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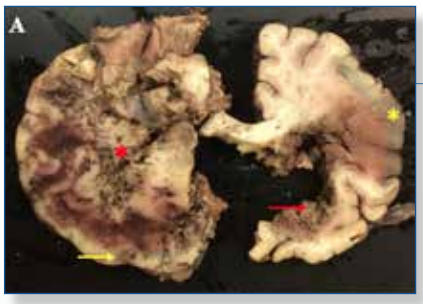

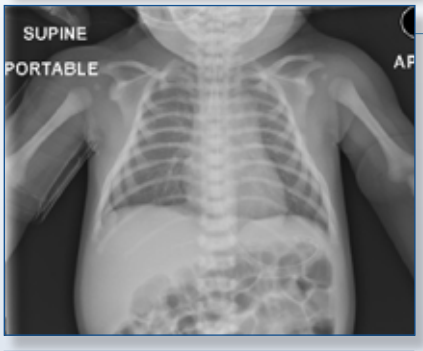

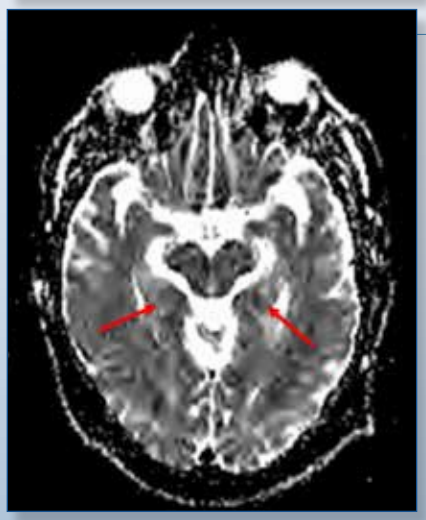

CASE REPORTS

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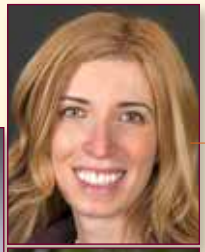

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IN THE NEWS


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PASSAGES: IN MEMORIAM

PEOPLE/PLACES

OBITUARY

An Instructive Case of Cerebral Mucormycosis

BELINDA SHAO, MD, MPH; MATTHEW J. HAGAN, BS; RAHUL A. SASTRY, MD; MICHAEL KRITSELIS, DO; JOHN E. DONAHUE, MD; STEVEN A. TOMS, MD

ABSTRACT

BACKGROUND: Mucormycosis can lead to fatal rhinocerebral infection.

CASE: A 53-year-old male with diabetes presented with altered mental status. He had been recently discharged from an admission for COVID-19 pneumonia treated with remdesivir and methylprednisolone. Imaging demonstrated a large left frontal mass with midline shift suspicious for a primary brain neoplasm. His neurologic exam rapidly declined and the patient was taken to the operating room for decompressive hemicraniectomy. Post-operatively, the patient remained comatose and failed to improve. Autopsy revealed a cerebral mucormycosis infection.

DISCUSSION: Despite concern for a primary brain neoplasm the patient was diagnosed postmortem with a mucormycosis infection. Other features supporting this diagnosis included nasal sinusitis on initial scans, his fulminant clinical decline, rapidly progressive imaging findings, and persistent hyperglycemia throughout his clinical course.

CONCLUSION: In an era of high steroid usage to treat COVID-19, mucormycosis infection must be considered in high-risk patients demonstrating disproportionate clinical decline.

KEYWORDS: mucormycosis, diabetic ketoacidosis, COVID-19, glioblastoma, immunosuppression, cerebral edema, decompressive hemicraniectomy

INTRODUCTION

Mucormycosis is a fungal infection that can cause a variety of clinical syndromes, particularly in patients with uncontrolled diabetes mellitus (DM) or underlying malignancy.[1] Patients who are immunocompromised secondary to steroid use are also at risk.[2] Most commonly, mucormycosis leads to rhino-orbital-cerebral (34%), cutaneous (22%), or pulmonary infection (20%).[1] There is a 50% mortality rate in those infected.[3] While rare, the prevalence of mucormycosis infection is increasing due to an increase in the immunocompromised population.[2] The current estimated incidence in the United States is three cases per million.[4] However, the prevalence of mucormycosis infection, and fungal infections in general, may be rising.[4-6]

Due to the rarity of the disease and the non-specific presentation of patients with mucormycosis, timely diagnosis is challenging. Frequently, by the time an accurate diagnosis has been made it may too late to effectuate meaningful treatment.[2] Here we present the case of a patient admitted to the hospital with non-specific neurologic symptoms who then experienced a rapid clinical decline with eventual postmortem diagnosis of mucormycosis.

CASE PRESENTATION

A 53-year-old male with a history of insulin dependent type II DM, lymphedema, compensated hepatitis C virus cirrhosis, hypertension, and recent COVID-19 infection presented to the emergency department following a transient episode of right upper extremity weakness and a ground level fall. The patient had been discharged four days prior to this visit after an admission for COVID-19 pneumonia, treated with remdesivir and methylprednisolone. Since discharge, he experienced progressive confusion, fatigue, and difficulty with ambulation.

On initial evaluation, the patient was alert and oriented to person and situation, but notably confused compared to his previous visit and was unable to report his address or his medical problems. His right upper extremity weakness had resolved and his motor, sensory, and language function had otherwise returned to baseline.

The patient's laboratory studies are reported in **Table 1** and notable for thrombocytopenia, which is his baseline, as well as hyperglycemia. Liver function tests were minimally elevated and at baseline. Computed tomography (CT) of the head demonstrated a left frontal mass-occupying lesion with midline shift as well as paranasal sinusitis (**Figure 1**).

Body imaging was negative for any potential primary malignancy. A chest x-ray revealed bilateral multifocal airspace disease consistent with his recently treated COVID-19 pneumonia. Subsequent magnetic resonance imaging (MRI) revealed an infiltrative and hemorrhagic left frontal mass extending across the corpus callosum, highly suspicious for a primary central nervous system (CNS) neoplasm (**Figure 2**). The patient was started on dexamethasone (6 mg every 6

Table 1. Patient laboratory results upon presentation.

Lab	Value
Complete blood count	
White blood cells (x109/L)	5.0
Red blood cells (x1012/L)	4.1
Hemoglobin (g/dL)	12.5
Hematocrit (%)	38.8
Platelets (x109/L)	41
Serum Chemistry	
Sodium (mEq/L)	134
Potassium (mEq/L)	4.7
Chloride (mEq/L)	103
Bicarbonate (mEq/L)	23
Blood urea nitrogen (mg/dL)	16
Creatinine (mg/dL)	0.79
Glucose (mg/dL)	244
Aspartate aminotransferase (iu/L)	65
Alanine aminotransferase (iu/L)	55
Alkaline phosphatase (iu/L)	111
Venous blood gas	
pH	7.42
pCO2 (mmHg)	38
pO2 (mmHg)	46
O2 saturation (%)	82

Figure 1. Head computed tomography (CT) upon presentation. Axial view revealing large region of hypodensity in the left frontal lobe, sulcal effacement, and extension across the corpus callosum toward the right frontal lobe (arrow). Visualization of left-to-right midline shift up to 6 mm anteriorly.

Figure 2. Initial brain magnetic resonance imaging (MRI). Axial T2 sequence revealing extensive high signal in the left frontal lobe extending across the corpus callosum with sulcal effacement and mass effect on the frontal horns (arrow). Demonstration of an irregular rim of enhancement consistent with hemorrhage (asterisks).

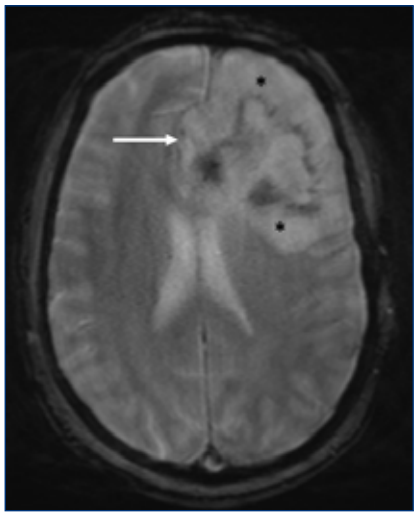
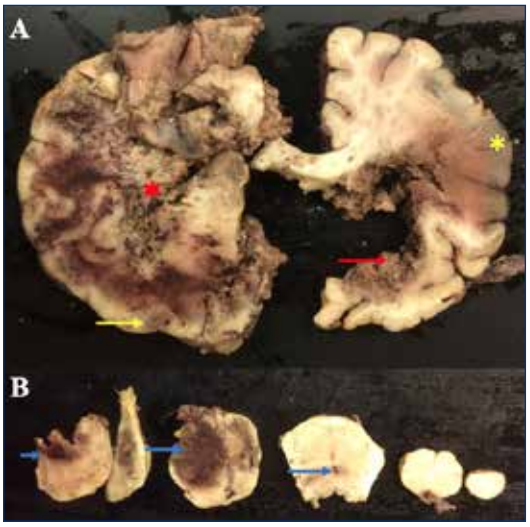


Figure 3. Gross pathology upon post-mortem autopsy.
(A) Cross section of the frontal lobes, demonstrating duskiness (yellow arrow/asterisk) bilaterally with central necrosis (red arrow/asterisk) involving the left frontal lobe. This extends posteriorly to involve the left parietal lobe and right posterior frontal lobe/temporal lobe.
(**B**) In the brainstem, there was a circular, well-circumscribed hemorrhage (blue arrows) that involved the right cerebral peduncle and surrounding midbrain at the level of the red nucleus and extends inferiorly to involve the pons at the level of the fifth cranial nerve.



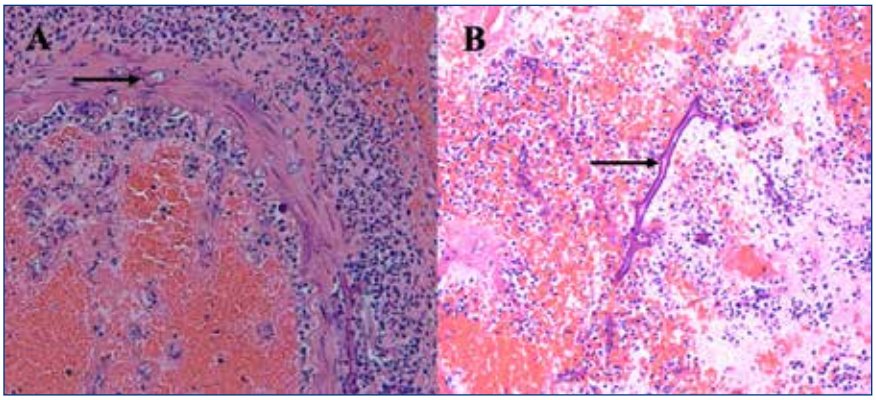
hours) for cerebral edema, and tentative plans for surgical biopsy and/or resection were made.

On hospital day one however, the patient's neurologic exam rapidly declined; he became disoriented and nonverbal, followed by extensor posturing. The patient was emergently intubated. Repeat CT brain studies that day revealed rapidly progressive cerebral edema and midline shift, and hypodense areas suspicious for lesion spread. Cerebral edema was treated with increasing doses of dexamethasone as well as mannitol and hypertonic saline. An insulin drip was initiated, as well. Given this fulminant decline and comatose state due to central herniation, the patient was taken emergently to the operating room for decompressive hemicraniectomy. Platelets were administered pre-operatively given his thrombocytopenia. Intraoperatively, immediately following bony decompression, the patient's brain swelled out of the calvarial defect, demonstrating severe cerebral edema. Given this as well as his thrombocytopenia, no intraoperative biopsy of the lesion was performed due to concern for intracerebral hematoma given the tissue's friability.

Post-operatively, the patient remained comatose. Given his disproportionate clinical decline, as well as new lesions and peripheral contrast enhancement on post-operative brain MRI, as well as a new leukocytosis of 15.0 x10^9/L and fever on post-operative day 1, an infection was suspected. The patient was started on empiric ampicillin, vancomycin, and meropenem. However, he continued to decline and on hospital day four he was transitioned to comfort measures only status.

Postmortem autopsy and neuropathology revealed a mass lesion with extensive hemorrhage and necrosis in the

Figure 4. Histologic slides upon post-mortem autopsy and neuropathology.
(**A**) High-power magnification photograph showcasing invasion of arteriolar lumen and tunica media by the fungal organisms (arrow). Hematoxylin and Eosin, 200X.
(**B**) High-magnification photograph highlighting the morphology of the fungal organisms. The organisms contain hyphae that are broad-based and non-septated with right-angle branching (arrow). Hematoxylin and eosin, 200X.



bilateral frontal and parietal lobes, corpus callosum, and deep gray matter structures, extending inferiorly into the brainstem through the left cerebral peduncle and into the pons (**Figure 3**). Microscopically, the mass was diagnosed as a hemorrhagic abscess with angioinvasion secondary to mucormycosis (**Figure 4**).

DISCUSSION

We present a patient with a left frontal brain lesion and fulminant neurological and radiographic decline in the setting of diabetes mellitus, recent steroid treatment for COVID-19 pneumonia, and possible underlying nasal sinusitis. Given the initial clinical picture, the patient's first suspected diagnosis was primary infiltrative CNS neoplasm; however, rapid and disproportionate clinical decline soon raised suspicion for other etiologies. The patient was ultimately diagnosed with a mucormycosis infection postmortem, with impressive hallmark gross and histological pathology findings featured in this vignette. While not necessary to make the diagnosis, other features supporting this diagnosis during the patient's clinical course included the contrast enhancement pattern of the lesions on MRI, nasal sinusitis on his initial CT, and marked hyperglycemia throughout his clinical course due to diabetes and both inpatient and pre-admission steroid usage.

