Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The coronavirus disease 2019 (COVID-19) pandemic continues its global spread. Coordinated effort on a vast scale is required to halt its progression and to save lives. Electronic health record (EHR) data are a valuable resource to mitigate the COVID-19 pandemic. We review how the EHR could be used for disease surveillance and contact tracing. When linked to “omics” data, the EHR could facilitate identification of genetic susceptibility variants, leading to insights into risk factors, disease complications, and drug repurposing. Real-time monitoring of patients could enable early detection of potential complications, informing appropriate interventions and therapy. We reviewed relevant articles from PubMed, MEDLINE, and Google Scholar searches as well as preprint servers, given the rapidly evolving understanding of the COVID-19 pandemic.

Coronavirus disease 2019 (COVID-19), an ongoing worldwide pandemic disease caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has a wide spectrum of disease severity with diverse presentation and organ system involvement. More than 148 million cases have been documented and more than 3.1 million deaths have resulted worldwide as of April 27, 2021.1 A coordinated scientific effort on a vast scale is necessary to mitigate the widespread misery, morbidity, and mortality inflicted by the pandemic.

Many similarities have been drawn between the current pandemic and the influenza pandemic of 1918. However, one major difference is the availability of several data sources to track and to mitigate the effects of the pandemic. In this review, we examine use of the electronic health record (EHR) to address the COVID-19 pandemic. EHR data can facilitate disease surveillance and contact tracing; enable risk stratification and real-time monitoring for early detection and management of severe disease; identify risk factors and disease complications, including long-term sequelae; provide insights into the pathophysiologic process using “omics” approaches; and serve as a platform for innovations related to artificial intelligence, remote monitoring, and early detection of pandemics.

DISEASE SURVEILLANCE AND CONTACT TRACING

Outbreaks of infectious diseases are traditionally monitored by active surveillance and contact tracing. Contact tracing is a time-consuming process whereby the individual representing the index case detected by surveillance is asked to provide details about other people who were in close contact during the time frame that puts them at risk of acquiring infection. Public health officials then trace these contacts and inform them about the possible exposure, leading to quarantine and testing.2 Given the extent of the COVID-19 pandemic and its rapid spread, conventional contact tracing is not feasible in most regions; however, mobile device data linked to the EHR are a potential alternative. Various apps for mobile devices have been developed to collect and to share COVID-19—related tracking information.3 App users can enter information when they test positive with COVID-19, and other users are then alerted if they were close to an infected individual during a prespecified amount of time before testing positive.4
This information can also be shared with public health officials, depending on the permissions and capabilities of the app, and it could be linked to the EHR of health systems, triggering an alert in the system when an individual tests positive for COVID-19 (Figure 1). The public-private collaboration Sync for Science is an example of how individuals could share such EHR data with researchers. These approaches may improve modeling of COVID-19 transmission as shown in studies from Brazil and the United States that used mobile phone geolocation data. However, it is important to balance public good with personal privacy in employing such techniques. Tracking of cases and data on infection rates, deaths, hospitalization, and patient recovery metrics at the local/county, state/district, national, and global levels is critical to inform policy and strategy related to the pandemic. This has led to creation of publicly available online tracking tools such as the COVID-19 Dashboard developed by the Johns Hopkins University.

ELECTRONIC HEALTH RECORD–BASED ALGORITHMS FOR RISK STRATIFICATION

Risk Stratification

Phenotyping algorithms can be deployed across EHR systems to rapidly ascertain comorbidities, multiorgan complications, and disease severity in patients with COVID-19. Predictive electronic algorithms could identify patients heading toward invasive ventilator support and allow early interventions to reduce risk of progression. These algorithms leverage rule-based strategies or machine learning to help identify patients with a particular clinical profile by querying a wide spectrum of EHR data elements, such as coded diagnoses and procedures or clinical notes through natural language processing, laboratory tests, medications, and imaging studies. As case numbers continue to rise throughout the world, substantial EHR data are being generated for patients

