/   ventricular recipatory failure w/   ventricular recipatory failure w/     AC, ESRD on HD, retropertioneum cancer   Nidorey-heart transplant, rheumatoid arthrits, protein-adolic cirrhosis w/ascites   SOB, diarrhea   SOB, diarrhea     Ridney-heart transplant, rheumatoid arthrits, protein-adolic cirrhosis w/ascites   Cough, fever, had transplant, theumatoid arthrits, protein-adolic cirrhosis w/ascites   SOB, diarrhea   SOB, diarrhea     Prostate cancer, alcoholic cirrhosis w/ascites, alcohol   Prostate cancer, alcoholic cirrhosis w/ascites, alcoholic cirrhosis w/ascites, alcoholic cirrhosis w/ascites, alcoholic and thrombosis   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory     Prostate cancer, alcoholic cirrhosis w/ascites, alcoholic and thrombosis   Cough, fever, had thrombosis   Diarrhea, pneumonia, acute respiratory   Diarrhea, pneumonia, acute respiratory   Diarrhea, pneumonia, acute respiratory   Diarrhea, pneumonia, acute respiratory     Insulin-dependent DM2 w/CKD AFIB, HTN, HLD, long QT, long Term   Cough, haddhee, pneumonia, acute respiratory   Diarrhea, pneumonia, acute respiratory   Diarlhea, pneumonia, acute respiratory   Diarlhea, pneumonia, acute respiratory     Insulin-dependent DM2, w/CKD, AFIB, HTN, HLD, long YT, Indo   Cough, haddhee, pneumonia, acute respiratory   Diarlhea, pneumonia, acute respiratory <t< td=""><td>60-89</td><td>1</td><td>Insulin-dependent DM2 w/CKD, COPD, nicotine, AFib, HTN,</td><td>SOB, diarrhea, weakness, low back pain,</td><td>Acute respiratory failure w/hypoxia,</td></t<>	60-89	1	Insulin-dependent DM2 w/CKD, COPD, nicotine, AFib, HTN,	SOB, diarrhea, weakness, low back pain,	Acute respiratory failure w/hypoxia,
Arise of the section of the sectin of the section of the section of the section			HLD, NSTEMI, pacemaker, long QT, h/o VTE, long-term	pneumonia, acute respiratory failure w/	ventricular tachycardia
Kidney-heart transplant, rheumatoid arthritis, protein- cuoirie malnutrition     Gough, chest pain, preumonia, AK, tachycardia     SOB, diarrhea hypoxia, AK       Filth, HLD, HUV, alcoholic cirrhosis w/ascites     Fever, tachycardia     SOB, fever, AI       Filth, HLD, HUV, alcoholic cirrhosis w/ascites     Fever, tachycardia     SOB, fever, AI       Prostate cancer, alcoholic cirrhosis w/ascites, bio pulmonary TB     Fever, tachycardia     SOB, fever, AI       Prostate cancer, alcoholic cirrhosis w/ascites, bio pulmonary TB     Fever, tachycardia, evere sepiratory     SOB, fever, AI       Filth, HLD, Jold MI, NSTEMI, Jong QT, ESBD on HD, protein- calorie malnutrition, OSA, thyroid cancer     Cough, fever, headsche, chest pain, tachycardia, enholism and thrombosis     SOB, fever, AI       Insulin-dependent DM2, w/CKD, AFib, HTN, HLD, Jong QT, Iong-term AC, CRO, Kidney transplant, protein-calorie malnutrition     SOB, cante embolism and thrombosis     AKI, tachycardia, tackycardia, ta				myposia, ando, arered merical status, metabolic encephalopathy, fluid overload, ventricular tachycardia	
calorie malnutrition     calorie malnutrition     Hypoxia, M       HTN, HLD, HUY, alcoholic cirrhosis w/ascites     Fever, tachycardia     SOB, fever, haedache, chest pain, tachycardia, ambolism, acute embolism, acute embolism, acute embolism, acute embolism, acute embolism, tachycardia, acute embolism, acute embolism, tachycardia, acute embolism, acute embolism, tachycardia, acute embolism, tachycardia, acute embolism, tachycardia, acute embolism, acute embolism, tachycardia, acute embolism, acute embolism, tachycardia, acute embolism, tachycardia, acute embolism, tachycardia, acute embolism, acute embolism, acute embolism, acute embolism, acute respiratory failure w/hypoxia, ARD, ARD, AKI, tachycardia, acute embolism and thrombosis     Chest pain, tachycardia, embolism, embolism, embolism, acute embolism, acute embolism, acute embolism, acute embolism, acute respiratory failure w/hypoxia, AKI, HTN, HLD, CKD, protein-calorie malnutrition     SoB, fever, headache, pneumonia, acute respiratory failure w/hypoxia, AKI, encephalopathy, fuid overload, sepsis w/ acute embolism and thrombosis       AFIb, HTN, HLD, Old MI, pacemaker, DIM, HLD, CKD, protein-calorie malnutrition     SoB, fever, headache, pneumonia, acute respiratory failure w/hypoxia, AKI     Fever, headache, the pneumonia, acute respiratory failure w/hypoxia, AKI     Fever, headache, the adache, th		m	Kidney-heart transplant, rheumatoid arthritis, protein-	Cough, chest pain, pneumonia, AKI, tachycardia	SOB, diarrhea, respiratory failure w/
HTN, HLD, HLV, alcoholic cirrhosis w/ascites, alcoholismic server, alcoholismic server, alcoholismic abuse, N/o pulmonary TB   Fever, headache, chest pain, tachycardia, abuse, N/o pulmonary TB   SOB, fever, headache, chest pain, tachycardia, abuse, N/o pulmonary TB   SOB, fever, headache, chest pain, tachycardia, acute embolismic acute embolismic acute embolismic acute and numborsis   SOB, fever, headache, chest pain, tachycardia, acute embolismic acute embolismic acute embolismic acute embolismic acute acprision and thrombosis   SOB, fever, headache, chest pain, tachycardia, acute embolismic acute erespiratory failure w/hypoxia, AKI   SOB, fever, headache, pneuronia, acute respiratory failure w/hypoxia, AKI   Pever, pneuronia, acute respiratory failure w/hypoxia, AKI     AFib, HTN, HLD, CKD, protein-calorie   Mry achybo xia, AKI   None   None   Polemeter acute erespiratory failure w/hypoxia, AKI   Pever, pneuronia, acute respiratory failure			calorie malnutrition	-	hypoxia, AKI, tachycardia
Prostate cancer, alcoholic cirrhosis w/ascites, alcohol     Cugh, fever, headache, chest pain, tachycardia, acute embolism and thrombosis     embolism acute embolism and thrombosis       HTN, HLD, old MI, NSTEMI, long OT, ESRD on HD, protein- calorie malnutrition, OSA, thyroid cancer     Cugh, fever, headache, chest pain, tachycardia, acute embolism and thrombosis     Chest pain, tachycardia, acute embolism and thrombosis       ITN, HLD, old MI, NSTEMI, long OT, ESRD on HD, protein- calorie malnutrition     Cugh, fever, headache, chest pain, tachycardia, acute embolism and thrombosis     Chest pain, tachycardia, acute embolism and thrombosis       Insulin-dependent DM2 w/CKD, AFIb, HTN, HLD, old MI, pacemaker, long OT, long-term AC, CKD, kidney transplant, protein-calorie malnutrition     Cugh, fever, headache, chest pain, tachycardia, acute embolism and thrombosis     Parte embolism and thrombosis       AFIb, HTN, HLD, old MI, pacemaker, long OT, long-term AC, brow encespinatory failure w/hypoxia, ARID, chord acute embolism and thrombosis     Paver, headache, chest pain, tachycardia, acute erspinatory failure w/hypoxia, ARID, AKI, tachycardia, acute erspinatory failure w/hypoxia, ARID, AKI, tachycardia, acute respiratory failure w/hypoxia, ARID, thuch, CKD, protein-calorie     Diarrhea, pre- erspiratory failure w/hypoxia, ARID, AKI, tachycardia, acute respiratory failure acute respiratory failure w/hypoxia, AKI, tachycardia, acute respiratory		4	HTN, HLD, <b>HIV</b> , alcoholic cirrhosis w/ascites	Fever, tachycardia	SOB, fever, AKI, tachycardia, acute