Rhino-orbital-cerebral involvement is the most common manifestation of mucormycosis,[7] often presenting with fever (44%), nasal ulceration or necrosis (38%), impaired vision (30%), opthalmoplegia (29%), sinusitis (26%), and headache (25%).[8] Notably, the patient described did not report or demonstrate these symptoms on his initial presentation, although retrospectively his initial head CT imaging report did comment on nasal sinusitis.

The most common underlying disorder in those diagnosed with mucormycosis is diabetes, specifically type II DM.[9] Classically, mucormycosis infection is associated with diabetic ketoacidosis. While our patient was not ever clinically diagnosed with diabetic ketoacidosis and his blood gases and serum bicarbonate levels were normal throughout admission, his serum glucose values were elevated both before and during his hospitalization. This was likely due to his acute disease processes and steroid usage both during his discussed hospitalization as well as his prior hospitalization for COVID-19 pneumonia. Patients can be at risk for mucormycosis infection with blood sugar levels greater than 200 for more than seven days, even without ketoacidosis.[10] Furthermore, in about 9% of cases, patients have no predisposing risk factors for mucormycosis.[11] In sum, diagnosis of mucormycosis requires a high index of suspicion in at-risk patients presenting with fever, sinusitis, altered mental status, and necrosed tissue on the nose or palate. Diagnosis confirmation is ultimately made by histopathology and tissue culture showing broad aseptate hyphae.[12,13]

In the contemporary period of high COVID-19 prevalence, co-infection is expected to occur at some background rate. This is especially true given that the standard therapy for severe COVID-19 pneumonia is corticosteroids which could precipitate mucormycosis infection due to their immunosuppressive and hyperglycemic effects.[14,15] Concurrent COVID-19 and mucormycosis infection has been reported previously in case reports[15-18] as well as analyzed in a systematic literature review of 101 patients.[19] In the present clinical vignette, our patient had many medical comorbidities predisposing him to mucormycosis including poorly controlled insulin-dependent DM and cirrhosis.[20,21] This was likely exacerbated by his recent infection with COVID-19 given its immunosuppressive treatment with dexamethasone, ultimately leading to his rapidly progressive mucormycosis infection, neurological decline, and eventual demise. Notably, Elhamamsy et al. (2021)[18] reported a case series of three nondiabetic immunocompetent patients who presented with rhino-orbital cerebral mucormycosis in the setting of a COVID-19 infection. They were subsequently treated with corticosteroids at dosages higher than those recommended by the World Health Organization. The authors concluded that guidelines regarding corticosteroid dosages to treat COVID-19 should be adhered to. Similarly, the patient in the present case report was receiving dosages of dexamethasone higher (6mg every 6 hours) than recommended for COVID-19 therapy (6mg daily for 7-10 days).[22] Of course, the

indication for steroids in this case was cerebral edema and not COVID-19 infection, however. Lastly, the authors suggest that immune dysregulation caused by COVID-19 may contribute to an increased risk of mucormycosis infection.[18]

Due to the aggressive and invasive nature of the disease, timely initiation of treatment is tantamount. The primary medical treatment is the antifungal amphotericin B.[11] The liposomal formulation of amphotericin B is commonly used as it has a lower side effect profile.[23] The recommended starting dose for liposomal amphotericin B is 5mg/day[24-26] although some literature supports the use of doses closer to 10mg/day.[27] Aggressive early surgical debridement has been associated with improved outcomes.[28] Removal of the affected necrotic and infarcted tissue can be disfiguring and may necessitate removal of the orbit and palate. In patients with mucormycosis and COVID-19 coinfection, surgery appears to decrease mortality and disease progression.[26] When anatomically feasible, endoscopic interventions have also been employed successfully.[29] In addition to antifungal therapy and surgery, patients must be medically optimized to attenuate risk factors for disease progression and recurrence. These measures include treating underlying diabetes and metabolic acidosis as well as stopping any immunosuppressive therapies.[30]

CONCLUSION

In high-risk patients with contrast-enhancing cerebral masses that demonstrate disproportionate progression of neurologic decline, edema, and lesion spread, rhinocerebral mucormycosis must be considered and not missed. This illustrative vignette may be particularly useful in an era of high COVID-19 prevalence and its requisite management with steroids that can exacerbate hyperglycemia and immunosuppression in patients with diabetes and sinusitis.

References

1. Jeong W, Keighley C, Wolfe R, et al. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. *Clinical Microbiology and Infection.* 2019;25(1):26-34.
2. Skiada A, Lass-Floerl C, Klimko N, Ibrahim A, Roilides E, Petrikkos G. Challenges in the diagnosis and treatment of mucormycosis. *Med Mycol.* 2018;56(suppl_1):93-101.
3. Palejwala SK, Zangeneh TT, Goldstein SA, Lemole GM. An aggressive multidisciplinary approach reduces mortality in rhinocerebral mucormycosis. *Surg Neurol Int.* 2016;7:61.
4. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. *J Fungi (Basel).* 2019;5(1).
5. Rees JR, Pinner RW, Hajjeh RA, Brandt ME, Reingold AL. The epidemiological features of invasive mycotic infections in the San Francisco Bay area, 1992-1993: results of population-based laboratory active surveillance. *Clin Infect Dis.* 1998;27(5):1138-1147.
6. Webb BJ, Ferraro JP, Rea S, Kaufusi S, Goodman BE, Spalding J. Epidemiology and Clinical Features of Invasive Fungal Infection in a US Health Care Network. *Open Forum Infect Dis.* 2018;5(8):ofy187.
7. Gupta S, Goyal R, Kaore NM. Rhino-Orbital-Cerebral Mucormycosis: Battle with the Deadly Enemy. *Indian J Otolaryngol Head Neck Surg.* 2020;72(1):104-111.
8. Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis. *Surv Ophthalmol.* 1994;39(1):3-22.
9. Roden MM, Zaoutis TE, Buchanan WL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis.* 2005;41(5):634-653.
10. Kontoyiannis DP, Wessel VC, Bodey GP, Rolston KV. Zygomycosis in the 1990s in a tertiary-care cancer center. *Clin Infect Dis.* 2000;30(6):851-856.
11. Bhandari J, Thada P, Nagalli S. Rhinocerebral Mucormycosis. [webpage]. 2021; https://www.ncbi.nlm.nih.gov/books/NBK559288/.
12. Balai E, Mummadi S, Jolly K, Darr A, Aldeerawi H. Rhinocerebral Mucormycosis: A Ten-Year Single Centre Case Series. *Cureus.* 2020;12(11):e11776.
13. Challa S. Mucormycosis: Pathogenesis and Pathology. *Current Fungal Infection Reports.* 2019;13(1):11-20.
14. Group TCST. Effect of 12 mg vs 6 mg of Dexamethasone on the Number of Days Alive Without Life Support in Adults With COVID-19 and Severe Hypoxemia: The COVID STEROID 2 Randomized Trial. *JAMA.* 2021;326(18):1807-1817.
15. Mehrabi Z, Salimi M, Niknam K, et al. Sinoorbital Mucormycosis Associated with Corticosteroid Therapy in COVID-19 Infection. *Case Reports in Ophthalmological Medicine.* 2021;2021:9745701.
16. Dilek A, Ozaras R, Ozkaya S, Sunbul M, Sen EI, Leblebicioglu H. COVID-19-associated mucormycosis: Case report and systematic review. *Travel Med Infect Dis.* 2021;44:102148.
17. Garg D, Muthu V, Sehgal IS, et al. Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature. *Mycopathologia.* 2021;186(2):289-298.
18. Elhamamsy S, Bayer T, Al-Kaffas M, et al. Rhino-Orbital Cerebral Mucormycosis in Non-Diabetic Patients with COVID-19. *R I Med J (2013).* 2021;104(8):19-21.
19. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. *Diabetes Metab Syndr.* 2021;15(4):102146.
20. Elsiesy H, Saad M, Shorman M, et al. Invasive mucormycosis in a patient with liver cirrhosis: case report and review of the literature. *Hepat Mon.* 2013;13(8):e10858.
21. Abbas Z, Jafri W, Rasool S, Abid S, Hameed I. Mucormycosis in patients with complicated cirrhosis. *Singapore Med J.* 2007;48(1):69-73.
22. Dexamethasone in Hospitalized Patients with Covid-19. *New England Journal of Medicine.* 2020;384(8):693-704.
23. Lemke A, Kiderlen AF, Kayser O. Amphotericin B. *Applied Microbiology and Biotechnology.* 2005;68(2):151-162.
24. Handzel O, Landau Z, Halperin D. Liposomal amphotericin B treatment for rhinocerebral mucormycosis: how much is enough? *Rhinology.* 2003;41(3):184-186.
25. Hussain S, Baxi H, Riad A, et al. COVID-19-Associated Mucormycosis (CAM): An Updated Evidence Mapping. *Int J Environ Res Public Health.* 2021;18(19).
26. Aranjani JM, Manuel A, Abdul Razack HI, Mathew ST. COVID-19–associated mucormycosis: Evidence-based critical review of an emerging infection burden during the pandemic's second wave in India. *PLOS Neglected Tropical Diseases.* 2021;15(11):e0009921.
27. Lanternier F, Poiree S, Elie C, et al. Prospective pilot study of high-dose (10 mg/kg/day) liposomal amphotericin B (L-AMB) for the initial treatment of mucormycosis. *Journal of Antimicrobial Chemotherapy.* 2015;70(11):3116-3123.

28. Di Carlo P, Pirrello R, Guadagnino G, et al. Multimodal Surgical and Medical Treatment for Extensive Rhinocerebral Mucormycosis in an Elderly Diabetic Patient: A Case Report and Literature Review. *Case Reports in Medicine.* 2014;2014:527062.
29. Saedi B, Sadeghi M, Seilani P. Endoscopic management of rhinocerebral mucormycosis with topical and intravenous amphotericin B. *J Laryngol Otol.* 2011;125(8):807-810.
30. Spellberg B, Ibrahim AS. Recent advances in the treatment of mucormycosis. *Curr Infect Dis Rep.* 2010;12(6):423-429.

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Disclosures

The authors report no relevant disclosures pertaining to the present manuscript.

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Successful Fracture Healing for Femoral Neck Nonunion with Bone Marrow Aspirate Concentrate

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ABSTRACT

INTRODUCTION: Femoral neck fractures in the young patient require prompt anatomic reduction and stabilization to preserve the vascular supply to the femoral head and minimize future need for arthroplasty. Secondary to unique biomechanical and vascular considerations, these injuries are prone to nonunion.

CASE REPORT: A 29-year-old male with a chronic femoral neck fracture nonunion who experienced successful fracture healing and symptom resolution following Bone Marrow Aspirate Concentrate (BMAC) administration.

DISCUSSION: Femoral neck nonunion in young patients is a challenging problem with treatment strategies aimed at improving the biological and biomechanical fracture environment. While the use of both vascularized and nonvascularized bone grafting has shown promising results, they have high complication rates and substantial donor site morbidity. BMAC has demonstrated multiple uses throughout orthopedic surgery and may result in an improved fracture healing environment with minimal patient morbidity.

CONCLUSION: The success of the BMAC procedure for this patient is promising and may be considered in similar patients, with or without revision internal fixation methods.

KEYWORDS: Bone Marrow Aspirate Concentrate, BMAC, femoral neck nonunion, femoral neck fracture, fracture nonunion, fracture healing

INTRODUCTION

Femoral neck (FN) fractures in young patients are typically the result of high energy trauma, and pose a complex problem for the treating orthopedic surgeon.[1] Given the tenuous blood supply to the FN, successful treatment of these fractures relies on anatomic reduction and primary bone healing.[2] FN fractures in young patients often have high Pauwel's angles and may be inherently unstable which predisposes these injuries to a high risk of complications.[1,2] A recent meta-analysis including 1558 fractures from 41 studies demonstrated a 14.3% rate of nonunion, 9.3% rate of avascular necrosis (AVN), and 18% reoperation rate.[3] Other studies have noted nonunion rates as high as 33%.[4] FN nonunion in this population is associated with persistent pain, disability, and poor patient satisfaction. Adjunct methods to enhance fracture biology when addressing FN non-unions have been advanced. In this case report, we present the novel use of bone-marrow aspirate concentrate (BMAC) for successful treatment of a persistent FN nonunion in a 29-year-old male patient.

Statement of Consent

The following described patient gave consent for his de-identified clinical course and radiographic and clinical images to be used in the creation of this case report.

CASE REPORT

We report the case of a 29-year-old nonsmoking healthy male who sustained a femoral shaft fracture with ipsilateral nondisplaced transcervical FN fracture and a tibial shaft fracture after a motorcycle collision. His FN fracture was fixed with three 6.5mm partially threaded cannulated screws, followed by retrograde and antegrade intramedullary nailing for his femoral and tibial shaft fractures, respectively.

One year postoperatively, the patient presented with symptomatic hardware in cold weather. His fractures appeared healed both clinically and radiographically, and thus indicated for elective removal of hardware (**Figure 1**).

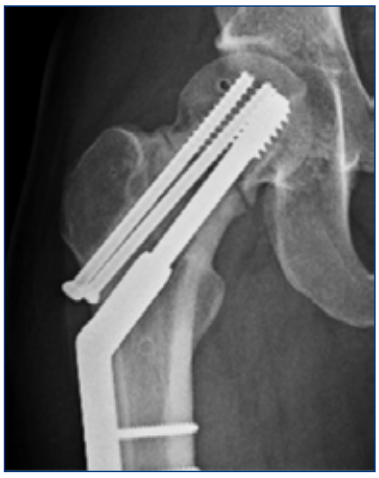
Two years later, he reported several weeks of hip and groin discomfort, and subsequently sustained a pathologic displaced FN fracture without associated trauma (**Figure 2**). The patient underwent urgent open reduction and internal fixation with a sliding hip screw and two 6.5mm partially threaded anti-rotation screws through a Smith-Petersen approach. Intraoperatively, minimal bridging callus and necrotic-appearing bone edges were noted, consistent with atrophic nonunion. Preoperative inflammatory markers were normal and cultures and pathology obtained intraoperatively were negative for infection.