ARTICLE HIGHLIGHTS

- This review summarizes the potential of the electronic health record for COVID-19 surveillance, contact tracing, identification of genetic susceptibility variants, risk stratification, and real-time monitoring.
- We discuss how such approaches can be useful in gaining insights into COVID-19 risk factors, pathophysiologic changes, disease complications, and drug repurposing.
- We describe how new consortia are assembling to identify factors influencing susceptibility to COVID-19 and disease severity through linkage of “omics” data to electronic health record data.
who have tested positive for COVID-19 and subsequently developed related complications. One study used data from the health system in Ontario, Canada, to develop a logistic regression–based model that included age and the presence of certain comorbidities (diabetes, renal disease, and immunocompromised state) to predict mortality. In UK Biobank participants, a model including clinical risk factors and 64 single-nucleotide variants was developed to predict risk of severe COVID-19.

Phenotyping and Common Data Models
The Electronic Medical Records and Genomics (eMERGE) network has created the Phenotype KnowledgeBase to catalog and share electronic phenotyping algorithms across different institutions and to conduct large-scale genomic studies. To date, 94 phenotyping algorithms have been validated, and 53 of those are finalized and publicly available. Whereas many of these are relevant to COVID-19, the eMERGE network is currently developing phenotyping algorithms specific for COVID-19—related complications, including acute myocardial injury, arrhythmias, ischemic stroke, thromboembolic disease, bleeding diathesis, acute kidney injury, and progression to chronic kidney disease, among others. A challenge is to develop algorithms that detect these complications within a narrow window temporally related to acute COVID-19 infection.

Portability of phenotyping algorithms across platforms can be challenging because of heterogeneity of data representations in different institutions and bio-repositories. Recently, PhenX—a catalog of measurement protocols and bioinformatics tools to promote unified study design, data integration, and analyses among researchers—added a COVID-19 page for compiling and distributing COVID-19 protocols currently in use. Common data models, such as the Informatics for Integrating Biology and the Bedside (i2b2) and the Observational Medical Outcomes Partnership, may help harmonize data from diverse EHR systems. Tools to standardize the execution of computable phenotype representations, tools to assess and quantify the portability of phenotyping algorithms, and machine learning–based methodologies for constructing and sharing phenotype classifiers across sites are being developed to facilitate COVID-19 research.

RISK FACTORS AND COMPLICATIONS

Social Determinants of Health
Numerous studies have demonstrated that COVID-19 is not evenly distributed among the population, with higher rates of COVID-19 positivity, hospitalizations, and deaths in individuals with any of the following characteristics: male sex, older age, nonwhite ethnicity, higher body mass index, lower income, and smokers. Reasons for these disparities are likely to include factors such as increased number and severity of comorbid conditions, inability to work from home, and lack of access to health care. Indeed, mobile phone geolocation data reveal that increased rates of infection among disadvantaged socioeconomic groups are in part due to the inability of these groups to reduce mobility to the degree of other groups. Documenting social determinants of health in the EHR can increase our understanding of how these factors are associated with risk of infection and severity of illness.

