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REVIEW ARTICLE

Community-Acquired Pneumonia due to Endemic Human Coronaviruses compared to 2019 Novel Coronavirus: A Review

Julio A. Ramirez[1,2], MD; Ruth Carrico[1,2], PhD; Rodrigo Cavallazzi[2,5], MD; Leslie Beavin[1,2], MD; Anupama Raghuram[1,2], MD; Mark V. Burns[1,2], MD; Kamran Mahmood[1,2], MD; Darmaan Aden[1,2], MD; Angeline Prabhu[1,2], MD; Dawn Balcom[1,2], DNP; Stephen Furmanek[1,2], MPH; Leslie Wolf[1,2,4], PhD; Kenneth E. Palmer[5], PhD; Mahder Tella[1,2], MPH; Connor Glick[1,2], MS; Forest W. Arnold[1,2], DO; for the Center of Excellence for Research in Infectious Diseases (CERID) Coronavirus Study Group[2]*

[1]Division of Infectious Diseases, Department of Medicine, School of Medicine, University of Louisville, Louisville, KY, USA; [2]Center of Excellence for Research in Infectious Diseases (CERID) Coronavirus Study Group, University of Louisville, Louisville, KY, USA (see Appendix); [3]Division of Pulmonary, Critical Care, and Sleep Disorders Medicine, Department of Medicine, School of Medicine, University of Louisville, Louisville, KY, USA; [4]Louisville Metro Department of Public Health and Wellness, Louisville, KY, USA; [5]Center for Predictive Medicine for Biodefense and Emerging Infectious Diseases, University of Louisville, Louisville, KY, USA

[*]j.ramirez@louisville.edu

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Abstract

The human coronaviruses (HCoVs) are an important etiology of community-acquired respiratory tract infections. Community-acquired pneumonia (CAP) may be caused by serotypes of endemic HCoVs or highly pathogenic HCoVs. In this review we compared clinical characteristics, management, outcomes, and infection control practices for patients with CAP due to endemic HCoVs versus patients with CAP due to 2019 novel coronavirus (SARS-CoV-2).

Introduction

There are four serotypes of HCoVs that are endemic and three highly pathogenic HCoVs (**Figure 1**). Endemic HCoVs cause respiratory tract infection in children and adults globally. We recently reported our experience with adults hospitalized with CAP due to endemic HCoVs in the city of Louisville, Kentucky.[1] The first cases of CAP due to highly pathogenic HCoVs, the severe acute respiratory syndrome coronavirus (SARS-CoV), were identified in China in 2002.[2] Cases of CAP due to a second highly pathogenic HCoV, the Middle East respiratory syndrome coronavirus (MERS-CoV), were identified in Saudi Arabia and Qatar in 2012.[3, 4] More recently, cases of CAP due to the 2019 novel coronavirus (2019-nCoV) were identified in the city of Wuhan, China at the end of 2019.[5] Based on phylogeny, this new coronavirus is recognized as a sister of the SARS-CoV, and the Coronavirus Study Group of the International Committee on Taxonomy of Viruses is proposing to designate this new virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[6] The World Health Organization is now officially calling the disease COVID-19 (**CO** for corona, **VI** for virus, **D** for disease, and **19** for the year 2019). Having a name for the virus (2019-nCoV or SARS-CoV-2) and a different name for the disease (COVID-19) will help with the nomenclature of future coronavirus outbreaks. The spectrum of disease for patients presenting with COVID-19 is depicted in **Figure 2**.

In this manuscript we first compared the clinical characteristics and outcomes of patients with CAP due to endemic HCoVs admitted to hospitals in the city of Louisville [1] versus patients with CAP due to the 2019-nCoV admitted to hospitals in the city of Wuhan.[7] We subsequently reviewed our current understanding of the risk factors, diagnosis, infection control practices, and management of patients with CAP due to endemic HCoVs and the 2019-nCoV or SARS-CoV-2.