Prostate career, alcoholic cirrhosis w/ascites, alcoholi di Mi NSTEMI, long QT, Barbo HD, protein- alorie malnutrition, OSA, thyroid cancer     Cough, fever, headache, chest pain, tachycardia, embolism and thrombosis     Chest pain, tachycardia, expression and thrombosis     Chest pain					embolism and thrombosis
abuse, <i>i/to</i> pulmonary TB   acute embolism and thrombosis   embolism i     HTN, HLD, old MI, NSTEMI, long QT, ESRD on HD, protein- calorie malnutrition   occure embolism and thrombosis   embolism and thrombosis     HTN, HLD, old MI, NSTEMI, long QT, long QT, long-term AC, CKD, Ridney transplant, protein-calorie malnutrition   Fever, diarrhea, pne tachycardia, severe sepsis w/shock, acute embolism and thrombosis   embolism acute embolism and thrombosis     AFIb, HTN, HLD, old MI, pacemaker, long QT, long-term AC, cKD, breast cancer, protein-calorie malnutrition   So cough, header houndonis, acute respiratory failure w/th malnutrition   Fever, pneuron so cough, header houndonis   embolism acute embolism so cough, header houndonis     AFIb, HTN, HLD, old MI, pacemaker, long QT, long-term AC, cKD, breast cancer, protein-calorie malnutrition   So cough, header with hypoxia, ARD shock, acute enbolism and thrombosis   eever sepsis w/f hour encopholo so cough, header houndonis   eever sepsis w/f dependence, acute sepsis w/f hour encopholosis     AFIb, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, neuronia, acute respiratory failure w/hypoxia, AR   None     AFIb, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, neuronia, acute respiratory failure w/hypoxia, AR   None     AFIb, HTN, HLD, long-term AC, dirrhosis, protein-calorie insulture w/hypoxia, AR   SOB, diarrhea, neuronia, acute respiratory failure w/hypoxia, AR   SOB, diarrhea, neuronia, acute respiratory failure w/hypoxia, AR     AFIb, HTN,		5	Prostate cancer, alcoholic cirrhosis w/ascites, alcohol	Cough, fever, headache, chest pain, tachycardia,	Chest pain, tachycardia, acute
HTM, HLD, old MM, NSTEM, Jong QT, <b>ESRD on HD, protein-</b> Fever, diarrhea, pneumonia, acute respiratory   Diarrhea, pneumonia, acute respiratory     calorie malnutrition, OSA, thyroid cancer   Rilure w/hypoxia, ARDS, vertilator   Rikl, tachyc     rable   Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT,   SOB, cough, headache, pneumonia, acute   erewite application     Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT,   SOB, cough, headache, pneumonia, acute   erewite application     Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT, long-term AC,   SOB, cough, headache, pneumonia, acute   erewite application     Insulin-dependent DM2, nicotine, HTN, HLD, old MI, pacemaker, long QT, long-term AC,   SOB, cough, headache, pneumonia, acute   Fever, pneum     AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC,   Witypoxia, AKI   Reverte respiratory failure   Diarrhea, wee     CKD, breast cancer, protein-calorie   minutrition   witypoxia, AKI   None   None     ITN, CLL w/o remission   Insulin-dependent DM2, nicotine, HTN, HLD, old MI,   SOB, fever, headache, pneumonia, acute respiratory failure   Diarrhea, wee     AFib, HTN, HLD, OKD, protein-calorie   Intered mental status   None   None     AFib, HTN, HLD, long-term AC, orter-calorie   SOB, fever, headache, pneumonia, acute respiratory failure   SOB, fever, headache				acute embolism and thrombosis	embolism and thrombosis
calorie malnutrition, OSA, thyroid cancer failure w/hypoxia, ARDS, ventilator respiratory   calorie malnutrition, OSA, thyroid cancer failure w/hypoxia, ARDS, ventilator respiratory   Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT, long-term AC, CKD, <b>kidney transplant</b> , protein-calorie SOB, cough, headache, pneumonia, acute Fever, pneum   Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT, long-term AC, CKD, <b>breast</b> cancer, protein-calorie SOB, cough, headache, pneumonia, acute Fever, pneum   AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC, CKD, <b>breast</b> cancer, protein-calorie SOB, cough, headache, pneumonia, acute Fever, pneum   AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC, circhosis SOB, favers, pneumonia, acute respiratory failure Diarrhea, were   AFib, HTN, HLD, CKD, protein-calorie malnutrition SOB, faver, headache Diarrhea, were None   AFib, HTN, HLD, CKD, protein-calorie malnutrition SOB, diarrhea, pneumonia, acute respiratory failure Diarrhea, were   AFib, HTN, HLD, CKD, protein-calorie malnutrition SOB, diarrhea, pneumonia, acute respiratory failure Diarrhea, were   AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie SOB, diarrhea, terespiratory failure Diarrhea, terespiratory failure   AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie SOB, diarrhea, terespiratory failure SOB, diarrhea, terespiratory failure   AFib, HTN, HLD, long-term AC, cirrhosis, protein-calori <td></td> <td>9</td> <td></td> <td>Fever, diarrhea, pneumonia, acute respiratory</td> <td>Diarrhea, pneumonia, acute</td>		9		Fever, diarrhea, pneumonia, acute respiratory	Diarrhea, pneumonia, acute
Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, Iong QT, Iong-term AC, CKD, <b>kidney transplant, protein-calorie</b> AKI, tachyc, tachyc enemonia, acute embolism and thrombosis   AKI, tachyc, acute embolism and thrombosis     Insulin-dependent DM2 w/CKD, <b>kidney transplant, protein-calorie</b> Sols, cough, haadache, protein-calorie   AKI, tachyc, acute embolism and thrombosis     AFib, HTN, HLD, old MI, pacemaker, Iong QT, Iong-term AC, CKD, <b>kidney transplant, protein-calorie malnutrition</b> Sols, cough, haadache, protein-calorie malnutrition   Fever, pneur     AFib, HTN, HLD, old MI, pacemaker, Iong GT, Iong-term AC, CKD, <b>braast cancer, protein-calorie malnutrition</b> Sols, cough, haadache, sepsis w/shock, acute   Fever, pneur     AFib, HTN, HLD, CKD, <b>protein-calorie malnutrition</b> Sols, fever, hadadche   Weakness, Ak   Sols, fever, hadadche   Sols, fever, hounonia, acute respiratory failure w/h, dependence, had     AFib, HTN, HLD, CKD, <b>protein-calorie malnutrition</b> Sols, fever, hounonia, acute respiratory failure w/hypoxia, ARD   None     AFib, HTN, HLD, Iong-term AC, <b>cirrhosis, protein-calorie</b> Sols, diarrhea, pneumonia, acute respiratory failure w/hypoxia, houndia, setter respiratory failure w/hypoxia, houndia, settererespiratory failure setry houndia, houndia, setter respiratory fa			calorie malnutrition, OSA, thyroid cancer	failure w/hypoxia, ARDS, ventilator	respiratory failure w/hypoxia, ARDS,
Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT, long-term AC, CKD, <b>kidney transplant, protein-calorie</b> tachycardia, severe sepsis w/shock, acute embolism and thrombosis   acute embolism and thrombosis     Insulin-dependent DM2, w/CKD, AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC, CKD, <b>breast cancer</b> , <b>protein-calorie</b> SOB, cough, headache, pneumonia, acute   Fever, pneurr     AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC, CKD, breast cancer, protein-calorie   SOB, cough, headache, pneumonia, acute respiratory failure   Fever, pneur     MTN, CLL W/o remission   MTN, HLD, old MI, pacemaker, long QT, long-term AC, CKD, breast cancer, protein-calorie   W/hypoxia, AKD, werload, sepsis w/sh   Fever, pneur     MTN, CLL W/o remission   MTN, HLD, old MI, ecotine, HTN, HLD, old MI, ecotine, and thrombosis   Diarrhea, wee     AFib, HTN, HLD, CKD, protein-calorie   MIN, HLD, CKD, protein-calorie   None   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, prever, headache     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, prever, headache   SOB, diarrhea, prevers, headache   SOB, diarrhea, prevers, headache     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   SOB, diarrhea, preverspiratory failure   SOB, diarrhea, preverspiratory   SOB, diarrhea, preverspiratory <t< td=""><td></td><td></td><td></td><td>dependence, AKI, encephalopathy,</td><td>AKI, tachycardia, sepsis w/shock,</td></t<>				dependence, AKI, encephalopathy,	AKI, tachycardia, sepsis w/shock,
Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, Iong OT, Iong V, HTN, HLD, old MI, pacemaker, Iong OT, Iong V, HTN, HLD, old MI, pacemaker, Iong OT, Iong-term AC, is an intrition insulin-dependent DM2, nicotine, HTN, HLD, old MI, is an intrition   Rewer, pneumonia, acute respiratory failure with hypoxia, AKI, is a spis w/shi dependence were phologating, acute respiratory failure w/hypoxia, AKI   Fever, pneumonia, acute respiratory failure with hypoxia, AKI     AFib, HTN, HLD, Old MI, pacemaker, Iong OT, Iong-term AC, is an invition   Mypoxia, AKI   Rewer, pneumonia, acute respiratory failure with hypoxia, AKI     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, pneumonia, acute respiratory failure w/hypoxia, ARDS, AKI, is acute respiratory failure w/hypoxia, ARDS, AKI, is acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, trachycardia sepsis w/shock is acute respiratory failure w/hypoxia, trachycardia sepsis w/shock is acute respiratory failure w/hypoxia, trachycardia acute respiratory failure w				tachycardia, severe sepsis w/shock, acute	acute embolism and thrombosis
Insulin-dependent DM2 w/CKD, kidney transplant, protein-calorie malnutrition   SOB, cough, headache, pneumonia, acute erepiratory failure with hypoxia, ARDS, AKl, failure with hypoxia, ARDS, AKl, enter who and the molesis with back acute embolism and thrombosis she incephalopathy, fluid overload, sepsis w/s asepsis w/s asepsis w/s dependent with who with poxia, ARDS, AKl, enter who and thrombosis with provis, ARD, but who remission   Fever, pneumonia, acute expiratory failure with hypoxia, ARDS, AKl, enter who and thrombosis with poxia, ARD, but oremission   Fever, pneumonia, acute expiratory failure with hypoxia, ARDS, AKl, enter and thrombosis with poxia, ARD, but oremission   Fever, pneumonia, acute expiratory failure with hypoxia, ARD, but oremission     AFID, HTN, HLD, old MI, enter of the insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, old MI, enter or insulin-dependent DM2, nicotine, HTN, HLD, ind future with not in acute respiratory failure with provis, indirectine, indir				embolism and thrombosis	
Iong-term AC, CKD, <b>kidney transplant, protein-calorie</b> respiratory failure with hypoxia, ARDS, AKI,   failure w/h     mainutrition   andinutrition   shock, acute embolism and thrombosis   sepsis w/s     AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC,   Weakness, pneumonia, acute respiratory failure   Diarrhea, weas     AFib, HTN, HLD, old MI, pacemaker, protein-calorie malnutrition   Withypoxia, AKI   Teipter with hypoxia, AKI   dependence were, sepsis w/s     RTM, CLL w/o remission   Insulin-dependent DM2, nicotine, HTN, HLD, old MI,   Weakness, pneumonia, acute respiratory failure   Diarrhea, wee     RTM, CLL w/o remission   Insulin-dependent DM2, nicotine, HTN, HLD, old MI,   Altered mental status   None     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, preumonia, acute respiratory   SOB, diarrhea, preumonia, acute respiratory   SOB, diarrhea, precephalor     AFib, HTN, HLD, OKD, protein-calorie malnutrition   SOB, diarrhea, preumonia, acute respiratory   SOB, diarrhea, precephalor   SOB, diarrhea, precephalor     AFib, HTN, HLD, OKD, protein-calorie   SOB, diarrhea, precephalor   None   Weakness, AK     AFib, HTN, HLD, ONG-term AC, cirrhosis, protein-calorie   SOB, diarrhea, precephalor   SOB, diarrhea, precephalor     AFib, HTN, HLD, Inng-term AC, cirrhosis, protein-calorie   Precephalor <td></td> <td>7</td> <td>Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT,</td> <td>SOB, cough, headache, pneumonia, acute</td> <td>Fever, pneumonia, acute respiratory</td>		7	Insulin-dependent DM2 w/CKD, AFib, HTN, HLD, long QT,	SOB, cough, headache, pneumonia, acute	Fever, pneumonia, acute respiratory
malnutritionmalnutritionencephalopathy, fluid overload, sepsis w/ shock, acute embolism and thrombosisdependence sepsis w/sAFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC, CKD, breast cancer, protein-calorie malnutrition HTN, CLL w/o remission Insulin-dependent DM2, nicotine, HTN, HLD, old MI, cirrhosisencephalopathy, fluid overload, sepsis w/ shock, acute embolism and thrombosis w/hypoxia, AKIdependenc sepsis w/st sepsis w/stAFib, HTN, HLD, old MI, cirrhosisWhypoxia, AKI None Altered mental statusNone withypoxia, AKIrespiratory none sepsis w/st breakness, AKAFib, HTN, HLD, CKD, protein-calorie malnutrition inhutritionSOB, diarrhea, pneumonia, acute respiratory failure w/hypoxia, ARDS, AKI, encephalopathy, tachycardia, sepsis w/shock failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, protein-calorieAFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie malnutritionSOB, diarrhea, pneumonia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, acut			long-term AC, CKD, <b>kidney transplant, protein-calorie</b>	respiratory failure with hypoxia, ARDS, AKI,	failure w/hypoxia, ventilator
AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC,   snock, acute embolism and thrombosis   sepsis w/sr     CKD, breast cancer, protein-calorie malnutrition   W/hypoxia, AKI   respiratory failure     HTN, CLL w/o remission   w/hypoxia, AKI   new cute respiratory failure   Diarrhea, wea     HTN, CLL w/o remission   SOB, fever, headache   None   nespiratory     Insulin-dependent DM2, nicotine, HTN, HLD, old MI,   SOB, fever, headache   None   veakness, AK     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, wea     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pialure w/hypoxia, ARDS, AKI, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia, acute respiratory   Plarrhea, pneur			malnutrition	encephalopathy, fluid overload, sepsis w/	dependence, AKI, fluid overload,
AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC, CKD, breast cancer, protein-calorie malnutrition   Weakness, protein-calorie malnutrition   Diarrhea, wea     CKD, breast cancer, protein-calorie malnutrition   SOB, fever, headache   None   respiratory     HTN, CLL w/o remission   SOB, fever, headache   None   respiratory     Insulin-dependent DM2, nicotine, HTN, HLD, old MI, cirrhosis   Altered mental status   None   veakness, AK     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, meumonia, acute respiratory   SOB, diarrhea, meumonia, acute respiratory   SOB, diarrhea, mercein-caporia     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, meumonia, acute respiratory   SOB, diarrhea, meumonia, acute respiratory   SOB, diarrhea, mercein-caporia     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia, acute respiratory   SOB, diarrhea, mercein-caporia     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia, acute respiratory   SOB, diarrhea, mercein-caporia     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia, acute respiratory   SOB, diarrhea, mercein-caporia     Mainutrition   AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia, acute respi				shock, acute embolism and thrombosis	sepsis w/shock
CKD, breast cancer, protein-calorie malnutrition   w/hypoxia, AKl   respiratory     HTN, CLL w/o remission   SOB, fever, headache   None     Insulin-dependent DM2, nicotine, HTN, HLD, old Ml,   SOB, fever, headache   None     rirhosis   SOB, ferer, headache   Woekness, Ak     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, pneumonia, acute respiratory     AFib, HTN, HLD, CKD, protein-calorie malnutrition   SOB, diarrhea, pneumonia, acute respiratory   SOB, diarrhea, failure w/hypoxia, ARDS, AKl,   acute respi     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory   SOB, diarrhea, che   acute respi     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia,   Diarrhea, che     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia,   Diarrhea, che     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia,   Diarrhea, che     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia,   Diarrhea, che     AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie   Pneumonia, acute respiratory failure w/hypoxia,   Diarrhea, che		6	AFib, HTN, HLD, old MI, pacemaker, long QT, long-term AC,	Weakness, pneumonia, acute respiratory failure	Diarrhea, weakness, pneumonia, acute
HTN, <b>CLL w/o remission</b> Insulin-dependent DM2, nicotine, HTN, HLD, old MI, Altered mental status <b>cirrhosis</b> AFib, HTN, HLD, CKD, <b>protein-calorie malnutrition</b> SOB, diarrhea, pneumonia, acute respiratory SOB, diarrhea failure w/hypoxia, ARDS, AKI, acute respiratory acute respiratory AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che <b>acute respi</b> AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> malnutrition AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che tachycardia			CKD, breast cancer, protein-calorie malnutrition	w/hypoxia, AKI	respiratory failure w/hypoxia, AKI
Insulin-dependent DM2, nicotine, HTN, HLD, old MI, Altered mental status cirrhosis dirrhosis diarrhea, preumonia, acute respiratory SOB, diarrhea AFib, HTN, HLD, CKD, protein-calorie malnutrition SOB, diarrhea, pneumonia, acute respiratory SOB, diarrhea failure w/hypoxia, ARDS, AKI, acute respiratory ARDS, AKI, acute respiratory ARDS, AKI, acute respiratory failure w/hypoxia, protein-calorie Pneumonia, acute respiratory failure w/hypoxia, protein-calorie preumonia, acute respiratory failure w/hypoxia, acute respiratory failure w/hypoxia, protein-calorie preumonia, acute respiratory failure w/hypoxia, protein-calorie pneumonia, acute respiratory failure w/hypoxia, protein-calorie preumonia, acute respiratory failure w/hypoxia, pricedia sepsis w/shock tachycardia acute respiratory failure w/hypoxia, pricedia acute respiratory failure w/hypoxia, broke acute respiratory failure w/hypoxia, pricedia acute respiratory failure w/hypoxia, pricedia acute respiratory failure w/hypoxia, pricedia acute respiratory failure w/hypoxia, broke acute respiratory acute acute respiratory failure w/hypoxia, broke acute respiratory failure w/hypoxia, broke acute respiratory failure w/hypoxia, broke acute acu		10	HTN, CLL w/o remission	SOB, fever, headache	None
cirrhosis AFib, HTN, HLD, CKD, protein-calorie malnutrition AFib, HTN, HLD, CKD, protein-calorie malnutrition AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie malnutrition AFib, HTN, HLD, long-term AC, cirrhosis, protein-calorie AFib, hordia		11	Insulin-dependent DM2, nicotine, HTN, HLD, old MI,	Altered mental status	Weakness, AKI, metabolic
AFib, HTN, HLD, CKD, <b>protein-calorie malnutrition</b> SOB, diarrhea, pneumonia, acute respiratory SOB, diarrhea failure w/hypoxia, ARDS, AKI, acute respiratory ARDS, AKI, acute respi encephalopathy, tachycardia, sepsis w/shock ARDS, AKI, tachycardia, sepsis w/shock ARDS, AKI, AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che <b>malnutrition</b> AKI, encepl			cirrhosis		encephalopathy, altered mental
AFib, HTN, HLD, CKD, <b>protein-calorie malnutrition</b> SOB, diarrhea, pneumonia, acute respiratory SOB, diarrhea failure w/hypoxia, ARDS, AKI, acute respiratory acute respi encephalopathy, tachycardia, sepsis w/shock ARDS, AKI, tachycardia AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che <b>malnutrition</b> AKI, encepl					status, bradycardia
failure w/hypoxia, ARDS, AKI, acute respi encephalopathy, tachycardia, sepsis w/shock ARDS, AKI, tachycardia AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che <b>malnutrition</b> AKI, encepl AKI, encepl shock		12	AFib, HTN, HLD, CKD, protein-calorie malnutrition	SOB, diarrhea, pneumonia, acute respiratory	SOB, diarrhea, chest pain, pneumonia,
encephalopathy, tachycardia, sepsis w/shock ARDS, AKI, tachycardia, sepsis w/shock ARDS, AKI, tachycardia AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che <b>malnutrition</b> AKI, encepl Shock				failure w/hypoxia, ARDS, AKI,	acute respiratory failure w/hypoxia,
tachycardii AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che <b>acute respi</b> AKI, encepl AKI, encepl				encephalopathy, tachycardia, sepsis w/shock	ARDS, AKI, encephalopathy,
AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b> Pneumonia, acute respiratory failure w/hypoxia, Diarrhea, che. acute respi AKI, encepl AKI, encepl shock					tachycardia, sepsis w/shock
tachycardia acute respi AKI, encepl shock		13	AFib, HTN, HLD, long-term AC, <b>cirrhosis, protein-calorie</b>	Pneumonia, acute respiratory failure w/hypoxia,	Diarrhea, chest pain, pneumonia,
Icept			mainutrition	tachycardia	acute respiratory failure w/hypoxia,
(Continued on best page					AKI, encephalopathy, sepsis w/ shock
					(Continued on next page)