Follow-up imaging over the next 12 months showed minimal bridging bone or callous formation (**Figure 3**) and the patient complained of ongoing pain. Given prior intraoperative findings demonstrating limited biological healing potential and radiographic evidence of atrophic nonunion,

Figure 1. Transcervical femoral neck fracture and transverse femoral shaft fracture 6 months status post fixation with three 6.5mm cannulated screw and a retrograde femoral nail.

Figure 2. Displaced transcervical femoral neck fracture of unclear chronicity, discovered one year after elective removal of hardware.

Figure 3. Femoral neck nonunion, 12 months after revision fixation.



operative techniques aimed at optimizing biological environment were considered include vascularized and non-vascularized bone graft. Bone marrow aspirate concentrate (BMAC) has not been an extensively described technique for femoral neck nonunion but has shown some promise in the treatment of nonunions and as an adjunct therapy. Given the desire of the patient to avoid invasive surgery, and the very low complication rate of this technique, the patient elected to attempt use of BMAC for augmentation of fracture healing.

In the OR, ipsilateral iliac crest BMAC was harvested, and subsequently injected into the non-union site. A 1-cm incision was made posterior to the anterior superior iliac spine. 100cc of bone marrow aspirate was obtained and injected into two sterile centrifuge containers with a Jamshadi needle. The containers were placed in a centrifuge for 15 minutes and the bone marrow concentrate layer was then drawn into 10cc sterile syringes (**Figure 4**).[5] The antero-superior 6.5mm cannulated screw was removed percutaneously, and the screw pathway was cleared of any fibrous debris with a 5mm drill. A metal cannula was gently inserted into the screw pathway with the end placed at the site of the known nonunion and 5 cc of BMAC was injected into the FN fracture nonunion. Next, 4.5 cc of BMAC was then injected

Figure 4. Bone marrow aspirate from ipsilateral iliac crest after centrifuge concentration.

Figure 5. Intraoperative fluoroscopy images demonstrating injection of BMAC at fracture site through temporarily removed screw tract (star) and through intraarticular injection (arrow).

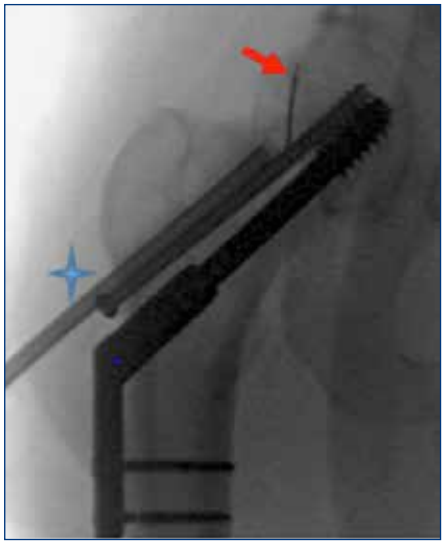


Figure 6. 12 months postop from BMAC injection, showing bridging and healing at superior aspect of the femoral neck nonunion and increased callous formation at inferior neck.

intraarticular into the hip joint using an 18-gauge spinal needle (**Figure 5**). A 7.3 mm partially threaded screw was used to replace the previous 6.5mm cannulated screw. The patient was made weightbearing as tolerated and discharged postoperatively without incident.

Postoperatively, radiographs and CT scan 12 months following surgery showed successful radiographic union of the fracture anteriorly and superiorly, which is exactly where the BMAC injections were placed (**Figure 6).** There was also interval callous formation and healing at the inferior neck. He reported complete resolution of his pain at this time.

DISCUSSION

In this case report, we present the case of a young male with a FN nonunion that demonstrated bony bridging and resolution of pain after BMAC injection at the fracture site. FN nonunion following fractures in young patients is challenging to manage.[4,6] There are two main treatment options – hip preservation or prosthetic replacement.[7] In most cases, joint preservation is preferable to arthroplasty in young patients, given high functional demands and substantial future life expectancy. Furthermore, arthroplasty can be performed if the effort for preservation fails.[8,9] The decision between the two strategies often depends on the presence of avascular necrosis with collapse of the femoral head, after which there are few treatment options besides a total hip arthroplasty. At the patient's age of 29, total hip arthroplasty has demonstrated poor results with high need for revision surgery and associated complications.[9]

Joint preserving treatment options for persistent nonunion have historically been aimed at improving the fracture's biomechanical environment, biologic environment, or both.[6] The most commonly utilized strategy for optimizing the biomechanical healing environment is an intertrochanteric valgus-producing osteotomy, also called a Pauwel's osteotomy, which converts shears force into compression forces at the fracture site. The Pauwel's intertrochanteric valgus osteotomy has promising outcomes with union reported in 44 of 48 patients in one study and in 58 of 66 patients in another study.[10,11] There are a multitude of similar cohort studies showing comparably high union rates.[12] Potential disadvantages of a valgus osteotomy include a decreased abductor lever arm, which may result in a Trendelenburg gait, iatrogenic leg length discrepancy, increasing contact pressures on the femoral head which may progress osteonecrosis and osteoarthritis, and potential nonunion at the new osteotomy site.[6] Reported strategies aimed at improving biology at the fracture site include muscle-pedicle bone grafting and vascularized bone grafting. Sen and colleagues reported that use of non-vascularized autogenous fibular grafting in combination with a fixed angle blade plate resulted in union in 21 of 22 patients (91%) over a period of 4.4 months.[7] Leung and Shen likewise reported a 100% union rate in 15 patients with vascularized iliac bone grafting and cannulated screw fixation of the FN fracture at 5–7 year follow up.[13] Adverse outcomes from autologous grafting are primarily related to donor site morbidity.[14]

Guidelines for treatment of this challenging problem of FN nonunion involve assessing for the presence of avascular necrosis to determine the feasibility of joint salvage versus arthroplasty, as well as assessing the cause of nonunion and potential need for altering the biomechanical and/or biological environment. However, there is no clearly agreed upon superior technique for accomplishing these goals. In this case we present successful treatment of a patient with an atrophic FN nonunion and normal neck-shaft angle using BMAC. BMAC is a form of osteogenic autograft that harvests mesenchymal stem cells (MSCs) from various anatomic regions including the iliac crest. The bone marrow harvested is centrifuged to allow for concentration of the MSCs for injection. The multipotent MSCs have osteogenic properties that facilitate bony healing by differentiation into osteoblast and osteoclast cell lines.

BMAC has several potential advantages over other techniques aimed at improving the biological environment. The described technique is a minimally invasive outpatient procedure and allows immediate postoperative weightbearing as well as an accelerated postoperative recovery. The risk of intraoperative and peri-operative complications with BMAC is likely far lower than with the two most common procedures used currently for treatment of FN nonunion in young patients, namely valgus intertrochanteric osteotomy and vascularized fibular autograft. Furthermore, the risk of donor site morbidity secondary to iliac crest bone marrow aspiration is low in comparison to autologous fibular and structural iliac crest grafting.[15] Clinical and radiographic results in the current case were consistent with successful union of the anterosuperior FN. The patient reported excellent clinical progression and return to all activities.

CONCLUSION

Femoral neck nonunion is a challenging problem, occurring in estimated 10–30% of FN fractures undergoing surgical reduction and fixation. It is particularly challenging in the young patient as arthroplasty has poor long-term outcomes and both biomechanical and biologic factors need to be considered. The use of BMAC to augment the biological healing environment in patients with delayed union or nonunion of the FN represents a novel technique with multiple benefits and potential uses. Nevertheless, this single case study serves as an early proof-of-concept and should not be interpreted to represent treatment recommendations. More rigorous research is needed to examine the utility and union rates following use of BMAC for the treatment of FN nonunion. With this case report we aim to distribute these results and inform orthopedic surgeons and other physicians of the potential of a valuable tool in management of FN nonunion in the young patient.

References

1. Robinson CM, Court-Brown CM, McQueen MM, Christie J. Hip fractures in adults younger than 50 years of age: Epidemiology and results. *Clin Orthop Relat Res*. 1995.
2. Panteli M, Rodham P, Giannoudis PV. Biomechanical rationale for implant choices in femoral neck fracture fixation in the non-elderly. *Injury*. 2015. doi:10.1016/j.injury.2014.12.031
3. Slobogean GP, Sprague SA, Scott T, Bhandari M. Complications following young femoral neck fractures. *Injury*. 2015;46(3):484-491. doi:10.1016/j.injury.2014.10.010
4. Lu-Yao GL, Keller RB, Littenberg B, Wennberg JE. Outcomes after displaced fractures of the femoral neck. A meta-analysis of one hundred and six published reports. *J Bone Jt Surg - Ser A*. 1994;76(1):15-25. doi:10.2106/00004623-199401000-00003
5. Chahla J, Mannava S, Cinque ME, Geeslin AG, Codina D, Laprade RF. Bone Marrow Aspirate Concentrate Harvesting and Processing Technique. 2017. doi:10.1016/j.eats.2016.10.024
6. Mathews V, Cabanela ME. Femoral Neck Nonunion Treatment. In: *Clinical Orthopaedics and Related Research*. Lippincott Williams and Wilkins; 2004:57-64. doi:10.1097/00003086-200402000-00010
7. Sen RK, Tripathy SK, Goyal T, et al. Osteosynthesis of femoral-neck nonunion with angle blade plate and autogenous fibular graft. *Int Orthop*. 2012;36(4):827-832. doi:10.1007/s00264-011-1344-1
8. Franzen H, Nilsson LT, Stromqvist B, Johnsson R, Herrlin K. Secondary total hip replacement after fractures of the femoral neck. *J Bone Jt Surg - Ser B*. 1990;72(5):784-787. doi:10.1302/0301-620x.72b5.2211756
9. Nilsson LT, Jalovaara P, Franzén H, Niinimäki T, Strömqvist B. Function after primary hemiarthroplasty and secondary total hip arthroplasty in femoral neck fracture. *J Arthroplasty*. 1994;9(4):369-374. doi:10.1016/0883-5403(94)90046-9
10. Marti RK, Schuller HM, Raaymakers ELFB. Intertrochanteric osteotomy for non-union of the femoral neck. *J Bone Jt Surg - Ser B*. 1989;71(5):782-787. doi:10.1302/0301-620x.71b5.2584247
11. Raaymakers ELFB, Marti R. Nonunion of the femoral neck: Possibilities and limitations of the various treatment modalities. *Indian J Orthop*. 2008;42(1):13-21. doi:10.4103/0019-5413.38575
12. Magu NK, Rohilla R, Singh R, Tater R. Modified Pauwels' intertrochanteric osteotomy in neglected femoral neck fracture. *Clin Orthop Relat Res*. 2009;467(4):1064-1073. doi:10.1007/s11999-008-0695-4
13. Leung PC. SWF of the femoral neck in younger adults. A new method of treatment for delayed and nonunions. CORR 1993 O-60. P 8403641. No Title.
14. Gaskill TR, Urbaniak JR, Aldridge JM. Free vascularized fibular transfer for femoral head osteonecrosis: Donor and graft site morbidity. *J Bone Jt Surg - Ser A*. 2009. doi:10.2106/JBJS.H.01105
15. Christophersen CM, Elattar O, Farber D. Pain and Complications following Bone Marrow Aspirate Concentrate (BMAC) Harvested from the Iliac Crest in Foot and Ankle Surgery. *Foot Ankle Orthop*. 2019;4(4):2473011419S0014. doi:10.1177/2473011419S00146

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Pyridoxine-Dependent Epilepsy as a Cause of Neonatal Seizures

HOI SEE TSAO, MD, MPH; SARAH D. CASE, MD

ABSTRACT

Pediatric seizures are a common reason for emergency department visits. The highest risk of seizures in children is during the neonatal period. A low index of suspicion is important to facilitate the early assessment, workup, and treatment of inborn errors of metabolism to optimize developmental outcomes. We present the rare case of a 9-day-old with seizures refractory to multiple anticonvulsant medications who was diagnosed with pyridoxine-dependent epilepsy. We review differences in the management of neonatal seizures from older patients, the utility of a trial of pyridoxine in refractory neonatal seizures, and the importance of preparing for emergent airway management given pyridoxine's ability to cause apnea and central nervous system depression.

KEYWORDS: neonate, pediatric, seizure, inborn error of metabolism, pyridoxine-dependent epilepsy

INTRODUCTION

One percent of pediatric emergency department visits is due to seizures.[1] Seizures occur in 4 to 10% of children[1] and the highest risk of seizures in children is during the neonatal period.[2] Among neonates with seizures, only a small percentage (13%) have neonatal epilepsy syndromes.[3] The majority of neonatal seizures occur secondary to neonatal encephalopathy or hypoxic-ischemic injury, metabolic disturbances, central nervous system or systemic infections, or structural brain lesions including strokes,[4] and require urgent and specific treatment to avoid further brain injury. Inborn errors of metabolism are an uncommon cause of neonatal seizures that should be considered as part of the workup of seizures in these young patients. Prompt treatment of inborn errors of metabolism is of vital importance to prevent developmental delay and other neurocognitive sequelae.[5,6]

CASE PRESENTATION

A 9-day-old female was transferred from an outside hospital for staring spells and upper extremity spasms. On the day of presentation, she was fussy, refused to feed and had episodes of staring off and 15 second bilateral arm spasms. The mother was breastfeeding and supplementing with formula that was correctly mixed. The patient had no fever, runny nose, cough, vomiting, diarrhea, decreased wet diapers, rash, sick contacts, or recent trauma.