Clinical Presentation and Outcomes

The demographics, comorbidities, and signs and symptoms of 42 patients hospitalized with endemic HCoVs as the only etiology of CAP from the city of Louisville [1] and the first 41 patients reported in the literature with CAP due to the 2019-nCoV from the city of Wuhan [7] are depicted in **Table 1**. The age distribution of both groups is depicted in **Figure 3**. Patients infected with the 2019-nCoVs are younger and present with less co-

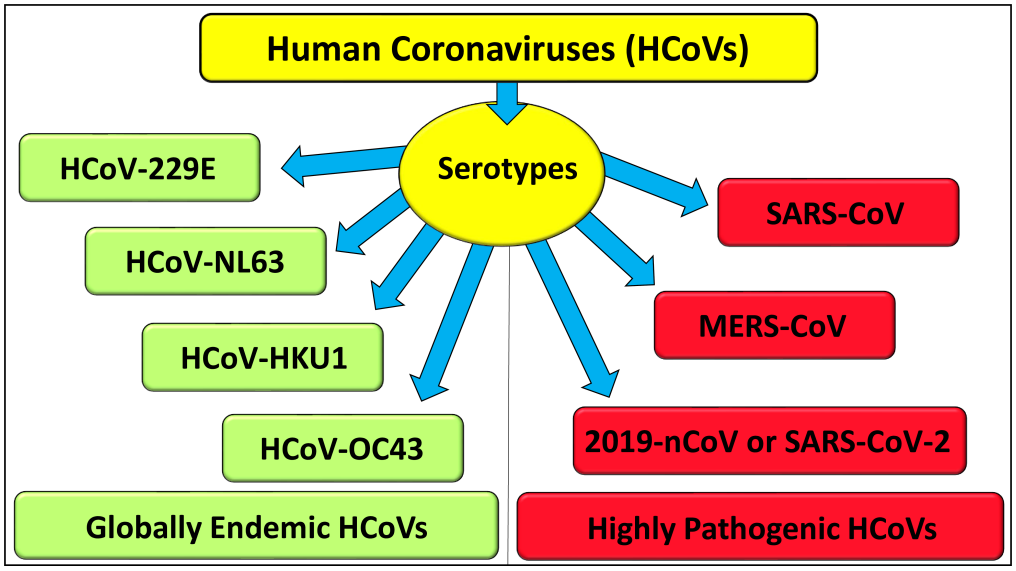

Figure 1. Serotypes of HCoVs globally endemic and highly pathogenic. SARS-CoV: Severe acute respiratory syndrome coronavirus. **Abbreviations:** MERS-CoV, Middle East respiratory syndrome coronavirus; 2019-nCoV, 2019 novel coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

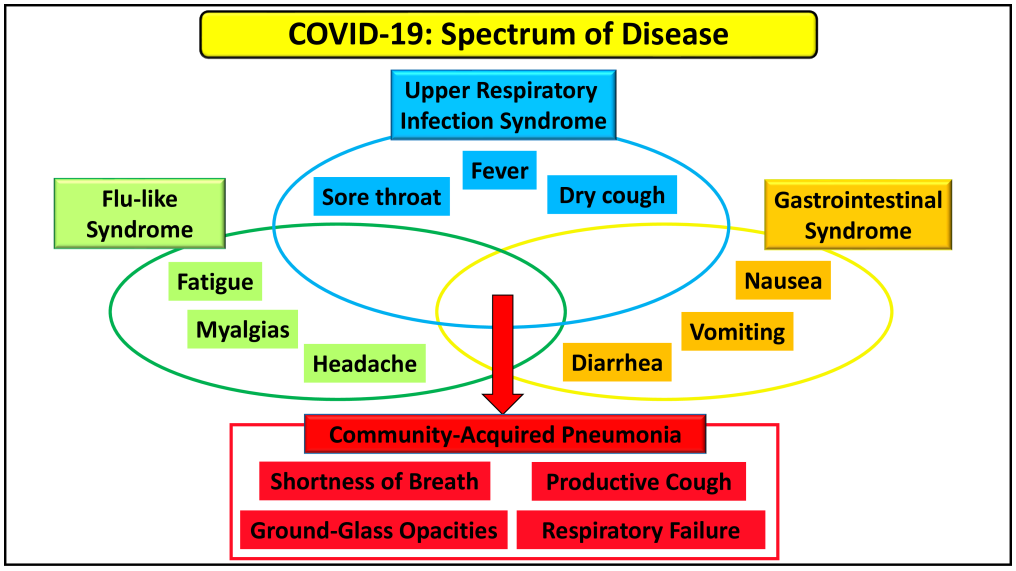

Figure 2. Spectrum of disease for patients presenting with COVID-19.