Comorbidities Associated With Complications of Severe COVID-19
The EHR can aid in the identification of comorbidities related to disease severity and associated complications. Elderly patients with multiple comorbidities make up most of the severely ill patients with COVID-19. These comorbid conditions include obesity, hypertension, diabetes mellitus, and cardiovascular disease, and their presence increases risk of myocardial injury and myocardial infarction, malignant arrhythmias, thromboembolic disease including pulmonary embolism and stroke, acute kidney
| Complication                              | Pathogenesis                                                                                                                                                                                                 | Imaging and laboratory data | Early detection                       | Clinical decision support                                                                 | References |
|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|---------------------------------------|-------------------------------------------------------------------------------------------|------------|
| Immunopathology and cytokine storm       | Proposed causes include down-regulation of ACE2 leading to unopposed angiotensin II in the setting of direct viral infection, genetic variation in inflammatory cascades, and antibody-dependent enhancement from prior exposure to other coronaviruses. | Elevated CRP, IL-6, leukocyte count | Baseline leukocyte count and CRP       | Electronic algorithms incorporating vital signs, laboratory values of inflammatory markers, supplemental oxygen requirements, decline in oxygen saturation could prompt anti-inflammatory therapies (ie, dexamethasone, colchicine, or canakinumab) or cardioprotective therapies (ie, angiotensin receptor blockers) if trials prove these to be effective. | 36-44      |
|                                          | Leads to multiorgan damage including myocardial injury and ARDS. May be involved in multisystem inflammatory syndrome.                                                                                                                                          |                            |                                       |                                                                                           |            |
| Myocardial injury                        | Defined by elevated troponin levels                                                                                                                                                                         | Elevated levels of troponin, NT-proBNP | Baseline troponin and NT-proBNP in all individuals at time of hospitalization/ emergency department evaluation | Periodic monitoring of troponin or NT-proBNP during hospitalization in high-risk individuals could inform decisions on length of stay and need for higher or lower level of care. Electronic algorithms incorporating multiple markers will provide useful prognostication and risk stratification information. | 34,35,45   |
|                                          | Presumably due to hostile inflammatory milieu in many cases, but may be due to direct viral infection, myocardial infarction, or malignant arrhythmias. Associated with adverse outcomes and death in COVID-19 patients.                                                                 |                            |                                       |                                                                                           |            |
|                                          | Could be used to identify high-risk individuals who should be admitted for close observation rather than discharged home.                                                                                                                                     |                            |                                       |                                                                                           |            |

Continued on next page
| Complication                        | Pathogenesis                                                                 | Imaging and laboratory data                        | Early detection                                                                 | Clinical decision support                                                                 | References |
|------------------------------------|------------------------------------------------------------------------------|----------------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|------------|
| Myocarditis                        | Presumed direct myocyte infection by SARS-CoV-2 through ACE2 receptor        | Cardiac MRI, ECG, and echocardiography             | Requires high index of clinical suspicion                                           | NLP of imaging reports, ECG monitoring, development of new heart failure symptoms, and real-time incorporation of laboratory data | 46-48      |
|                                    |                                                                               |                                                     |                                                                                   |                                                                                           |            |
| Myocardial infarction              | Prothrombotic, systemic inflammatory milieu and elevated shear stress due to increased coronary blood flow requirements can precipitate plaque rupture, resulting in type 1 acute myocardial infarction. | ECG, echocardiography, cardiac stress tests, coronary angiography | Modifications of existing diagnostic protocols examining patient history, ECG, telemetry, age, risk factors, and cardiac troponin levels | Real-time review of troponin levels, telemetry monitoring, and NLP of ECG and imaging reports could identify individuals requiring either coronary angiography or anticoagulation for type 1 or 2 acute myocardial infarctions, respectively. | 49,50      |
|                                    |                                                                               |                                                     |                                                                                   |                                                                                           |            |
| Malignant arrhythmia               | Thought to be due to a combination of myocardial injury, hypoxemia from lung injury, cytokine storm, heightened inflammatory milieu, genetic predisposition, or medication adverse effects | ECG and telemetry                                  | Telemetry monitoring in high-risk individuals, especially if prolonged QT is observed on ECG or the patient is taking high-risk medications | Rapid detection of malignant arrhythmias by telemetry monitoring should prompt medical and electrical defibrillation therapy. | 34,45,51   |
| Coagulopathy and pulmonary vessel thrombosis | Likely multifactorial: inflammatory cytokines, endothelial dysfunction, and | Chest CT angiography, V/Q scan, Doppler ultrasound | Detection of decreased oxygen saturation/ increased oxygen requirements, bradycardia, | Algorithms including real-time incorporation of laboratory values, vital signs, oxygen saturation/ supplemental oxygen | 34,35,52-56|