The patient was born via planned cesarean section at 41 weeks. Her mother had routine prenatal care, negative prenatal labs and no medical problems during pregnancy or delivery. She had no home medications, allergies, or significant family history.

At the outside hospital emergency department (ED), vital signs were as shown in **Table 1**. Physical examination revealed eyes that intermittently deviated to the right or left for 15 seconds at a time with no extremity spasms. The eye deviation episodes coincided with cyanosis, bradypnea or apnea, and oxygen desaturation to the low 80s. Between episodes, pupils were equal and reactive bilaterally. The remainder of her examination was normal other than having slowed capillary refill and cool skin peripherally. During the bradypnea/apnea episodes, bulb suctioning the airway and using a nonrebreather mask improved oxygen saturation to 100%. The patient had bloodwork and a lumbar puncture performed (**Tables 2 and 3).** She received 15 mL/kg normal saline, ampicillin and gentamicin, and was transferred to a tertiary children's hospital ED.

Table 1. Vital signs at outside hospital and pediatric emergency department.

Vital Sign	Outside Hospital	Pediatric Emergency Department
Temperature (°C)	34.7 (rectal)	36.1 (rectal)
Heart Rate (Beats Per Minute)	176	188
Blood Pressure (mmHg)	Not recorded	97/59
Respiratory Rate (Breaths Per Minute)	46	96
Oxygen Saturation	91% on room air	97% on room air
Weight		4.4 kg (Birth weight: 4.6 kg)

At the pediatric ED, vital signs were as shown in Table 1. On physical examination, she was pink, active, and crying. She had transient leftward eye deviation and bilateral arm jerking. Her abdomen was distended with grimacing and crying on palpation. She was intubated for airway protection

Table 2. Electrolyte and complete blood count results obtained at outside hospital, pediatric emergency department and pediatric intensive care unit (PICU).

Lab Value	Outside Hospital	Pediatric Emergency Department	Pediatric Intensive Care Unit (PICU)
Electrolytes			
Na (Ref: 131–143 mmol/L)	138	140	142
K (Ref: 3.7–5.9 mmol/L)	5.2	5.8	4.7
Cl (Ref: 99–116 mmol/L)	106	106	110
CO_2 (Ref: 22–32 mEq/L)	<10	7	17
BUN (Ref: 5–27 mg/dL)	13	27	18
Cr (Ref: 0.30–1.00 mg/dL)	0.68	0.71	0.5
Glucose (Ref: 50–80 mg/dL)	351	174	78
Calcium (Ref: 9.0–10.9 mg/dL)	10.7	10.4	9.3
Anion Gap (Ref: 3–13 mEq/L)	22	27	15
Complete Blood Count			
White Blood Count (Ref: 4.4–21.0 x 10^9/L)	29.3		17.6
Hemoglobin (Ref: 14.0–21.0 g/dL)	13.1		12.4
Hematocrit (Ref: 42.0–55.0%)	38.6		36.4
Platelets (Ref: 150–450 x 10^9/L)	625		499
Neutrophils (Ref: 14–77%)	30%		68%
Bands (Ref: 0–6%)	1%		0%
Lymphocytes (Ref: 12–78%)	64%		19%
Monocytes (Ref: 0–12%)	4%		11%
Eosinophils (Ref: 0–6%)	1%		0%
Basophils (Ref: 0–1%)	0%		1%
Metamyelocytes (Ref: 0%)	0%		1%

Table 3. Metabolism, toxicology, blood gas, urinalysis, cerebrospinal fluid (CSF), respiratory viral panel and culture results obtained at outside hospital, pediatric emergency department and pediatric intensive care unit (PICU).

Lab Value	Outside Hospital	Pediatric Emergency Department	Pediatric Intensive Care Unit (PICU)
Metabolism Labs			
Lactate (Ref: 0.2–1.9 mEq/L)		>17.1	
Lactate Dehydrogenase (LDH) (Ref: 100–220 IU/L)			375
Ammonia (Ref: 2–50 µmol/L)			70
Uric Acid (Ref: 1.9–5.4 mg/dL)			7.6
Creatine Kinase (CK) (Ref: 34–204 IU/L)			555
β–Hydroxybutyrate (Ref: 0.02–0.27 mmol/L)			2.96
Toxicology Labs			
Serum Acetaminophen Level			Undetectable
Serum Salicylate Level			Undetectable
Urine Drug Screen			Positive for barbiturates, benzodiazepines, fentanyl
Blood Gas	**Arterial**	**Venous**	**Arterial**
pH	7.01	6.995	7.382
pCO_2 (mmHg)	30	46	30
pO_2 (mmHg)	250	47	150
HCO_3– (mmol/L)	7.6	13	19
Base Excess	–22.5	–20	–7
Urinalysis			Normal other than 1+ ketones
CSF			
White Cell Count (Ref: 0–8 cells/mm^3)	2		
Red Cell Count (Ref: <1 cell/mm^3)	27		
Glucose (Ref: 40–80 mg/dL)	128		
Total Protein (Ref: 15–45 mg/dL)	106.7		
CSF HSV PCR	Negative		
Respiratory Viral Panel		Negative	
Cultures (blood, urine, CSF)	No growth at 5 days		

with fentanyl and midazolam. An orogastric tube was placed for stomach decompression. Pediatric surgery was consulted. Acyclovir was given.

Repeat bloodwork and a respiratory viral panel were performed (Tables 2 and 3). Chest radiograph (**Figure 1**) showed diffuse hazy opacities bilaterally. Abdomen radiographs (**Figures 2 and 3**) showed non-specific diffuse air-filled loops of small and large bowel to the level of the rectum without complete obstruction and no free air. CT pan-scan was normal.

Figure 1.

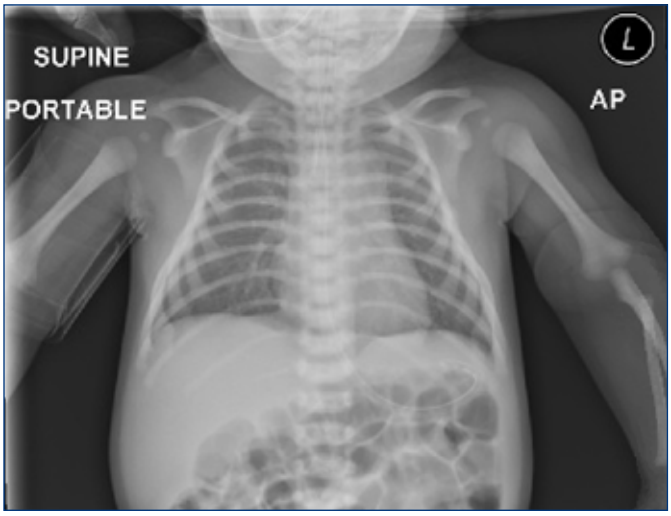


Figure 2.

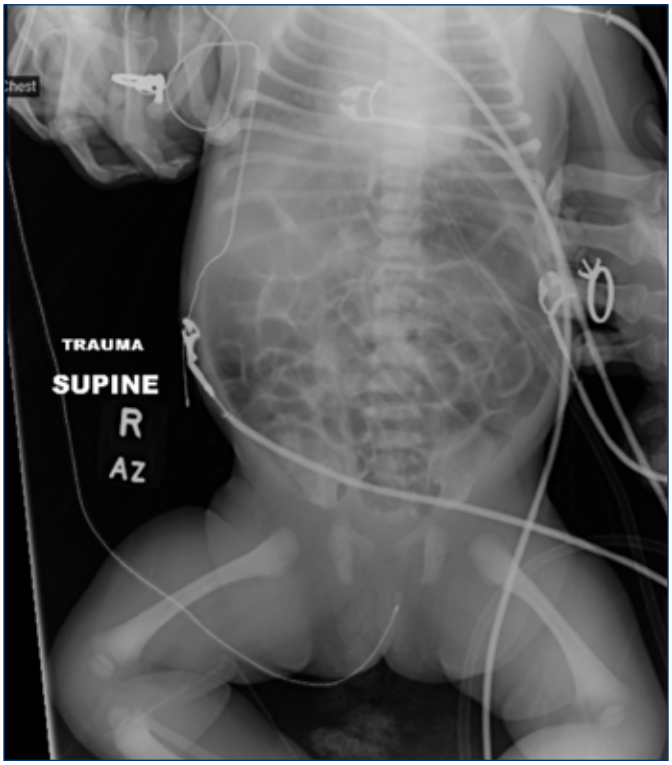
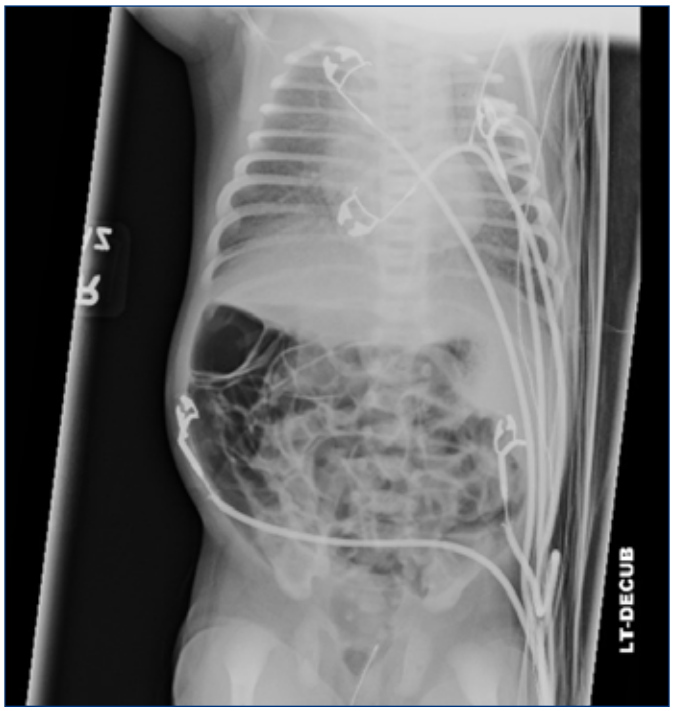


Figure 3.



She was admitted to the pediatric intensive care unit (PICU) where she continued to have intermittent leftward eye deviation with arm jerking. She was given a phenobarbital bolus and Neurology was consulted. The patient was placed on continuous electroencephalogram (EEG) and started on maintenance phenobarbital. Additional lab work was performed (Tables 2 and 3) several hours after admission.

The patient was extubated given her improved labs. Shortly after extubation, she developed episodes of eye deviation, head turning to the right, and flexion of all extremities. She was given phenobarbital and levetiracetam without improvement, corresponding with refractory status epilepticus on EEG. Pyridoxine was then given with seizure resolution clinically and on EEG. The Genetics/Metabolism team was consulted, and the workup revealed an ALDH7A1 gene mutation consistent with pyridoxine-dependent epilepsy. She was discharged with oral pyridoxine.

DISCUSSION

The differential for pediatric seizures includes infectious, neurologic (including hypoxic-ischemic encephalopathy), metabolic (including inborn errors of metabolism in neonates), traumatic, vascular, toxicologic, and oncologic etiologies. The evaluation of a neonatal seizure should focus on the preceding events and description of the seizure, including precipitating factors such as trauma, ingestion, immunizations, fever, or systemic illness. In formula-fed infants, families should be asked about the formula preparation process to assess for electrolyte derangements such as

hyponatremia from formula over-dilution. Maternal history to elicit includes group B streptococcus status, antibiotic treatment during delivery, and the presence of herpes simplex virus (HSV) lesions or risk factors. A thorough physical examination should be performed with a focus on the neurologic exam and assessment for microcephaly/macrocephaly, dysmorphism, signs of trauma, and bulging fontanelles.[7]

The workup for neonatal seizures includes a rapid glucose test, serum electrolytes, calcium, magnesium, ammonia and lactate to screen for inborn errors of metabolism, and complete blood counts. A sepsis workup including blood cultures, urinalysis, urine culture and cerebrospinal fluid studies should be obtained. Empiric antibiotic and anti-HSV coverage should be given. A head CT should be considered depending on the provider's clinical suspicion for structural brain lesions such as intracranial hemorrhage or stroke. EEG may be needed following stabilization in patients with refractory seizures.[7]

The management of neonatal status epilepticus involves stabilization of the airway, breathing and circulation.[7] Reversible causes such as glucose, sodium, magnesium, and calcium abnormalities should be corrected.[8] Phenobarbital is the most commonly used first-line therapy for neonatal seizures. Fosphenytoin is the second most commonly used. Phenobarbital and phenytoin are both equally but incompletely effective as neonatal anticonvulsants, with cessation of seizure activity in less than half of neonates with either medication.[9] Phenobarbital is much more effective at achieving complete seizure freedom for 24 hours in neonates compared with levetiracetam.[10] IV phenobarbital (20 mg/kg) should therefore be used as first-line medication for neonatal seizures, as is recommended in most neonatal seizure algorithms.[11,12] If timely IV access cannot be obtained, a short-acting benzodiazepine can be used in the interim. Second-line medications differ between neonatal seizure algorithms and include benzodiazepines, phenytoin, lidocaine,[11] fosphenytoin or levetiracetam.[12] Second-line neonatal seizure medications should therefore ideally be individualized for patients and selected with input from a pediatric neurologist. For seizures that are unresponsive to one or more second-line anticonvulsants, a trial of pyridoxine may be warranted ideally with EEG monitoring.[13,14] In neonates, pyridoxine can be given as 100 mg IV. Oral pyridoxine can be considered in older children (15-30 mg/kg/day divided three times daily). IV or oral pyridoxine can lead to central nervous system depression and apnea,[13] so clinicians should be prepared for emergent airway management.