Table 1. Demographics, comorbidities, and signs and symptoms of 42 patients with CAP due to endemic CoVs from the city of Louisville and the first 41 patients reported in the literature with CAP due to the 2019-nCoV from the city of Wuhan.

Variable	Louisville Endemic CoV (*n*=42)	Wuhan 2019-nCoV (*n*=41)
Demographics		
Age, years	71 [54, 82]	49 [41, 58]
Sex (%)		
Men	18 (43)	30 (73)
Women	24 (57)	11 (27)
Current Smoker (%)	9 (21)	3 (7)
Comorbidities		
Any Comorbidity (%)	39 (93)	13 (32)
Diabetes (%)	15 (36)	8 (20)
Hypertension (%)	30 (71)	6 (15)
Cardiovascular disease (%)	15 (36)	6 (15)
Chronic obstructive pulmonary disease (%)	15 (36)	1 (2)
Malignancy or active neoplastic disease (%)	7 (17)	1 (2)
Liver Disease (%)	3 (7)	1 (2)
Signs and symptoms		
Highest temperature, ℃ (%)		
<37.3	20 (48)	1 (2)
37.3-38.0	4 (10)	8 (20)
38.1-39.0	11 (26)	18 (44)
>39.0	7 (17)	14 (34)
Systolic pressure, mm Hg	120 [103.0, 133.0]	125 [119.0, 135.0]
Respiratory rate >24 breaths per min (%)	17 (40)	12 (29)

Abbreviations: CAP, community-acquired pneumonia.
Dichotomous variables are reported as frequency/total (%); continuous variables are reported as median [interquartile range].

morbidities when compared to patients infected with endemic HCoVs. **Table 2** compares the laboratory and radiographic findings of both groups. Patients with CAP due to 2019-nCoV presented with lower white blood cells count and higher elevations in liver enzymes. In both groups of patients, procalcitonin levels were low, as expected of patients with viral CAP. The presence of pulmonary infiltrates with bilateral involvement was present in almost 100% of patients in both groups. The treatments and outcomes of both groups are depicted in **Table 3**. In the initial report of CAP due to 2019-nCoV, the high mortality of 15% was likely a reflection of a more critically ill population of patients being initially recognized with the disease. A second case series, including 139 hospitalized patients with 2019-nCoV, reported a mortality of 4%.[8] This mortality is similar to the one that we reported for hospitalized patients with endemic HCoVs of 2%.

Risk Factors and Diagnosis

The incubation period of 2019-nCoV is thought to range from 3 to 14 days, with most patients developing clinical manifestations within the first week following exposure. Since an infected person may be asymptomatic for up to 14 days, a patient with fever and/or symptoms of respiratory tract infection should be considered at risk of 2019-nCoV infection if: 1) the patient, within the prior 14 days, resided in or traveled to China, or 2) the patient, within the prior 14 days, had close contact with a confirmed or suspected case of 2019-nCoV infection. In a patient at risk of 2019 nCoV infection, the diagnosis is confirmed by performing a PCR of specimens from the upper respiratory tract (e.g. nasopharyngeal or oropharyngeal secretions) using 2019-nCoV primers.

Infection Control Measures

There are four areas of infection control practice that are relevant for the safety of healthcare workers caring for patients with CAP due to endemic HCoVs as well as the 2019-nCoV. They include early recognition and isolation, selection and use of personal protective equipment, performance of hand hygiene, and environmental infection control. The specific infection control recommendations for endemic HCoVs and 2019-nCoV are depicted in **Table 4**.