Continued on next page
| Complication               | Pathogenesis                                                                 | Imaging and laboratory data | Early detection                                      | Clinical decision support                                                                 | References |
|----------------------------|------------------------------------------------------------------------------|----------------------------|-----------------------------------------------------|------------------------------------------------------------------------------------------|------------|
| ischemic stroke            | higher incidence of stroke in patients with severe COVID-19 may result from  | brain MRI, head CT         | evidence of hypercoagulability or elevated inflammatory markers could prompt more frequent neurochecks in hospitalized patients or admission of patients for close monitoring who otherwise might be dismissed from emergency departments. | real-time NLP of nursing notes for neurochecks could prompt stroke pager activation for early imaging and subsequent treatment with fibrinolytic therapy. | 54,57-59   |
| acute renal failure        | more common with underlying chronic kidney disease                           | increased serum creatinine or cystatin C | obtain baseline serum creatinine or cystatin C level. Closely monitor urine output in hospitalized patients. These are especially important in patients with underlying chronic kidney disease or who present with sepsis. | automated algorithms tracking urine output and creatinine or cystatin C trends can alert providers of likely acute renal failure and highlight any nephrotoxic medications that could be held. | 60,61      |
injury, acute respiratory distress syndrome, cytokine storm, and death.\textsuperscript{33,34} Table 1 summarizes these complications and highlights how electronic algorithms linked to clinical decision support can be used for their early detection and management. Figure 2 depicts multisystemic complications that can occur in an infected patient.

**Laboratory Markers of Severe Disease**
Clinical laboratory results are present as structured data in the EHR and can be mined with relative ease, cross-sectionally as well as to profile temporal changes.\textsuperscript{65} The Consortium for Clinical Characterization of COVID-19 by EHR (4CE) consortium,\textsuperscript{66} the eMERGE network, and other consortia are studying the association of laboratory abnormalities with outcomes in COVID-19. Laboratory findings associated with poor outcomes include an increasing white blood cell count with lymphopenia; prolonged prothrombin time; and elevated levels of liver enzymes, lactate dehydrogenase, D-dimer, interleukin 6, C-reactive protein, and procalcitonin.\textsuperscript{7,67,68} Markers of cardiac,\textsuperscript{69} immune,\textsuperscript{70} coagulation,\textsuperscript{71} muscle,\textsuperscript{72} and ACE2, angiotensin-converting enzyme 2; AI, artificial intelligence; aPTT, activated partial thromboplastin time; ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, computed tomography; DIC, disseminated intravascular coagulation; DVT, deep venous thrombosis; ECG, electrocardiography; ECMO, extracorporeal membrane oxygenation; EHR, electronic health record; IL-6, interleukin 6; MRI, magnetic resonance imaging; NLP, natural language processing; NT-proBNP, N-terminal pro-B type natriuretic peptide; PAP, positive airway pressure; PE, pulmonary embolism; PT, prothrombin time; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

| Complication            | Pathogenesis                                                                 | Imaging and laboratory data | Early detection                                                                 | Clinical decision support                                                                 | References |
|-------------------------|------------------------------------------------------------------------------|------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|------------|
| Respiratory failure     | Likely multifactorial, including direct infection of alveolar cells, inflammation including cytokine storm, pulmonary embolism, and neurologic involvement. This can lead to dyspnea with adequate oxygenation, hypoxemia requiring supplemental oxygen or PAP therapy, or ARDS requiring mechanical ventilation, prone positioning, and ECMO. | Chest radiograph, chest CT, ultrasound | Oxygen saturation at home, physician’s office, emergency department, or hospital | Real-time electronic monitoring of oxygen saturation, supplemental oxygen requirements, arterial or venous blood gases with pH, and respiratory rate can alert providers of the high likelihood of impending respiratory failure prompting consideration of escalation to intensive care. | 62-64      |
hepatic, \(^{32}\) and renal,\(^{73}\) injury or dysfunction are also associated with severe disease. Electronic algorithms incorporating real-time laboratory data, especially cardiac troponins and inflammatory markers, could be useful in early detection of complications and linked to clinical decision support for appropriate escalation of care to decrease morbidity and mortality.