Days between positive				
SARS-CoV-2 tests	Patient	Comorbidities <sup>b</sup>	Symptom(s) of COVID-19 episode 1	Symptom(s) of COVID-19 episode 2
	15	Insulin-dependent DM2 w/CKD, HTN, HLD, old MI, ESRD on	Fever, headache, diarrhea, weakness, low back	Weakness, pneumonia, acute
		<b>HD</b> , heart transplant	pain, pneumonia, acute respiratory failure w/	respiratory failure w/hypoxia,
			hypoxia, metabolic encephalopathy, fluid	encephalopathy, fluid overload,
			overload	tachycardia, sepsis w/o shock
	16	HTN, HLD	Weakness, pneumonia, AKI, metabolic	Fever, weakness, chest pain,
			encephalopathy	pneumonia, tachycardia
	17	HTN, protein-calorie malnutrition	Pneumonia, acute respiratory failure w/hypoxia,	SOB, pneumonia
			AKI, encephalopathy	
	18	Esophageal cancer	None	None
	20	Insulin-dependent DM2 w/CKD, nicotine, HTN, ESRD on HD,	Fever, headache, chest pain, acute respiratory	Chest pain
		HIV	failure w/hypoxia	
	21	Nicotine, long QT	Low back pain	Low back pain
	22	Monoclonal gammopathy, respiratory TB,	None	Fever
		histoplasmosis, blastomycosis		
	23	COPD, nicotine	Pneumonia	SOB, pneumonia, acute respiratory
				failure w/hypoxia