In a recent report of 138 patients hospitalized with 2019-nCoV infection, the authors estimated that nosocomial transmission of the virus may have occurred in

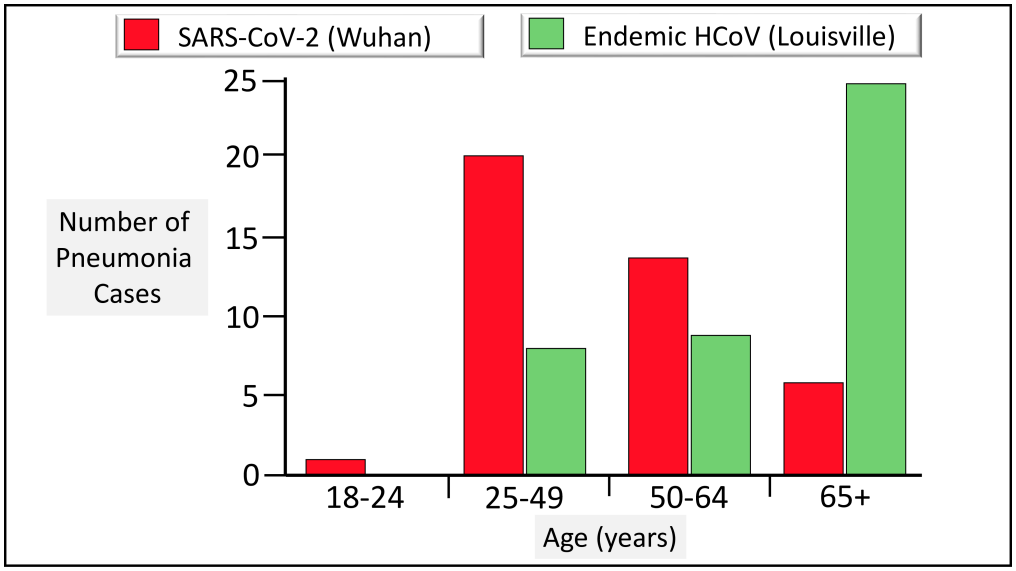

Figure 3. Age distribution of 42 patients with CAP due to endemic human CoVs from the city of Louisville and the first 41 patients reported in the literature with CAP due to the 2019-nCoV or SARS-Cov-2 from the city of Wuhan.

Table 2. Laboratory and radiographic findings of 42 patients with CAP due to endemic CoVs from the city of Louisville and the first 41 patients reported in the literature with CAP due to the 2019-nCoV from the city of Wuhan.

Variable	Louisville endemic CoV (*n*=42)	Wuhan 2019-nCoV (*n*=41)
White blood count per 1000/μL	11.0 [9.1, 15.2]	6.2 [4.1, 10.5]
$<$4	2/41 (5)	10/40 (25)
4–10	14/41 (34)	18/40 (45)
$>$10	25/41 (61)	12/40 (30)
Platelets per 1000/μL	229 [173, 266]	164.5 [131.5, 263.0]
$<$100	2/42 (5)	2/40 (5)
$\geq$100	40/42 (95)	38/40 (95)
Albumin, g/dL	36.0 [34.0, 40.0]	31.4 [28.9, 36.0]
Alanine transferase (ALT), U/L	27 [21, 36]	32 [21, 50]
Aspartate transaminase (AST), U/L	23 [20, 32]	34 [26, 48]
$\leq$40	32/39 (82)	26/41 (63)
$>$40	7/39 (18)	15/41 (37)
Bilirubin ,mg/dL	0.6 [0.5, 0.9]	0.7 [0.6, 0.8]
Potassium ,mmol/L	4.0 [3.7, 4.4]	4.2 [3.8, 4.8]
Serum sodium ,mmol/L	138 [135, 140]	139 [137, 140]
Procalcitonin (μg/mL)	0.1 [0.1, 0.3]	0.1 [0.1, 0.1]
$<$0.1	7/14 (50)	27/39 (69)
$\geq$0.1 to $<$0.25	3/14 (21)	7/39 (18)
$\geq$0.25 to $<$0.5	2/14 (2)	2/39 (5)
$\geq$0.5	2/14 (2)	3/39 (8)
Hypersensitive troponin, pg/mL	20.5 [10.0, 38.5]	3.4 [1.1, 9.1]
$>$28	12/28 (43)	5/41 (12)
Bilateral involvement of chest radiographs	41/42 (98)	40/41 (98)

Abbreviations: CAP, community-acquired pneumonia; CoV, coronavirus.
Dichotomous variables are reported as frequency/total (%); continuous variables are reported as median [interquartile range].