**Target Organ Damage**

Although most individuals appear to recover completely after infection with SARS-CoV-2, some have persistent target organ damage. Whereas there are significant data on acute and short-term complications, not much is known about long-term target organ damage in COVID-19 survivors. EHR data will be important for tracking and understanding of persistent target organ damage consequent to COVID-19. Target organ damage can include cardiovascular (eg, myocarditis, pericarditis, microvascular angina, arrhythmias), pulmonary (eg, interstitial lung disease, chronic pulmonary emboli), neurologic (eg, myelopathy, neuropathy, neurocognitive disorders), renal (eg, chronic kidney disease), and others (eg, multisystem inflammatory syndrome in children).\(^{74}\) For example, in a study\(^{77}\) of patients who had recovered from COVID-19 with initial diagnosis occurring between 64 and 92 days previously, most continued to have elevated high-sensitivity

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**FIGURE 2.** Electronic health record—based strategies for early detection of complications in severe COVID-19. Complications include pulmonary, cardiovascular, renal, and neurologic. Myocardial injury in COVID-19 can occur through several nonmutually exclusive mechanisms, including myocarditis, myocardial infarction, cytokine storm, heart strain from pulmonary embolism, and malignant arrhythmias. Blue text highlights areas where early detection through informatics approaches can lead to improvement in patient care. ACE2, angiotensin-converting enzyme 2; ARDS, acute respiratory distress syndrome; CRP, C-reactive protein; IL-6, interleukin 6; MI, myocardial infarction; WBC, white blood cell.
| Repository                        | Description                                                                                                                                                                                                 | Citations                                                                                     |
|----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| **Previously existing repositories** |                                                                                                                                                                                                             |                                                                                              |
| UK Biobank                       | Contains patient health information, clinical laboratory and radiology information, genomic data, and other relevant information from more than 500,000 participants in the United Kingdom. Data regarding COVID-19 are updated frequently and are available to researchers through an application process. Summary statistics are freely available. | https://www.ukbiobank.ac.uk/ 93                                                            |
|                                  |                                                                                                                                                                                                             | https://pan.ukbb.broadinstitute.org/ 94                                                     |
|                                  |                                                                                                                                                                                                             | http://phee.web.sph.umich.edu/SAIGE-UKB/ 95                                                 |
| FinnGen                          | A public-private collaborative effort that brings together Finnish universities, hospital and hospital districts, and a nationwide network of Finnish biobanks to combine genome information with digital health care data from national health registries. FinnGen contains data of more than 135,000 participants (data freeze 3) and is actively collecting data on COVID-19 status of participants based on the Finnish National Infectious Diseases Register and regularly updates this information. Data access can be obtained through collaboration with a FinnGen partner. Summary statistics are freely available. | https://www.finngen.fi/en 96                                                               |
| eMERGE                           | A consortium of multiple academic medical centers throughout the United States with EHR and genotype data for more than 136,000 participants. As part of phase 4, several sites are developing phenotyping algorithms for the early detection of complications from COVID-19. Data can be accessed through collaboration with an eMERGE partner. Electronic phenotyping algorithms from eMERGE are posted to the PheKB website. | https://emerge-network.org/ 97                                                              |
|                                  |                                                                                                                                                                                                             | http://phekb.org 13,14                                                                       |
| MVP                              | A research program that links EHR and genomic data from more than 825,000 US military veterans registered at the Veterans Health Administration. Investigators are analyzing complications of COVID-19 infection; disease severity and outcomes; and response to various medications, including the influence of race and ethnicity on disease susceptibility, severity, and outcomes. | https://www.research.va.gov/mvp/ 98                                                        |
| GenOMICC                         | A global community of scientists and physicians established in 2016 to gather genomic information on patients with critical illness, including COVID, Middle Eastern respiratory syndrome virus, and influenza. They have partnered with the UK-wide COG viral sequencing group and have published a GWAS examining associations of COVID-19 with disease severity as discussed in the main text. | https://genomicc.org/ 99                                                                    |
| **New consortia assembled in the COVID-19 era** |                                                                                                                                                                                                             |                                                                                              |
| COVID-19 Host Genetics Initiative| A consortium created to foster the sharing of resources, such as protocols to facilitate COVID-19 host genetics research; to organize and coordinate analyses across participating sites; and to provide a platform to share summary-level and individual-level data among the scientific community. This initiative currently includes ~190 individual studies, a number that will grow as more biobanks/EHR-linked biorepositories contribute COVID-19–related data. | https://www.covid19hg.org/ 100-102                                                          |
| N3C                              | A repository of patient-level data from many clinical centers within the United States that will use common data models to reveal patterns of risk factors, comorbidities, and testing among COVID-19 patients. This collaborative currently includes more than 120,000 positive COVID-19 patients and hundreds of thousands of negative controls. | https://ncats.nih.gov/n3c 103                                                                |
| 4CE                              | A consortium that collects COVID-19 cases from 96 hospitals in 5 countries including France, Germany, Italy, Singapore, and the United States. It seeks                                                                                                                                 | https://covidclinical.net/ 66,104                                                            |
troponin levels, lower left ventricular systolic function, and imaging evidence of ongoing myocardial inflammation.