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<sup>o</sup>Data are based on manual review of ICD-10 codes within 30 days before and after the index date and the second positive test date. MI, myocardial infarction; AC, anticoagulation; HTN, hypertension; HDL, hyperlipidemia; SOB, shortness of breath; DM2, type 2 diabetes mellitus; CKD, chronic kidney disease; AFib, atrial fibrillation; VTE, venous thromboembolism; ESRD, end-stage renal disease; HD, hemodialysis; TB, tuberculosis; OSA, obstructive sleep apnea; AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CLL, chronic lymphocytic leukemia; COPD, chronic obstructive pulmonary disease. HD, hemodialysis; TB, tuberculosis; OSA, obstructive sleep apnea; AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CLL, chronic lymphocytic leukemia; COPD, chronic obstructive pulmonary disease.



Interval	Ptid	Outcome of Interest	-40	-20	0	20	4	40	60		80	100		120	140	160
	PT2,M,60-69(>90d)	no			00	0				0*		0				
>=90 Days	PT8,M,70-79(>90d)	MV1			0			0	0	þ		0	(			
between two positives	PT14,F,40-49(>90d)	no			0		0	0				(	C			
	PT19,M,50-59(>90d)	ICU2	0	0	0	>						00	o			
	PT1,M,70-79	no			0			0	0	0000	0 (					
	PT3,M,60-69	no			00 0	5			0		00	c	00	(	0	
	PT4,M,50-59	no			Ó		• *	0		00						
	PT5,M,60-69	no			0 (	С	0	0								
	PT6,M,70-79	MV1			0		00		0 0	) C					<b>O</b> *	
	PT7,F,70-79	MV*			<u>o</u> *		0		0	0	0	ō	0 0	000	0	
	PT9,F,U	no			0 0	000				🏟 🛛	)					
50-89 Days Detween	PT10,M,50-59	no			0	0	0 0		0							
wo positives	PT11,F,70-79	no			0		0			0	0 0	0				
	PT12,M,70-79	ICU1, MV1			0				0	00	0	C	)			
	PT13,F,80-89	ICU2			0 0	0 0	OO				¢					
	PT15,M,60-69	ICU2,MV2			00	0 🚥			0	0						
	PT16,M,40-49	no			0	0	000	00	0	)	0					
	PT17,M,50-59	ICU*,MV1			0	0	(	C	00 (		0	000	¢	0	0	
	PT18,F,50-59	ICU2		0	Ó					00	œ		*			
	PT20,F,50-59	no			0	0			0 0	) (	00	0	00			
	PT21,F,40-49	no			O		0		0	0	00	0	0	0	00	
	PT22,M,20-29	no			0		0	0	0	0	0					
	PT23,F,60-69	ICU2			0		0		0	00	o þ					
			-40	-20	0	20	4	40	60		80	100		120	140	160
				Days fro	om the Fir	st Pos	itive Tes	t (Day	( 0)							
ospitalization	Event O COVID-19 RNA * Drug	Value nega posit		dexa	imethasone izumab				al Ventila st and 2n		CU: Inten re 1/2			the 1st/2	2nd positive	