Pyridoxine-dependent epilepsy is an autosomal recessive epileptic encephalopathy caused by antiquitin deficiency. Antiquitin is an enzyme involved in lysine catabolism in the brain and liver. When there is a deficiency in antiquitin, there is a buildup of intermediate products in the catabolism pathway proximal to antiquitin, and a decrease in breakdown products distal to antiquitin. These factors collectively lead to increased seizure activity and developmental delay.[15]

The classic presentation of pyridoxine-dependent epilepsy is neonatal seizures not responsive to traditional anticonvulsants and at least partially responsive to pyridoxine.[16] Diagnosis is based on seizure recurrence when pyridoxine is withheld and seizure resolution with pyridoxine supplementation,[11,13] biochemical evaluation including elevated urine alpha-aminoadipic semialdehyde and/or plasma pipecolic acid,[15,17,18] and mutation analysis of the ALDH7A1 gene.[17,18] There is a wide spectrum of clinical presentations in terms of prodromal symptoms, associated seizure types, and biochemical derangements in pyridoxine-dependent epilepsy.[16]

Clinicians should have a low threshold to suspect pyridoxine-dependent epilepsy in refractory neonatal seizures. Pyridoxine-dependent epilepsy is a treatable cause of seizures and intellectual disability. Early treatment with lysine-lowering strategies and pyridoxine supplementation will optimize seizure control and childhood development.[13,16]

While seizures are a common reason for emergency department visits, neonatal seizures are unique in the early use of phenobarbital in the treatment of status epilepticus. Astute clinical suspicion, early diagnosis, and treatment of inborn errors of metabolism will facilitate acute stabilization of these children, optimize developmental outcomes,[19] and ensure that genetic counseling can be initiated if indicated.[5]

CONCLUSION

Physicians should be aware of the unique early use of phenobarbital in the treatment of neonatal status epilepticus, which is different from older children or adults. There is a broad differential for neonatal seizures that includes inborn errors of metabolism such as pyridoxine-dependent epilepsy. Prompt suspicion, workup and treatment of metabolic disorders is imperative to prevent developmental delay and other complications. A trial of pyridoxine can be used in the management of refractory neonatal seizures but can lead to central nervous system depression and apnea. Physicians should be prepared for emergent airway management such as intubation when administering pyridoxine.

References

1. Chen C-Y, Chang Y-J, Wu H-P. New-onset seizures in pediatric emergency. *Pediatr Neonatol.* 2010;51(2):103-111.
2. Silverstein FS, Jensen FE. Neonatal seizures. *Ann Neurol.* 2007;62(2):112-120.
3. S Shellhaas RA, Wusthoff CJ, Tsuchida TN, Glass HC, Chu CJ, Massey SL, Soul JS, Wiwattanadittakun N, et al. Profile of neonatal epilepsies: Characteristics of a prospective US cohort. *Neurology.* 2017;89(9):893-899.
4. Mizrahi EM. Chapter 14: Neonatal Seizures. In: Pellock JM, Bourgeois BFD, Dodson WE, eds. *Pediatric Epilepsy: Diagnosis and Therapy.* Third ed. New York: Demos Medical Publishing, LLC; 2008:233-234.

5. Rahman S, Footitt EJ, Varadkar S, Clayton PT. Inborn errors of metabolism causing epilepsy. *Dev Med Child Neurol.* 2013;55(1):23-36.
6. Olson DM. Neonatal seizures. *Neoreviews.* 2012;13(4):e213-e223.
7. Friedman MJ, Sharieff GQ. Seizures in children. *Pediatr Clin North Am.* 2006;53(2):257-277.
8. Sidhu R, Velayudam K, Barnes G. Pediatric seizures. *Pediatr Review.* 2013;34(8):333-341; 342.
9. Painter MJ, Scher MS, Stein AD, Armatti S, Wang Z, Gardiner JC, Paneth N, Minnigh B, et al. Phenobarbital compared with phenytoin for the treatment of neonatal seizures. *N Engl J Med.* 1999;341(7):485-489.
10. Sharpe C, Reiner GE, Davis SL, Nespeca M, Gold JJ, Rasmussen M, Kuperman R, Harbert MJ, et al. Levetiracetam Versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial. *Pediatrics.* 2020;145(6).
11. World Health Organization. Guidelines on neonatal seizures. World Health Organization. https://apps.who.int/iris/bitstream/handle/10665/77756/9789241548304_eng.pdf?%20sequence=1. Published 2011. Accessed 17 November, 2021.
12. Krawiec C, Muzio MR. Neonatal seizure. StatPearls Publishing. StatPearls [Internet] website. https://www.ncbi.nlm.nih.gov/books/NBK554535/. Published 2020. Accessed 5 December, 2021.
13. Baxter P. Pyridoxine-dependent and pyridoxine-responsive seizures. *Dev Med Child Neurol.* 2001;43(6):416.
14. Baxter P. Epidemiology of pyridoxine dependent and pyridoxine responsive seizures in the UK. *Arch Dis Child.* 1999;81(5):431-433.
15. Stockler S, Plecko B, Gospe SM, Coulter-Mackie M, Connolly M, van Karnebeek C, Mercimek-Mahmutoglu S, Hartmann H, et al. Pyridoxine dependent epilepsy and antiquitin deficiency: Clinical and molecular characteristics and recommendations for diagnosis, treatment and follow-up. *Mol. Genet. Metab.* 2011;104(1):48-60.
16. van Karnebeek CD, Tiebout SA, Niermeijer J, Poll-The BT, Ghani A, Coughlin II CR, Van Hove JLK, Richter JW, et al. Pyridoxine-dependent epilepsy: an expanding clinical spectrum. *Pediatr Neurol.* 2016;59:6-12.
17. Mills PB, Footitt EJ, Mills KA, Tuschl K, Aylett S, Varadkar S, Hemingway C, Marlow N, et al. Genotypic and phenotypic spectrum of pyridoxine-dependent epilepsy (ALDH7A1 deficiency). *Brain.* 2010;133(Pt 7):2148-2159.
18. Mills PB, Struys E, Jakobs C, Plecko B, Baxter P, Baumgartner M, Willemsen MA, Omran H, et al. Mutations in antiquitin in individuals with pyridoxine-dependent seizures. *Nat Med.* 2006;12(3):307-309.
19. Burton BK. Inborn errors of metabolism in infancy: a guide to diagnosis. *Pediatrics.* 1998;102(6):e69-e69.

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Opioid-Associated Amnestic Syndrome

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KEYWORDS: acute amnestic syndrome, bilateral hippocampal restricted diffusion, opioid-associated amnesia, substance use disorder, toxicology

INTRODUCTION

The hippocampus plays a critical role in learning and memory. The hippocampi, and specifically the neurons in the cornu ammonis 1 (CA1) region, are particularly vulnerable to episodes of ischemia, hypoxia, and other forms of metabolic stress.[1] There have been recent reports of an opioid-associated amnestic syndrome associated with bilateral hippocampal restricted diffusion on MRI.[2,3,5,6]

CASE PRESENTATION

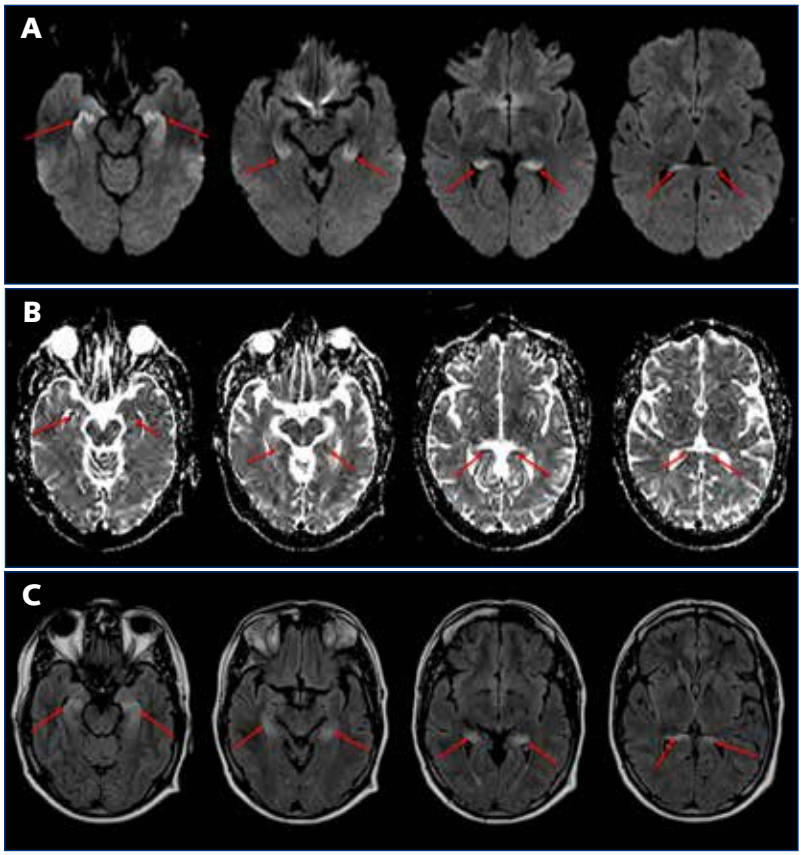
A 47-year-old man with polysubstance use disorder including alcohol, opioids, cocaine, and cannabinoids was found unresponsive with a needle in his cubital fossa. He received naloxone. He required emergent intubation. Upon presentation to the emergency department, routine immunoassay-based toxicology screening in urine was negative and blood alcohol level was undetectable. Computed tomography of the head was normal.

The patient was extubated within 24 hours. Shortly after, he was noted to have severe memory deficits. Formal neuropsychological testing was performed as an inpatient. Frontal and executive functioning were notable for organizational difficulties, impulsivity, disinhibition, and confabulation. He had severe anterograde amnesia, as well as elements of retrograde amnesia. Language and spatial functioning were preserved. The rest of his neurological exam was normal.

MRI of the brain with and without gadolinium contrast was obtained on hospital day 6. MRI showed bilateral hippocampal restricted diffusion, with matching hyperintensities on fluid-attenuated inversion recovery (FLAIR) sequence (**Figure 1**). There was no abnormal gadolinium enhancement. Computed tomography angiogram of the head and neck was normal. Routine electroencephalogram showed mild bitemporal focal slowing, with no epileptiform abnormalities. Cerebrospinal fluid (CSF) revealed 0 white blood cells per µL, glucose 57mg/dL (serum 90 mg/dL), and protein 70 mg/dL. Oligoclonal bands were absent. Gram stain showed no organisms. CSF cultures were negative.

The patient's family members indicated that he was using synthetic opioids immediately prior to his hospitalization. Routine immunoassay-based toxicology screening does not

Figure 1. Axial MRI of the brain in opioid-associated amnestic syndrome.
(A) Diffusion weighted imaging (DWI) showed bilateral, symmetric hyperintensities involving the entirety of the hippocampi (arrows). **(B)** Apparent diffusion coefficient (ADC) sequence confirmed the presence of bilateral hippocampal restricted diffusion (arrows). **(C)** Fluid-attenuated inversion recovery (FLAIR) sequence revealed bilateral hippocampal hyperintensities matching the areas of restricted diffusion (arrows).



typically test for synthetic opioids, and this explains why his urine toxicology screen was negative.[2-6] Since the patient's family members verified that he was using synthetic opioids, confirmatory high-resolution mass spectrometry was not ordered. A repeat neuropsychological evaluation done 2 weeks later showed no significant improvement. The patient was referred for cognitive rehabilitation and was instructed to follow up with neuropsychology. He received counseling for his polysubstance use disorder.

DISCUSSION

Opioid-associated amnestic syndrome (OAS) is a recently described clinical-radiological entity consisting of deficits in anterograde and retrograde memory with characteristic hippocampal abnormalities on MRI.[2,3,5,6] Proposed mechanisms of opioid-related hippocampal injury include inhibition of inhibitory interneurons through stimulation of mu receptors, direct neurotoxicity induced by opioids, or sequelae of hypoxemia.[3,5]

Based on a recently proposed case definition, our patient would be considered a 'probable' case of OAS because he had new onset amnesia lasting >24 hours, recent opioid use that was confirmed by family members, and typical MRI findings.[6] Clinicians should be mindful that, currently, most conventional toxicology screening panels do not detect the presence of synthetic opioids.[2-6] This could potentially cause delays in diagnosis. For instance, in a case series, 75% of OAS patients who tested positive for fentanyl on dedicated confirmatory testing had previously tested negative for opioids on routine urine drug screen.[3] If clinically indicated, high-resolution mass spectrometry may be ordered to investigate the presence of synthetic opioids.