“Long COVID”
Many individuals experience persistent symptoms and a decline in health-related quality of life after COVID-19. These can include a variety of nonspecific symptoms, such as chest pain, shortness of breath, fatigue, headache, loss of taste and smell, and brain fog. Whether COVID-19 survivors will completely recover from these persistent symptoms is not yet clear. Congress recently allocated $1.15 billion for the National Institutes of Health to support research into “long COVID.” This includes efforts to develop an EHR-based registry detailing symptoms that is linked to blood, tissue, and other samples from patients. The EHR data will be valuable to further characterize "long COVID."

**ELECTRONIC HEALTH RECORD—BASED OMICS APPROACHES**

**Viral Genomics**
The SARS-CoV-2 is a positive-sense single-stranded RNA virus with a genome of about 30 kilobases. It has a high mutation rate similar to other RNA viruses, potentially allowing altered infectivity, pathogenesis, and development of drug resistance and vaccine evasion. Presently, EHR systems do not track the genetic variants detected in patients, but as sequencing of SARS-CoV-2 genomes becomes more common, such information could be incorporated in the EHR to trace clusters of community-acquired transmission and to identify specific concerning variants. This information can also be used to monitor success of control measures, treatments, and vaccination efforts. Tracing mutation hot spots and conserved regions in the viral genome could inform future drug and vaccine development and appropriate contact and travel restrictions to curb spread of new variants.

**Host Genomic Studies**
Host genomes influence disease severity for many respiratory pathogens, including COVID-19. Early studies primarily addressed epidemiologic and clinical characteristics of COVID-19 and the characteristics of the SARS-CoV-2 genome. As interindividual variation in
COVID-19 disease severity became apparent, a search began for host genetic variants that may underlie this variability. The linkage of EHR data to patient genotype/sequence data from DNA biorepositories allowed rapid assembly of large national and international consortia to better understand the contribution of common DNA sequence variants to COVID-19 disease severity \(^9^1,^9^2\) (Table 2; Figure 3).

The first genome-wide association study (GWAS) \(^9^1\) of COVID-19 severity included approximately 2000 COVID-19 patients with respiratory failure from 7 hospitals in Europe. Genetic variants in loci involved in inflammation pathways that functionally interact with the SARS-CoV-2 cellular receptor angiotensin-converting enzyme 2 and the ABO blood groups were associated with severe disease; risk was higher in patients with blood group A than in patients with other blood groups, and lower risk was found in patients with blood group O compared with other blood groups, consistent with previous studies implicating the ABO locus in susceptibility to infection with SARS-CoV-2 \(^9^1,^1^0^7,^1^0^8\). An additional GWAS and transcriptome-wide association study from the Genetics of Mortality in Critical Care (GenOMICC) consortium in the United Kingdom \(^1^0^9\) included 2244 patients with severe disease and identified variants in multiple genes, many of which are known to be involved in innate immunity, to be associated with disease severity. Some of these variants hint at specific targets for novel drug development. A GWAS \(^1^0^2\) meta-analysis of 46 studies including...
49,562 case patients and more than 2,000,000 controls with diverse ancestries found 15 variants (13 of them novel) associated with COVID-19. This study differed from the prior GWAS in that it examined infection susceptibility in addition to hospitalization and severe illness. The 25 genetic susceptibility variants discovered to date are listed in the Supplemental Table (available online at http://www.mayoclinicproceedings.org). As additional genetic susceptibility loci are discovered, it may be possible to combine these into a polygenic risk score for severe disease that could be integrated in the EHR for risk stratification.110,111