those known to be at a particularly high risk for COVID-19 or those with persistent or recurrent symptoms may undergo frequent testing, thereby increasing the likelihood of receiving some false-positive or false-negative results.

Outcomo of

Immunocompromising conditions, including end-stage renal disease on dialysis; HIV; cirrhosis, including alcohol-related; solid organ transplant; cancer; and protein-calorie malnutrition, were more common in our study population affected by COVID-19 than in the general population without COVID-19. Consistent with prior evidence that immunocompromised populations with COVID-19 have elevated risks of COVID-19 severity and morbidity and mortality (6–9), among the subset of patients in our study with immunocompromising conditions, more than two-thirds required hospitalization for the second positive PCR test after the interval negative PCR test. Patients with HIV in our sample had at least one other significant comorbidity, namely, either alcoholic cirrhosis (PT4 and PT14) or ESRD on hemodialysis (PT20). Reinfection may therefore raise clinical suspicion for an underlying immune defect, which may have also influenced the duration to achieve viral clearance.

Over 90% of patients in our study exhibited symptoms or clinical manifestations consistent with COVID-19 at the time of the second positive test, satisfying a CDC criterion for the investigation of suspected SARS-CoV-2 reinfection, particularly among those with 45 to 89 days between positive PCR tests. However, a biased detection of symptomatic reinfection is possible (10), and some of the symptoms could be related to the multitude of other underlying chronic medical conditions present among these patients, while the second positive COVID PCR test could be due to prolonged shedding or a false positive. Overall, 70% (12/17) of patients hospitalized at the first positive test were also hospitalized at the second test, suggesting that in many cases reinfection was not associated with less severe disease in our study population. In a recent review of 16 reported cases of reinfection confirmed by sequencing (10), for those 12 cases in whom

severity could be compared between episodes, one-half of reinfections were less severe, which the authors suggested may reflect partial immune protection. However, the demographics of that study population differed from ours, as 8 of the 16 cases were between the ages of 20 to 30 years and 7 were health care workers, with a high potential for reinfection.

Overall, in our study, 37% of those hospitalized had severe disease characterized by ICU admission. This value is higher than previous estimates that 17% to 35% of hospitalized COVID-19 patients are treated in an ICU (2). Acute kidney injury (AKI) has been reported to occur in approximately 9% of hospitalized COVID-19 patients and a higher proportion of those requiring ICU admission (2). We observed AKI as a more common complication associated with COVID-19, including after both COVID-19 diagnoses in several individuals, but we were unable to determine whether they were independent or persistent events.