To the best of our knowledge this is the first reported case of OAS in Rhode Island. As opioid use/misuse becomes more prevalent in Rhode Island and in the United States, clinicians should be aware of OAS.[7] Whenever patients present with new onset amnesia or severe cognitive deficits in the context of opioid overdose they should undergo inpatient evaluation, which will include brain MRI.[6] In cases where clinical follow-up was available, OAS patients have shown lasting amnestic deficits ranging from weeks to months, or even years.[2,6]

References

1. Schmidt-Kastner R. Genomic approach to selective vulnerability of the hippocampus in brain ischemia-hypoxia. Neuroscience. 2015 Nov 19;309:259-79. doi: 10.1016/j.neuroscience.2015.08.034. Epub 2015 Sep 14. PMID: 26383255.
2. Barash JA, Somerville N, DeMaria A Jr. Cluster of an Unusual Amnestic Syndrome - Massachusetts, 2012-2016. MMWR Morb Mortal Wkly Rep. 2017 Jan 27;66(3):76-79. doi: 10.15585/mmwr.mm6603a2. PMID: 28125568; PMCID: PMC5724909.
3. Barash JA, Ganetsky M, Boyle KL, Raman V, Toce MS, Kaplan S, Lev MH, Worth JL, DeMaria A Jr. Acute Amnestic Syndrome Associated with Fentanyl Overdose. N Engl J Med. 2018 Mar 22;378(12):1157-1158. doi: 10.1056/NEJMc1716355. PMID: 29562161.
4. Kale N. Urine Drug Tests: Ordering and Interpreting Results. Am Fam Physician. 2019 Jan 1;99(1):33-39. PMID: 30600984.
5. Barash JA, Kofke WA. Connecting the dots: an association between opioids and acute hippocampal injury. Neurocase. 2018 Apr;24(2):124-131. doi: 10.1080/13554794.2018.1475572. Epub 2018 May 18. PMID: 29774783.
6. Barash JA, Whitledge J, Watson CJ, Boyle K, Lim C, Lev MH, DeMaria A Jr, Ganetsky M. Opioid-associated amnestic syndrome: Description of the syndrome and validation of a proposed definition. J Neurol Sci. 2020 Oct 15;417:117048. doi: 10.1016/j.jns.2020.117048. Epub 2020 Jul 17. PMID: 32739497.
7. Schneider R, Carlson L, Rosenthal S. Mapping the Opioid Epidemic in Rhode Island: Where Are We Missing Resources? R I Med J (2013). 2020 Feb 3;103(1):46-50. PMID: 32013306.

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Disclosure

Prior meetings: An abstract summarizing this case report will be presented at the Maine Osteopathic Association (MOA) Midwinter Symposium, Virtual Meeting, 01/2022

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Video: Apraxia

JOSEPH H. FRIEDMAN, MD

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This patient has a rare neurodegenerative disorder, corticobasal syndrome. It has that name because it causes parkinsonism (a syndrome with slowed movements, stooped posture and shuffling gait), a basal ganglia disorder, and aphasia or apraxia, both caused by dysfunction in the cerebral cortex.

Apraxia is an inability to voluntarily perform a maneuver that the person is physically able to perform. In this case, she has difficulty continuing to perform rapid alternating hand movements on the left after doing a few. More severe was her inability to slide her left foot up and down her right shin. Apraxia is due to dysfunction in the parietal lobe and is seen in a number of disorders, most commonly stroke. It is rarely so severe as in this case.

Author

Joseph H. Friedman, MD, is Editor-in-chief Emeritus of the *Rhode Island Medical Journal,* Professor and the former Chief of the Division of Movement Disorders, Department of Neurology at the Alpert Medical School of Brown University, Chief of Butler Hospital's Movement Disorders Program and first recipient of the Stanley Aronson Chair in Neurodegenerative Disorders.

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Causes of Death in COVID-19 Patients with Cardiac Injury

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ABSTRACT

BACKGROUND: The causes of death in COVID-19 patients with cardiac injury are uncertain.

METHODS: We conducted a case-control study and reviewed the electronic medical record of 109 deceased COVID-19 patients with cardiac injury on admission and 32 deceased COVID-19 patients without cardiac injury at two hospitals in Rhode Island.

RESULTS: Among the 109 deceased COVID-19 patients who had cardiac injury on admission, 79 patients (72.5%) died of hypoxic respiratory failure, 21 patients (19.2%) of multi-organ failure and septic shock, 6 patients (5.5%) of cardiac arrhythmia, 3 patients (2.8%) of severe kidney failure as the immediate causes of death. We observed a similar pattern of distribution when compared to deceased patients without cardiac injury on admission (n=32).

CONCLUSION: The main causes of death of COVID-19 patients with cardiac injury were non-cardiac, mostly hypoxic respiratory failure. Cardiac-related arrhythmia only accounted for a small proportion of cases.

KEYWORDS: COVID-19, cardiac injury, cause of death, admission-to-death time, hypoxic respiratory failure

INTRODUCTION

The COVID-19 pandemic had spread to over 200 countries worldwide infecting more than 270 million people with more than five million deaths so far worldwide.[1, 2] It is well known that the COVID-19 virus could affect multiple organ systems,[3-5] including the cardiovascular system,[6-8] leading to severe organ damage and death.[9] Patients with cardiac injury had higher mortality rate than those without cardiac injury.[9-12] The pathogenesis involved in the COVID-19-related cardiac injury is unclear and may include myocardial inflammation,[7, 13] stress cardiomyopathy, direct myocardial destruction by the virus, among other causes, which can lead to arrhythmia,[14] cardiogenic shock, secondary thromboembolic events,[15] and sudden cardiac death.[16] For instance, up to 14% of the critically ill COVID-19 patients experienced cardiac arrest,[16] mainly due to pulseless electrical activity and asystole, as a possible manifestation of fulminant myocarditis or proximal pulmonary embolism.

Although there were previous reports regarding the causes of death in COVID-19 patients,[17-21] data regarding the causes of death in COVID-19 patients with cardiac injury was limited. Given the significance of cardiac involvement and the high mortality rate observed in patients with cardiac injury,[11, 12, 22] the current study sought to elucidate the immediate causes of death in COVID-19 patients with cardiac injury on admission, contrasting those without cardiac injury. We hypothesized that COVID-19 patients with cardiac injury would die more from cardiac-related causes compared to patients without cardiac injury.

METHODS

Overview

We conducted a retrospective case-control study through electronic medical record review of deceased COVID-19 patients from March 17, 2020 to January 11, 2021 at Roger Williams Medical Center and Our Lady of Fatima Hospital. The inclusion criteria were patients who were admitted during this time period with COVID-19 infection as one of the admission-diagnoses and died during the hospital stay. COVID-19 infection was confirmed by positive COVID-19 tests, which were defined as positive results in one or more than one of the following tests: SARS-CoV-2 transcription mediated amplification (TMA), Nucleic Acid Amplification Test (NAAT), and SARS-CoV-2 in Respiratory Virus Panel (RVP). Cardiac injury was defined as a troponin level >99th percentile of normal values (≥0.030 ng/ml) per pre-existing literature.[23]

Exclusion criteria: patients who were admitted into the hospital during the above-mentioned time period with positive COVID-19 tests who reached the end point of being discharged including death, but no troponin I level was checked (n=252). Patients diagnosed with acute coronary syndrome were excluded from this analysis since they have a legitimate non-COVID-19 explanation for increased troponin levels.

Data collection

Pre-existing past medical conditions and clinical courses were abstracted by two independent reviewers (Xiuhong Lyu and

Khushal Choudhary) to determine the immediate causes of death, with a third reviewer (John Miskovsky) who served as a final adjudicator in case of disagreements.

Clinically, the causes of death of these 141 patients (data not shown) were structured according to the WHO guideline for statement of cause of death, which included the immediate causes of death (disease or condition directly leading to death), antecedent causes of death (the condition leading to the immediate cause of death and the underlying disease/condition which gave rise to the conditions leading to the immediate cause of death, if present) and other significant conditions (comorbidity) which contributed to the death, but not related to the disease or condition causing it. Our study focused on the immediate cause of death.

The immediate causes of death that were adjudicated were: hypoxic respiratory failure defined as a patient who manifested with worsening hypoxemia initially with escalating oxygen needs at the time of death or at the time that their code status were changed to comfort measures only; cardiac arrhythmia defined as patients manifested as ventricular tachycardia, ventricular fibrillation, or atrial fibrillation, at the time of death without worsening hypoxemia or severe kidney failure that may have led to electrolyte abnormalities; multi-organ failure, defined as signs of failure of three or more organs at the time of death in the absence of worsening hypoxemia; septic shock, defined as severe hypotension in the setting of sepsis; and severe kidney failure defined as severe kidney injury with potassium level exceeding 7 mEq/L without worsening hypoxemia. Each category of immediate cause of death was mutually exclusive.

Laboratory data extracted, clinical course, and electrocardiogram characteristics were outlined in Tables 3 and 4. Acute kidney injury was defined according to the KDIGO clinical practice guidelines as an increase in serum creatinine by ≥0.3 mg/dl within 48 h or by 1.5 times of the baseline values. The clinical criteria for superimposed bacterial infection was defined as positive microbiology evidence in cultures, including cultures from expectorated sputum, secretions from endotracheal tube suctioning, and/or bronchoalveolar lavage sample.

Statistical Analysis

Descriptive statistics were obtained for all study variables. Continuous data were expressed as mean (SD) ± Standard Deviation values. Categorical data were expressed as percentages. All categorical variables were compared using the Fisher exact test or $\chi 2$ test, and continuous variables were compared using the t test, and Mann-Whitney test, where applicable. Data were analyzed using IBM SPSS statistics. Statistical charts were generated using Excel 2016 (Microsoft). For all the statistical analyses, two tailed $P<0.05$ was considered significant.

RESULTS

General characteristics of the deceased patients

General clinical characteristics of these patients were outlined in **Table 1**. Among 109 deceased patients with cardiac injury on admission, the age ranged from 52-98 years, with a mean age of 80.2±12, 54 were female (49.5%), 79.8% (87/109) were White, 6.4% (7/109) were of African-American descent,

Table 1. Overall clinical characteristics of 141 deceased COVID-19 patients according to presence or absence of cardiac injury on admission^

General characteristics	Total (n=141)	Cardiac injury (n=109)	No cardiac injury (n=32)	P value
	141	109 (77.3%)	32 (22.7%)	
Demographic information				
Age (years)	78.6±12.6	80.2±12	73.3±13.4	**0.006**
Female Sex (%)	71 (50.4%)	54 (49.5%)	17 (53.1%)	0.721
Body mass index (kg/m^2)	29.1±8	28.4±8	31.4±7.5	0.062
Race				
White	108 (76.6%)	87 (79.8%)	21 (65.6%)	0.313#
African American	10 (7.1%)	7 (6.4%)	3 (9.4%)	
Hispanic	15 (10.6%)	10 (9.2%)	5 (15.6%)	
Others (unknown)	8 (5.7%)	5 (4.6%)	3 (9.4%)	
Past Medical History				
Hypertension	109 (77.3%)	83 (76.1%)	26 (81.3%)	0.545
Hyperlipidemia	81 (57.4%)	62 (56.9%)	19 (59.4%)	0.802
Diabetes Mellitus	50 (35.5%)	38 (34.9%)	12 (37.5%)	0.784
Coronary artery disease	44 (31.2%)	37 (33.9%)	7 (21.9%)	0.195
History of Heart failure	28 (19.9%)	26 (23.9%)	2 (6.3%)	**0.028**
Atrial fibrillation	27 (19.1%)	23 (21.1%)	4 (12.9%)	0.307
Cerebrovascular disease	14 (9.9%)	12 (11%)	2 (6.3%)	0.737#
History of lung disease (COPD/asthma/pulmonary fibrosis)	40 (28.4%)	30 (27.5%)	10 (31.3%)	0.681
History of kidney disease	28 (19.9%)	23 (21.1%)	5 (15.6%)	0.495
History of liver disease	5 (3.5%)	5 (4.6%)	0	0.588#
History of malignancy	17 (12.1%)	12 (11%)	5 (15.6%)	0.538#

Abbreviation: *COPD, chronic obstructive pulmonary disease.
^Cardiac injury here was referred to on admission Troponin level equal or more than 0.030 ng/ml.
Fisher's exact test was used for statistics.

and 9.2% (10/109) were of Hispanic origin. The BMI ranged from 13.4 kg/m² to 72.1 kg/m², with a mean BMI of 28.4±8 kg/m². Compared to patients without cardiac injury, deceased patients with cardiac injury were older (80.2 vs 73.3 years, *P*=0.006), and with a higher prevalence of heart failure history (23.9% vs 6.3%, *P*=0.028). There were no significant differences in other demographic parameters, and other past medical comorbidity as outlined in **Table 1** between the two groups.

Immediate causes of death, organ injury, and admission to death time analysis

Regarding the immediate cause of death, among the 109 patients with cardiac injury on admission (see **Table 2, Figure 1**), 79 patients (72.5%) died of hypoxic respiratory failure, 13 patients (11.9%) of multi-organ failures, 8 patients (7.3%) of septic shock, 6 patients (5.5%) of cardiac arrhythmia, and 3 patients (2.8%) of severe kidney failure. There was no significant difference in the distribution of causes of death between cardiac injury vs non-cardiac injury groups (cardiac arrhythmia in cardiac injury, 5.5% vs. non-cardiac injury, 3.1%, *P*=0.369).

As shown in **Table 2** and **Figure 2**, at the time of death, in the cardiac injury group, 6 patients (5.5%) had only pulmonary injury, while 18 patients (16.5%) had two organ injuries (pulmonary with kidney or cardiac or liver injury), 58 patients (53.2%) with three organ injuries (pulmonary pulse two other organ injuries) and 27 patients (24.8%) had evidence of four organ injuries (pulmonary with cardiac, kidney and liver injuries). Overall, patients in the cardiac injury group had a higher rate of three or more organ injuries at the time of death (78% vs 43.7%, *P*=0.002) as compared to those without cardiac injury on admission.

As demonstrated in Table 2, the mean admission to death time in cardiac injury group was significantly shorter than those without cardiac injury on admission (10.5±9.2 vs 14.9±11.2 days, *P*=0.023).