Rare variant analyses have been enabled by exome and genome sequencing data. The COVID Human Genetic Effort discovered 24 rare, deleterious genetic variants in 8 genes mediating type I interferon antiviral immunity that are enriched in patients who develop life-threatening COVID-19 compared with patients with mild or asymptomatic presentations of COVID-19.38 In a study of 2 families112 with multiple young, previously healthy men who developed severe COVID-19 in The Netherlands, separate mutations in TLR7 leading to loss of function of an important innate immunity—sensing protein were identified. These studies highlight that rare genetic variants in various key genes and pathways could have an impact on COVID-19 disease susceptibility.

Proteomic and Metabolomic Studies
Integration of various omics approaches could provide novel insights into COVID-19 pathogenesis. Certain metabolomic profiles can distinguish COVID-19—positive patients from uninfected controls,126 whereas others can predict risk of death from COVID-19.121 Proteomic and metabolomic data can be combined with genotype expression data as demonstrated in a study116 that investigated whether commonly used drugs affect angiotensin-converting enzyme 2 and transmembrane protease serine 2 and therefore might alter risk of infection with SARS-CoV-2. Shen et al122 applied metabolomics and proteomic profiling to serum from 46 patients with COVID-19 and 53 controls to demonstrate that 93 proteins were differentially expressed in patients with severe COVID-19 and 204 metabolites correlated with COVID-19 severity. Furthermore, pathway analysis showed metabolic and immune dysregulation in COVID-19 patients, consistent with findings from other studies with different designs.

TREATMENT

Repurposing Drugs and Vaccines
The EHR captures medication data, providing an opportunity to evaluate the benefit of therapies for COVID-19 as well as adverse effects and complications of novel therapies. Such data may also be useful for profiling patients for clinical trial eligibility and for insights into drug repurposing. Using EHR data from the French National Health Data System, Semenzato et al123 showed that COVID-19 patients receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers had a lower risk of hospitalization, intubation, and death than patients using calcium channel blockers as their antihypertensive medications. Gupta et al124 used EHR data from hospitals in the United States to make the observation that hospitalized patients with COVID-19 receiving statins had lower mortality than those not taking statins. Castro et al125 used the EHR for an agnostic approach to identify ibuprofen, naproxen, and...
valacyclovir use as being associated with lower risk of hospitalization in patients with COVID-19. Data from the Mayo Clinic EHR revealed that individuals who received various vaccines (high-dose influenza, measles-mumps-rubella, Haemophilus influenzae type B, pneumococcal conjugate, hepatitis A, hepatitis B, or varicella) within the previous 5 years had decreased rates of COVID-19. The EHR-based omics studies mentioned may provide useful insights into new drug development or drug repurposing.

**Targeted Medical Therapy**

Variants can be associated with either improved therapeutic outcomes or adverse reactions for drugs being trialed for COVID-19; these variants are being tracked by the Pharmacogenomics Knowledge Base. These variants can be placed in the EHR to inform decisions related to selection of drug therapy. In addition, EHR-based algorithms and clinical decision support can be used to notify medical providers if patients meet preset criteria for use of certain medical therapies to improve care; these might include dexamethasone (if supplemental oxygen is required), monoclonal antibody therapy (on the basis of age and presence of certain comorbidities), or potential eligibility for experimental therapeutics and clinical trials.