Table 3. Treatment and outcomes of 42 patients with CAP due to endemic CoVs from the city of Louisville and the first 41 patients reported in the literature with CAP due to the 2019-nCoV from the city of Wuhan.

Variable	Louisville Endemic CoV (*n*=42)	Wuhan 2019-nCoV (*n*=41)
Shock with need for vasopressors (%)	3 (7)	3 (7)
Non-invasive ventilation (%)	3 (7)	10 (24)
Invasive mechanical ventilation (%)	3 (7)	2 (5)
Death (%)	1 (2)	6 (15)

Table 4. Specific infection control recommendations for patients infected with endemic human coronaviruses (HCoVs) and 2019 novel coronavirus (2019-nCoV) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

	Endemic HCoVs	2019-nCoV or SARS-CoV-2
Isolation	Standard precautions, private room not required	Airborne isolation room providing verified negative airflow in combination with contact isolation
Personal protective equipment	Not recommended	Barrier use (e.g., eye protection, gowns and gloves) to prevent contact with body fluids, such as respiratory secretions that may be projected during cough. Respirator use in accordance with airborne isolation.
Hand hygiene	Alcohol-based hand rubs	After removal of gloves, alcohol-based hand rubs
Environmental disinfection	Use of an EPA-registered disinfectant approved for use in healthcare.	Use of an EPA-registered disinfectant approved for use in healthcare.

Abbreviations: EPA, Environmental Protection Agency.

40% of the patients.[8] They considered transmission from patient to patient in 17 patients (12%) and transmission from patient to health care worker in 40 patients (29%). It is important that several patients in this report were not placed in respiratory isolation at the time of hospital admission because the initial patient's complaints were related to atypical abdominal symptoms. As depicted in **Figure 2**, some patients may have a gastrointestinal syndrome as initial presentation of Covid-19. In these cases, the virus may be transmitted via the fecal-oral route.

ICU Management

Some parallels can be made to the prior two epidemic strains, MERS-CoV and SARS-CoV in transmission and clinical features and thus ICU management strategies implemented in those epidemics could be applied currently. Clinicians at University of Toronto described specific challenges in oxygenating patients with SARS-CoV.[9] The use of oxygen therapy with aerosol humidifiers was suspected to increase the risk of droplet transmission. Additional routine ICU procedures were deemed high risk due to infection control concerns including intubation and extubation, nasopharyngeal swab, bag-valve-mask ventilation, suctioning, non-invasive positive pressure ventilation (NIPPV), and high frequency oscillation. Disconnection from the ventilator and manual bag ventilation was discouraged due to concerns for droplet spread even in cases of cardiac arrest unless an obvious mechanical failure was suspected.

Ventilator management of SARS-CoV mirrored that of acute respiratory distress syndrome (ARDS). Similar observations were made with the MERS-CoV outbreak as described by clinicians in Jeddah, Saudi Arabia.[10] Management of respiratory failure with NIPPV was strongly discouraged as it almost always lead to intubation and also carried significant risk of droplet spread.

In patients who develop ARDS leading to invasive ventilation, we consider a strategy of low tidal volume (4 to 6 ml/ Kg of predicted body weight) and the use of positive-end-expiratory pressure titrated according to the requirement of oxygen. The plateau pressure should be maintained at less than 30 cmH2O.[11] We also consider monitoring driving pressure, since higher driving pressure values have been associated with higher mortality in patients with ARDS.[12] In the setting of refractory hypoxia, other strategies should be considered such as prone position and extracorporeal membrane oxygenation.[13, 14]

Therapy

The majority of the proposed therapies for CAP due to human coronavirus came to light during the SARS-CoV and MERS-CoV outbreaks in 2003 and 2012, respectively. Treatment options evaluated in clinical studies included antivirals, such as ribavirin, antiretrovirals such as lopinavir/ritonavir, steroids, interferon, and macrolides. In most reports, these therapies have been used in combination without a clear clinical benefit.