Table 2. Immediate causes of death, organ injury at the time of death, and clinical course of 141 deceased patients according to presence or absence of cardiac injury on admission ^

	Available number	Total (N=141)	Cardiac injury (N=109)	No Cardiac injury (N=32)	P value
Immediate cause of death					**0.37#**
Hypoxic respiratory failure	99	106 (70.2%)	79 (72.5%)	20 (62.5%)	
Cardiac arrhythmia	7	7 (5%)	6 (5.5%)	1 (3.1%)	
Multi-organ failure (MOF)	19	19 (13.5%)	13 (11.9%)	6 (18.8%	
Septic shock	10	10 (7.1%)	8 (7.3%)	2 (6.3%)	
Severe kidney failure	6	6 (4.3%)	3 (2.8%)	3 (9.4%)	
Organ injury at the time of death					**0.002#**
Pulmonary only	13	13 (9.2%)	6 (5.5%)[b]	7 (21.9%)[a]	
Pulmonary plus another one organ injury(cardiac/ renal/liver)	29	29 (20.6%)	18 (16.5%)[b]	11 (34.4%)[a]	
Pulmonary plus two other organ injuries	67	67 (47.5%)	58 (53.2%)[b]	9 (28.1%)[a]	
Pulmonary plus another three organs injuries	32	32 (22.7%)	27 (24.8%)[a]	5 (15.6%)[a]	
Clinical course					
On admission FiO2	141	0.56±0.29	0.57±0.29	0.51±0.3	0.315
Incidence of pulmonary embolism/DVT	141	6 (4.3%)	6 (5.5%)	0	0.34#
Superimposed Bacteria infection	141	42 (29.8%)	27 (24.8%)	15 (46.9%)	**0.016**
BAL	141	14 (9.9%)	10 (9.2%)	4 (12.5%)	0.52#
ICU transfer rate	141	55 (39%)	39 (35.8%)	16 (50%)	0.147
FiO2 at the time of death	141	0.78±0.26	0.76±0.27	0.81±0.26	0.365
Admission to death time (days)	141	11.5±9.8	10.5±9.2	14.9±11.2	**0.023**

Abbreviations: MOF, multi-organ failure; FiO2, fraction of inspired oxygen; DVT, deep venous thrombosis; BAL, bronchoalveolar lavage; ICU, intensive care unit.
^ Cardiac injury here was referred to on admission Troponin level equal or more than 0.030 ng/ml.
# Fisher's exact test was used for statistics.
[a,b] stand for statistical difference existing between the two comparison group under the calculation of Chi-Square/Fisher Exact test.

Figure 1. Comparison between Non-cardiac injury group and Cardiac injury group regarding the immediate cause of death.

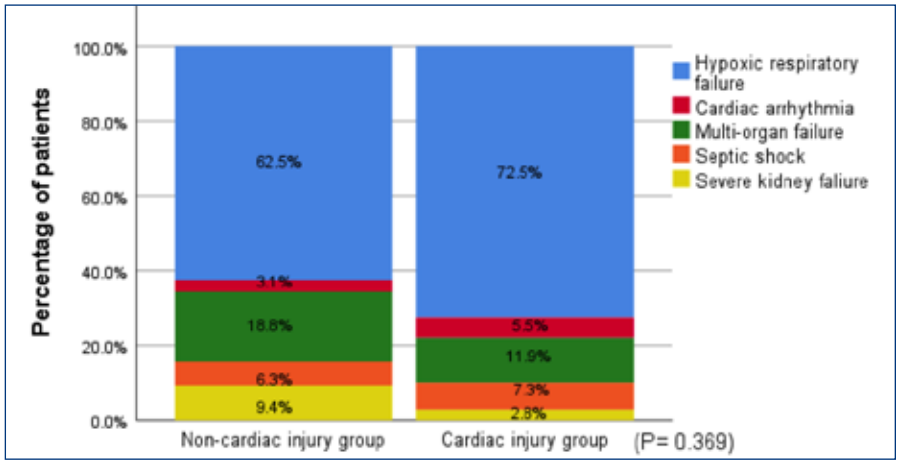

Figure 2. Comparison between Non-cardiac injury group and Cardiac injury group regarding organ injuries at the time of death.

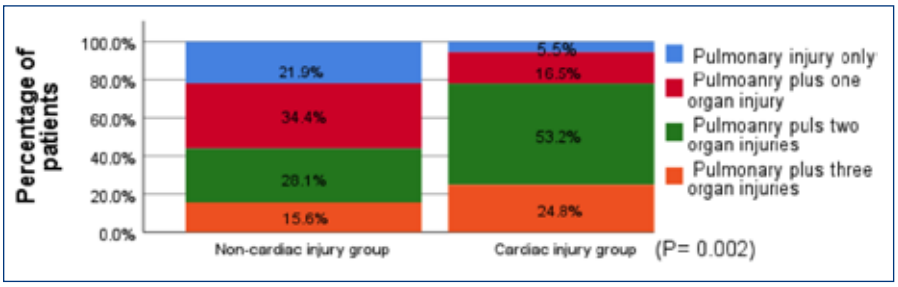

Table 3. Overall laboratory characteristics of 141 deceased COVID-19 patients according to presence or absence of cardiac injury on admission ^

Lab values	Available number	Total (n=141)	Cardiac injury (n=109)	No Cardiac injury (n=32)	P value
Kidney function					
BUN on admission (mg/dl)	141	42.9±26.8	47.7±27.8	26.6±13.6	**<0.001&**
Creatinine on admission (mg/dl)	141	2.1±1.6	2.3±1.8	1.5±0.8	**0.004&**
AKI on admission (%)	141	90(63.8%)	75(68.8%)	15(46.9%)	**0.023**
Liver function on admission					
Total bilirubin(mg/dl)	139	0.6±0.3	0.6±0.3	0.6±0.4	0.89
AST (U/L)	139	49.7±36.6	50.7±36.6	46.4±37.2	0.563
ALT(U/L)	139	30.5±25.5	29.1±23	35±32.7	0.636&
ALP(U/L)	138	76.4±37	76.7±35.6	75.4±41.5	0.857
Albumin (gm/dl)	139	3.5±0.4	3.5±0.5	3.6±0.3	0.224&
Cardiac function					
Troponin I level on admission (ng/ml)	141	0.5±2.9	0.7±3.3	0.02±0.006	0.251
Peak Troponin I Level(ng/ml)	122	0.9±2.9	1.1±3.2	0.2±0.5	0.006&
BNP on admission (PG/ML)	124	374±655.4	429.3±724.8	200.8±310.7	0.097
Inflammatory markers					
ESR on admission (MM/H)	63	55.8±29.9	55.2±31.4	57.7±25.4	0.776
Peak ESR (MM/H)	34	67.9±30.4	67.6±31.9	69.1±26.9	0.902
CRP on admission (mg/L)	136	143.3±96.8	148.4±100.6	126.8±82.4	0.271
Peak CRP (mg/L)	122	211.3±96.2	213.7±92.2	204±108.9	0.633
Ferritin on admission (ng/ml)	132	653.2±488.6	699.6±486.4	501.9±472.4	**0.048**
Peak Ferritin (ng/ml)	121	1017.4±507.3	1078.8±482.5	831.3±542.9	**0.02**
LDH on admission (U/L)	115	387.6±228.5	384±173.3	398.2±348.1	0.775
Peak LDH level (U/L)	92	1014.4±1708.7	831.3±895.6	1479.2±2868.6	0.132&
Coagulation parameters					
D-dimer on admission (mg/L FEU)	124	5.3±8.9	5.7±9	4.1±8.5	0.377
Peak D-dimer (mg/L FEU)	112	13.4±12.7	14±13.2	11.5±11.1	0.367
Procalcitonin on admission (ng/mL)	129	4.1±16.7	5.2±18.9	0.4±0.5	**0.014&**

Abbreviations: BUN, blood urea nitrogen; AKI, acute kidney injury; AST, aspartate aminotransferase; ALT, alanine transaminase; ALP, alkaline phosphatase; BNP, brain natriuretic peptide; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; LDH, lactate dehydrogenase.
^ Cardiac injury here was referred to on admission Troponin level equal or more than 0.030 ng/ml.
& Mann-Whitney U test was used for statistics.

Overall laboratory characteristics

As shown in **Table 3,** compared to deceased patients without cardiac injury, those with cardiac injury on admission had significant higher admission blood urea nitrogen level (47.7 vs 26.6 mg/dl, *P*<0.001), creatinine (2.3 vs 1.5 mg/dl, *P*=0.004), higher admission rate of acute kidney injury (68.8% vs 46.9%, *P*= 0.023), ferritin (699.6 vs 501.9 ng/ml, *P*=0.048), procalcitonin (5.2 vs 0.4 ng/mL, *P*=0.014) levels and peak ferritin level (1078.8 vs 831.3 ng/ml, *P*=0.02). There were no significant differences in admission brain natriuretic peptide level, inflammation markers and coagulation parameters during hospitalization between these two groups.

Clinical course, treatment summary, electrocardiogram characteristics, and transthoracic echocardiogram findings

Regarding clinical course, as shown in Table 2, compared to deceased patients without cardiac injury, those with cardiac injury on admission had lower rates of superimposed bacterial infection (24.8% vs 46.9%, *P*=0.016). There were no differences in the fraction of inspired oxygen (FiO2) level on admission and at the time of death, incidence of pulmonary embolism and/or deep venous thrombosis, rates bronchoalveolar lavage, or ICU transfers between these two groups (*P*>0.05).

Regarding treatment during hospitalization (data not shown), there were no significant differences in the percentage of oxygen administration methods at the time of death; use of Remdesivir, Steroid, Tocilizumab, Convalescent plasma, Azithromycin, Plaquenil and/or Zinc; or dose of anticoagulation received

Table 4. EKG characteristics of 141 deceased patients according to presence or absence of cardiac injury ^

Cardiac workup	Available number	Percentage	Cardiac injury	No Cardiac injury	P value
EKG Ischemic findings					**1#**
No new changes	87	66.4% (87/131)	66.3% (67/101)	66.7% (20/30)	
New ST elevation/ depression, T wave inversion	14	10.7% (14/131)	10.9% (11/101)	10% (3/30)	
Non-specific ST-T wave changes	30	22.9% (30/131)	22.8% (23/101)	23.3% (7/30)	
Arrhythmia					**0.52#**
Normal sinus rhythm	62	47% (62/132)	48% (49/102)	43.3% (13/30)	
Sinus Tachycardia	27	20.5% (27/132)	16.7% (17/102)	33.3% (10/30)	
Sinus Bradycardia	6	4.5% (6/132)	3.9% (4/102)	6.7% (2/30)	
New onset A-fib/a-flutter	12	9.1% (12/132)	9.8% (10/102)	6.7% (2/30)	
SVTs other than a-fib/a-flutter	7	5.3% (7/132)	5.9% (6/102)	3.3% (1/30)	
VF/VT	3	2.3% (3/132)	2.9% (3/102)	0	
Old A-Fib	15	11.4% (15/132)	12.7% (13/102)	6.7% (2/30)	

Abbreviations: EKG, electrocardiogram; a-fib, atrial fibrillation; a-flutter, atrial flutter; SVT, supraventricular tachycardia; VT, ventricular tachycardia; VF, ventricular fibrillation.
^ Cardiac injury here was referred to on admission Troponin level equal or more than 0.030 ng/ml.
# Fisher's exact test was used for statistics.

(prophylactic dose, intermittent therapeutic dose, or around-the-clock therapeutic dose) between cardiac injury group and non-cardiac injury group.

Regarding the EKG findings as shown in **Table 4**, there was also no statistical difference between the two groups (P>0.05). We also compared the echocardiographic findings between these two groups; no significant differences were found (P>0.05, data not shown).

DISCUSSION

Immediate cause of death in COVID-19 patients with cardiac injury

Several studies concluded that the most common immediate cause of death was hypoxic respiratory failure,[19, 24, 25] followed by multi-organ failure and septic shock in patients hospitalized with COVID-19.[17] In a study regarding the timing and cause of death in COVID-19 patients, De Roquetaillade et al concluded that COVID-19 related multi-organ dysfunction and secondary infection was the most common immediate cause of death in critically ill COVID-19 patients.[20] However, these conclusions were drawn from the general COVID-19 patient population without accounting for presence of cardiac injury. Currently, there is no report elucidating the immediate causes of death specifically in COVID-19 patients with cardiac injury. Given the special pathogenesis of COVID-19 related cardiac injury,[26] and the notion that COVID-19 patients with cardiac injury had higher mortality rates than those without cardiac injury,[6, 9-12] it was reasonable to hypothesize that patients with cardiac injury would die more of cardiac- related complications from COVID-19 infection, or that higher proportion of patients with cardiac injury would die of cardiac-related conditions as compared to those without cardiac injury.

Contrary to our belief, we report that the most common immediate causes of death of COVID-19 patients with cardiac injury were non-cardiac, mostly hypoxic respiratory failure, followed by multi-organ failure and septic shock, a pattern that is similar when compared to deceased patients without cardiac injury on admission. Only a very small portion of patients died of cardiac arrhythmia, mostly ventricular tachycardia and/or ventricular fibrillation, a difference that was not statistically significant between patients with and without cardiac injury. The distribution pattern of immediate causes of death was similar between cardiac injury and non-cardiac injury groups. However, the cardiac injury group had a higher rate of acute kidney injury on admission and multi-organ injury at the time of death, and shorter admission to death time, which indicated that these patients had a more serious clinical course and deteriorated quicker. Thus, cardiac injury per se is likely a reflection of a more severe COVID-19 infection affecting multiple organs where the heart is one of the injured organs and does not support the notion of a heart-specific target among patients with cardiac injury and COVID-19 hospitalization. Our current study also revealed that deceased patients with cardiac injury had a higher rate of acute kidney injury on admission compared to those without cardiac injury. This result was consistent with Guo et al, [27] who reported that general COVID-19 patients with cardiac injury had a higher rate of developing acute kidney injury (36.8% vs 4.7%) compared to a patient without cardiac injury. The rate of kidney injury was much higher in our population likely because our study population was the most serious COVID-19 patients who died in-hospital.