**Electronic Health Record—Based Innovations**

**Artificial Intelligence and the EHR**

Artificial intelligence is being integrated into dashboards within the EHR to assist clinicians in real-time monitoring. Wagner et al. used deep neural networks to examine clinical notes in the EHR for patients who eventually developed COVID-19. They identified multiple symptoms predictive of subsequent development of COVID-19 and included these in an augmented intelligence platform, allowing an EHR tool to assist clinicians for early diagnosis of COVID-19. The US Food & Drug Administration issued an Emergency Use Authorization for artificial intelligence—enhanced electrocardiography to detect left ventricular dysfunction in patients with COVID-19, and this has been successfully used in the clinical setting. In addition, artificial intelligence—enhanced electrocardiography for diagnosis of COVID-19, possibly even in presymptomatic patients, is being explored for potential use in portable devices to rapidly screen individuals.

**Remote Monitoring**

Infectious pandemics such as COVID-19 can overwhelm medical facilities, and there is a need for hospital-at-home models to care for less severely ill patients at home, thus decreasing transmission risk and freeing up hospital beds for more critically ill patients. Telemedicine can be used to manage not only mild disease but also severe disease by providing expanded access to critical care. Electronic phenotyping algorithms, including “real-time” natural language processing, can detect complications in patients with COVID-19, facilitate timely triage to intensive care units, and determine clinical trial eligibility. Such alerts can be linked to clinical decision support tools to provide guidance at the point-of-care and can identify individuals at high risk who may benefit from home oximetry, hospitalization, or early escalation of level of care in the hospital to the intensive care unit as well as identify individuals for clinical trials and drug repurposing. A critical care physician could monitor patients in small rural hospitals remotely, guiding local nurses, respiratory therapists, and hospitalists to adjust medications or ventilators and to perform interventions as needed.

**Early Detection of the Next Pandemic**

The COVID-19 pandemic has highlighted the importance of early detection of outbreaks, rapid response, and mitigation strategies to prevent escalation. The International Society for Infectious Diseases created ProMED, which allows various public health agencies to post information about potential or confirmed outbreaks of known or novel infectious diseases for the global community to view. The sobering experience with the COVID-19 pandemic should
motivate a global data collaborative for early detection of outbreaks that may lead to pandemics. This can include data from a variety of sources, including the EHR, Internet search engine queries of symptoms, and artificial intelligence monitoring of news reports around the world. Indeed, the Big Data and the Global Public Health Intelligence Network and the Meaningful Integration of Data Analytics and Services platform are exploring strategies for early recognition of the next pandemic.

CONCLUSION
To mitigate global pandemics such as COVID-19, international collaborations that share EHR data using common data models are key. Phenotyping algorithms based on billing codes, laboratory and medication data, and natural language processing of clinical notes are useful for monitoring disease epidemiology and severity. Such algorithms enable rapid automated phenotyping for genomic studies and drug repurposing efforts. Data sharing between EHRs of health systems, public health entities, and patients through mobile apps can improve disease tracking and contact tracing to limit spread. By linkage to clinical decision support tools for point-of-care patient management, EHR algorithms for early detection of complications can improve patient outcomes. Such surveillance can detect high-risk individuals who may benefit from increased monitoring either at home or through early hospitalization. Together, various EHR-centered approaches can improve patient care and advance the scientific understanding needed to combat and to end the COVID-19 pandemic.

SUPPLEMENTAL ONLINE MATERIAL
Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: COVID-19 = coronavirus disease 2019; EHR = electronic health record; eMERGE = Electronic Medical Records and Genomics; GWAS = genome-wide association study; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Grant Support: This work was funded by a supplemental award HG006379-0951 from the National Human Genome Research Institute. IJK is supported by National Human Genome Research Institute grant HG006379 and National Heart, Lung, and Blood Institute award K24 HL130710. B.A.S. was supported by the Mayo Clinic Clinician-Investigator Training Program.

Potential Competing Interests: The authors report no competing interests.

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