Remdesivir is a novel nucleotide analogue with activity against SARS and MERS-CoV in vitro and in animal studies.[15] Remdesivir was utilized as a compassionate use investigational drug in the first described US case of 2019-nCoV in January 2020. The patient had mild initial symptoms that progressed to pneumonia on the ninth day of admission, with rapid clinical improvement after treatment with remdesivir. This novel agent is being considered for further randomized clinical trials in China to establish efficacy in humans during the current 2019-nCoV outbreak. Investigators from the National Institute of Allergy and Infectious Diseases (NIAID) are preparing to test remdesivir, as well as lopinavir/ ritonavir (Kaletra), and interferon-beta for their activity against 2019-nCoV.[16]

Prospect for a Vaccine

The NIAID Vaccine Research Center is leading the efforts to develop a vaccine for the 2019-nCoV. Investigators are using a messenger RNA platform to produce the viral spike protein of 2019-nCoV. The NIAID anticipates the experimental vaccine will be ready for testing in a phase 1 trial in the coming months.[16]

Conclusions

Patients with CAP due to 2019-nCoV tend to be younger, and with less comorbidities than patients with CAP infected with endemic HCoVs, however, the clinical presentation and outcomes for both groups of patients is similar. Optimal implementation of infection control practices is important to contain the 2019-nCoV spread in the community and hospital setting. Patients hospitalized with CAP due to 2019-nCoV have a mortality of approximately 3%, very similar to the mortality of hospitalized patients with CAP due to endemic HCoVs. Mortality of hospitalized patients with CAP due to 2019-nCoV is expected to decrease as new therapeutic strategies are developed.

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Appendix: Center of Excellence for Research in Infectious Diseases (CERID) Coronavirus Study Group

CERID Leadership

Julio Ramirez, MD, Executive Director

Forest Arnold, DO, Associate Director

Ruth Carrico, PhD, Director of Epidemiological Research

Leslie Wolf, PhD, Director of Laboratory Research

Senen Peña, MD, Director of Research Operations

Emily Just, MA, Director of Administrative Operations

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Leslie Beavin, MD

Mark Burns, MD

Barbara Wojda, MD

Julio Ramirez, MD (Executive Director)

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Implementation Unit
Amr Aboelnasr (Lead)
Vidyulata Salunkhe
Daniya Sheikh
Prashant Tripathi
Mohammed Abbas
Ahmed Abdelhaleem
Mutasem Abuhalaweh
Ahmed Adel
Khaled Alsweis
Omar Altantawi
Ibrahim Asha
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Balachandran Rishinaradamangalam
Harideep Samanapally
Balaji Sekaran
Ayesha Shameem
Ahmed Ali Shebl
Nishita Tripathi
Darmaan Aden, MD (Fellow)
Kamran Mahmood, MD (Fellow)
Angeline Prabhu, MD (Fellow)

Data Management Unit
Mahder Tella, MPH (Lead)

Biostatistics Unit
Stephen Furmanek, MPH (Lead)
Mahder Tella, MPH
Connor Glick, MS

Research & Diagnostic Laboratory Unit
Leslie Wolf, PhD (Lead)

Biorepository Unit
Subathra Marimuthu, PhD (Lead)

Quality Assurance Unit
Mohammed Tahboub (Lead)
Iqbal Ahmed
Duremala Duremala
Raghava Sekhar
Sahaj Hardeep Singh

Regulatory & Compliance Unit
Maria Hill (Lead)

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Clinical Research Internship
Morgan Stanley (Lead)
Mohamed Abdelnabi
Mahmoud Abdelsamia
Yousra Alghalban
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Arpan Chawala
Lakshmi Cherukuwada
Arashpreet Chhina
Satya Durugu
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Jeremiah Olabiyi
Lucia Puga Sanchez
Nida Qadir
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Gowthami Ramineni
Ashraf Rjob
Syed Shah
Hammad Tanzeem

Medical Writing Unit
Forest Arnold, DO (Lead)

Informatics Unit
William Mattingly, PhD (Lead)
Matthew Grassman
Rakhi Shah
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Tonya Augustine (Lead)
Tessa Chilton
Trevor Bosley

University Outreach Unit
Ruth Carrico, PhD (Lead)

Community Outreach Unit
Dawn Balcom, PhD (Lead)

Administration Unit Emily Just, MA (Lead)
Eman Abbas
Morgan Stanley
Catherine Bryan

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Dan Kapp (Lead)