It is possible that hospitalized patients are more likely to undergo frequent testing, due to more severe disease or to support discharge to a rehabilitation facility or nursing home. This frequent testing can lead to alternating positive and negative tests, often on overlapping days. Given the high hospitalization rate in our study, repeated positive tests for some patients (e.g., PT5, PT7, PT12, and PT17) occurring during the time of an extended hospitalization with severe complications may not represent true reinfections. Moreover, prolonged viral shedding, as has been observed in severe COVID-19 cases (11), cannot be ruled out. A recent analysis in the Emory Healthcare System indicated that, among 22,443 patients who had at least 2 tests, the median (interquartile range [IQR]) duration between first and last positive test was 19 days (12, 32), and a duration of 45 and 90 days represented the 88th and 97th percentile, respectively (10).

In the absence of genomic evaluations to definitively confirm reinfection (3, 10), finding two positive molecular tests separated by negative tests, prolonged time, and resolution of symptoms remain the best surrogate measure of possible reinfection. In 169 previously reported cases to date (3), with an average of 115 days between first and second positive test, viral genome sequences were shown to be distinct, strongly suggesting a reinfection rather than a failure to clear an initial infection. Our identification and clinical characterization of 23 possible reinfections in a large data set, with a median of 77 days between positive tests, provides additional data suggesting that reinfections may be common. Since most patients in the Optum data set did not have repeated tests after their COVID-19 diagnosis, the true incidence rate of recurrent detectable SARS-CoV-2 cannot be estimated.

Our analysis was limited by a lack of information on RT-PCR platforms or semiguantitative RT-PCR cycle threshold ( $C_{\tau}$ ) values. As additional assays became available during the course of the pandemic, various test sensitivities may have contributed to testing discrepancies during our study period. The patients in our study nevertheless fulfilled CDC criteria for cases  $\geq$  90 days apart or 45 to 89 days apart based on positive RT-PCR, and based on our study definition, cases were classified as reinfection rather than relapse based on interval negative RT-PCR. Genomic sequencing of samples would have allowed for a direct assessment of whether the CDC investigative criteria matched the genomic data and thus lend further credibility to the recommendations. We were not able to confirm if COVID-19 was the primary diagnosis prompting hospitalization, if patients were incidentally found to test positive for SARS-CoV-2 upon admission for an unrelated illness, or later became symptomatic during the hospitalization course. Diagnoses may be more likely to be incidental if associated with ICD-10 codes for preprocedural exam (e.g., elective surgery); however, a preprocedural exam at the time of the second positive test was noted for only one patient in our study (PT2). Finally, repeatedly positive tests do not necessarily mean a reinfection, and persistent infection or relapse cannot be ruled out, particularly if signs and symptoms observed at the second positive test are similar to those seen in individuals with post-acute sequelae of COVID-19 (or "long COVID").

Despite these limitations, our study provides a comprehensive characterization of demographic, clinical, and SARS-CoV-2 testing data for patients with repeatedly

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positive SARS-CoV-2 tests in a large EHR database across the United States, which could help prioritize suspected cases of reinfection for investigation in the absence of sequencing data and for continued surveillance of potential long-term health consequences of SARS-CoV-2 infection. Further investigation into the risk of reinfection by type and degree of immunosuppressive condition, medications, and disease chronicity, as well as evaluation of immune response after initial SARS-CoV-2 infection, will be valuable for future goals of prevention, mitigation of risk factors, and reduction of illness severity.

### **MATERIALS AND METHODS**

This retrospective study used the COVID-19 data set collected by Optum (12), a unit of United Health Group that provides multiple services, including health plans, pharmacy benefits, data, and analytics. The data set implements a low-latency data acquisition model that aggregates deidentified EHR data from over 700 hospitals and 7,000 clinics across the continuum of care. As of 20 August 2020, the Optum COVID-19 data set included 73,702 patients with a COVID-19 diagnosis code (ICD10 U07.1) that was laboratory confirmed with a positive SARS-CoV-2 PCR test, of whom 690 had 2 positive PCR test results separated by at least 1 negative test result. The study sample was further restricted to patients who had 2 consecutive negative test results >24 h apart between 2 positive test results (n = 79); of these patients, 4 had at least 90 days between their 2 positive tests and another 19 had at least 60 days between their 2 positive tests were disregarded.

Demographic and clinical information, including age, gender, race/ethnicity, smoking status, and body mass index (BMI), was extracted. Smoking and BMI were based on the patient's most recent record within 1 year prior to the index date (first SARS-CoV-2-positive test date). Available EHR data for the 23 patients were manually reviewed. The prevalence of chronic medical conditions which are considered risk factors for COVID-19 was ascertained, including insulin-dependent type 2 diabetes, hypertension, chronic kidney disease (CKD), respiratory disease (including chronic obstructive pulmonary disease), car-diovascular disease (CVD), atrial fibrillation, and immunocompromising conditions (including alcohol-related; solid organ transplant; cancer; and protein-calorie malnutrition). Symptoms typical of COVID-19 were ascertained for each patient during each of two time periods, within 30 days before and after the index date and the second positive test date. In addition, severe clinical outcomes related to COVID-19 illness and medications commonly used to treat COVID-19 were ascertained during each time period, including the following: hospitalization, intensive care unit (ICU) admission, mechanical ventilation, tra-cheostomy, amputation, or death (at second positive test).

Continuous variables were expressed as median (25th and 75th percentile) and categorical variables as counts (percentages). Missing data were not imputed.

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