Our findings of a rate of 3-5% of ventricular tachycardia and/or ventricular fibrillation, was in agreement with the findings of Ruan et al,[24, 28] and Contou et al,[13, 25] who reviewed general and critically ill COVID-19 patients, with similar findings. Coromilas et al retrospectively summarized the data of 4526 patients from different countries and

demonstrated that 2.4% of hospitalized COVID-19 patients had ventricular tachycardia or ventricular fibrillation recorded at the time of death.[14] They further showed that 23.7% patients had non-shockable rhythms including bradycardia, pulseless electrical activity, or asystole at the time of death. None of the previous studies accounted for cardiac injury status. Our study builds on previous findings and supports the notion of severe hypoxemia and critical illness being the primary driver of cardiac arrest leading to death in this population, rather than myocardial injury or cardiac-specific abnormality leading to primary cardiac arrest. Based on our chart review, most of our COVID-19 patient deaths were initially preceded by worsening hypoxemia followed by bradycardia and then asystole, as Coromilas et al had also stated in their study.[14] However, there is a small proportion of patients who suddenly developed ventricular tachycardia/ventricular fibrillation without hypoxemia as a precipitant. These are the patients we attributed the causes of deaths to related cardiac arrhythmia. For cases with expected causes of cardiac arrhythmia such as severe kidney failure, with potassium level up to 7-8 mmol/L before they died of cardiac arrhythmia, these patients' immediate cause of death was attributed to hyperkalemia secondary to kidney failure; hence, they were not considered as a primary cardiac arrhythmic death in our study.

The potential pathogenesis underlying cardiac injury with worse clinical course

Our current study demonstrated that inflammatory markers were significantly elevated in all deceased patients (including cardiac injury and non-cardiac injury patients), which is in line with the theory of involvement of inflammation-mediated cytokine release syndrome and the micro-macro vascular thrombosis related coagulopathy pathway in the pathogenesis of COVID-19-mediated organ injury.[29, 30] While studies conducted by Wang et al,[24] and Mengozzi et al demonstrated higher inflammatory markers such as CRP,[31] D-dimer in the cardiac injury group, our data revealed that only ferritin and procalcitonin were significantly elevated in cardiac injury compared to non-cardiac injury patients. The difference is likely reflective of our sample being severe COVID-19 patients who were deceased and may support ferritin and pro-calcitonin being a more specific inflammatory marker of adverse outcomes compared to the rest (e.g., CRP, sedimentation rate, D-dimer). Interestingly, in our study, although cardiac injury group patients were older, having a higher rate of congestive heart failure history as compared to the non-cardiac injury group patients, the admission fraction of inspired oxygen level was similar in these two groups, which meant cardiac injury group patients were not necessarily sicker on admission from a respiratory standpoint. However, they did have higher rates of acute kidney injury on admission and higher rates of multi-organ injury at the time of death, indicating that cardiac injury might be an indicator for higher possibility of concurrent acute kidney injury on admission and multi-organ injury at death in severely ill COVID-19 patients. The pathogenesis behind this notion remains unclear and warrants further investigation. Furthermore, from our current data, it is hard to say whether the preexisting congestive heart failure history predisposed the patients to cardiac injury in COVID-19 patients, and/or kidney injury; or whether the cardiac injury/kidney injury on admission was purely reflection of multi-organ tropism from the COVID-19 virus.

Comparison of immediate cause of death result to published post-mortem autopsy

Wichamn et al reported that deep venous thrombosis was found in 58% patients (12 patients total),[32] while one-third of patients died immediately of pulmonary embolism as evidenced in the autopsy result. In our study, pulmonary embolism was documented in only 5.5% (6/109) patients. In a study conducted by Elezkurtaj et al on 26 patients,[18] the autopsy result revealed that septic shock and multi-organ failure was the most common immediate cause of death, often due to suppurative pulmonary infection, a finding that was similar to our study, irrespective of the cardiac injury status.

LIMITATIONS

When comparing the admission to death time between the two groups, the duration of pre-hospital illness was missing in the current study. It is unclear how this would change our current conclusion regarding the admission to death time. Secondly, we have to address that this is a relatively small sample size study, particularly among the patients without cardiac injury. In addition, the parameters extracted were just snapshots of the clinical course. Given the complicated course and evolving clinical picture of COVID-19 infection, the inclusion of serial cardiac biomarkers, such as troponin and BNP levels, as well as echocardiogram findings in a larger proportion of patients would have provided a broader understanding of the extent of cardiac injury in these patients, even though it might still not have changed the most common immediate cause of death. Lastly, there were no corresponding post-mortem autopsies to investigate specifically the cause of death since autopsy was declined by most relatives of the deceased. Future studies that compiled more complete clinical data, autopsy results and clinical chart review from multiple centers will be needed to assess the generalizability of our results.

CONCLUSIONS

The most common immediate cause of death in COVID-19 patients with cardiac injury was hypoxic respiratory failure. Cardiac arrhythmia accounted for a very small portion of the immediate cause of death, with similar prevalence between

the cardiac and non-cardiac injury patients. The distribution of immediate causes of death was similar between patients with and without cardiac injury, but deceased patients with cardiac injury had higher rates of kidney injury as well as multi-organ failure at the time of death. The treatment of COVID-19 patients with cardiac injury should still focus on the treatment of the underlying pulmonary pathology and support of the multi-organ failure.

References

1. Wang C, Wang Z, Wang G, Lau JY, Zhang K and Li W. COVID-19 in early 2021: current status and looking forward. *Signal Transduct Target Ther*. 2021;6:114.
2. Amawi H, Abu Deiab GaI, A Aljabali AA, Dua K, Tambuwala MM. COVID-19 pandemic: an overview of epidemiology, pathogenesis, diagnostics and potential vaccines and therapeutics. *Ther Deliv*. 2020;11:245-268.
3. Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, Bikdeli B, Ahluwalia N, Ausiello JC, Wan EY, Freedberg DE, Kirtane AJ, Parikh SA, Maurer MS, Nordvig AS, Accili D, Bathon JM, Mohan S, Bauer KA, Leon MB, Krumholz HM, Uriel N, Mehra MR, Elkind MSV, Stone GW, Schwartz A, Ho DD, Bilezikian JP, Landry DW. Extrapulmonary manifestations of COVID-19. *Nature Medicine*. 2020;26:1017-1032.
4. Batlle D, Soler MJ, Sparks MA, Hiremath S, South AM, Welling PA, Swaminathan S. Acute Kidney Injury in COVID-19: Emerging Evidence of a Distinct Pathophysiology. *Journal of the American Society of Nephrology*. 2020;31:1380-1383.
5. Puelles VG, Lütgehetmann M, Lindenmeyer MT, Sperhake JP, Wong MN, Allweiss L, Chilla S, Heinemann A, Wanner N, Liu S, Braun F, Lu S, Pfefferle S, Schröder AS, Edler C, Gross O, Glatzel M, Wichmann D, Wiech T, Kluge S, Pueschel K, Aepfelbacher M, Huber TB. Multiorgan and Renal Tropism of SARS-CoV-2. *New England Journal of Medicine*. 2020;383:590-592.
6. Zou F, Qian Z, Wang Y, Zhao Y and Bai J. Cardiac Injury and COVID-19: A Systematic Review and Meta-analysis. *CJC Open*. 2020;2:386-394.
7. Nishiga M, Wang DW, Han Y, Lewis DB and Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nature Reviews Cardiology*. 2020;17:543-558.
8. Fox SE, Akmatbekov A, Harbert JL, Li G, Quincy Brown J and Vander Heide RS. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. *Lancet Respir Med*. 2020;8:681-686.
9. He Y, Zheng X, Li X and Jiang X. Key factors leading to fatal outcomes in COVID-19 patients with cardiac injury. *Scientific Reports*. 2021;11:4144.
10. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B and Huang C. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiology*. 2020;5:802-810.
11. Al-Wahaibi K, Al-Wahshi Y and Mohamed Elfadil O. Myocardial Injury Is Associated with Higher Morbidity and Mortality in Patients with 2019 Novel Coronavirus Disease (COVID-19). *SN Compr Clin Med*. 2020:1-7.
12. Efros O, Barda N, Meisel E, Leibowitz A, Fardman A, Rahav G, Klempfner R and Grossman E. Myocardial injury in hospitalized patients with COVID-19 infection—Risk factors and outcomes. *PLOS ONE*. 2021;16:e0247800.
13. Basso C, Leone O, Rizzo S, De Gaspari M, van der Wal AC, Aubry MC, Bois MC, Lin PT, Maleszewski JJ and Stone JR. Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study. *Eur Heart J*. 2020;41:3827-3835.
14. Coromilas EJ, Kochav S, Goldenthal I, Biviano A, Garan H, Goldbarg S, Kim JH, Yeo I, Tracy C, Ayanian S, Akar J, Singh A, Jain S, Zimerman L, Pimentel M, Osswald S, Twerenbold R, Schaerli N, Crotti L, Fabbri D, Parati G, Li Y, Atienza F, Zatarain E, Tse G, Leung KSK, Guevara-Valdivia ME, Rivera-Santiago CA, Soejima K, De Filippo P, Ferrari P, Malanchini G, Kanagaratnam P, Khawaja S, Mikhail GW, Scanavacca M, Abrahão Hajjar L, Rizerio B, Sacilotto L, Mollazadeh R, Eslami M, Laleh Far V, Mattioli AV, Boriani G, Migliore F, Cipriani A, Donato F, Compagnucci P, Casella M, Dello Russo A, Coromilas J, Aboyme A, O'Brien CG, Rodriguez F, Wang PJ, Naniwadekar A, Moey M, Kow CS, Cheah WK, Auricchio A, Conte G, Hwang J, Han S, Lazzerini PE, Franchi F, Santoro A, Capecchi PL, Joglar JA, Rosenblatt AG, Zardini M, Bricoli S, Bonura R, Echarte-Morales J, Benito-González T, Minguito-Carazo C, Fernández-Vázquez F and Wan EY. Worldwide Survey of COVID-19-Associated Arrhythmias. *Circ Arrhythm Electrophysiol*. 2021;14:e009458.
15. Bois MC, Boire NA, Layman AJ, Aubry MC, Alexander MP, Roden AC, Hagen CE, Quinton RA, Larsen C, Erben Y, Majumdar R, Jenkins SM, Kipp BR, Lin PT and Maleszewski JJ. COVID-19-Associated Nonocclusive Fibrin Microthrombi in the Heart. *Circulation*. 2021;143:230-243.
16. Hayek SS, Brenner SK, Azam TU, Shadid HR, Anderson E, Berlin H, Pan M, Meloche C, Feroz R, O'Hayer P, Kaakati R, Bitar A, Padalia K, Perry D, Blakely P, Gupta S, Shaefi S, Srivastava A, Charytan DM, Bansal A, Mallappallil M, Melamed ML, Shehata AM, Sunderram J, Mathews KS, Sutherland AK, Nallamothu BK and Leaf DE. In-hospital cardiac arrest in critically ill patients with covid-19: multicenter cohort study. *BMJ*. 2020;371:m3513.
17. Guo A-X, Cui J-J, Ouyang Q-Y, He L, Guo C-X and Yin J-Y. The clinical characteristics and mortal causes analysis of COVID-19 death patients. 2020.
18. Elezkurtaj S, Greuel S, Ihlow J, Michaelis EG, Bischoff P, Kunze CA, Sinn BV, Gerhold M, Hauptmann K, Ingold-Heppner B, Miller F, Herbst H, Corman VM, Martin H, Radbruch H, Heppner FL and Horst D. Causes of death and comorbidities in hospitalized patients with COVID-19. *Scientific Reports*. 2021;11.
19. Contou D, Cally R, Sarfati F, Desaint P, Fraissé M and Plantefève G. Causes and timing of death in critically ill COVID-19 patients. *Critical Care*. 2021;25:79.
20. De Roquetaillade C, Bredin S, Lascarrou J-B, Soumagne T, Cojocaru M, Chousterman BG, Leclerc M, Gouhier A, Piton G, Pène F, Stoclin A and Llitjos J-F. Timing and causes of death in severe COVID-19 patients. *Critical Care*. 2021;25.
21. Elezkurtaj S, Greuel S, Ihlow J, Michaelis E, Bischoff P, Kunze CA, Sinn BV, Gerhold M, Hauptmann K, Ingold-Heppner B, Miller F, Herbst H, Corman VM, Martin H, Radbruch H, Heppner FL and Horst D. Causes of Death and Comorbidities in Patients with COVID-19. *medRxiv*. 2020:2020.06.15.20131540.
22. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B and Huang C. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiology*. 2020;5:802.
23. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA and White HD. Fourth Universal Definition of Myocardial Infarction (2018). *Journal of the American College of Cardiology*. 2018;72:2231-2264.
24. Wang K, Qiu Z, Liu J, Fan T, Liu C, Tian P, Wang Y, Ni Z, Zhang S, Luo J, Liu D and Li W. Analysis of the clinical characteristics of 77 COVID-19 deaths. *Scientific Reports*. 2020;10.
25. Olivas-Martínez A, Cárdenas-Fragoso JL, Jiménez JV, Lozano-Cruz OA, Ortiz-Brizuela E, Tovar-Méndez VH, Medrano-Borromeo C, Martínez-Valenzuela A, Román-Montes CM, Martínez-Guerra B, González-Lara MF, Hernandez-Gilsoul T, Herrero AG, Tamez-Flores KM, Ochoa-Hein E, Ponce-De-León A, Galindo-Fraga A, Kershenobich-Stalnikowitz D and Sifuentes-Osornio J. In-hospital mortality from severe COVID-19 in a tertiary care center in Mexico City; causes of death, risk factors and the impact of hospital saturation. *PLOS ONE*. 2021;16:e0245772.

26. Yadav R, Bansal R, Budakoty S and Barwad P. COVID-19 and sudden cardiac death: A new potential risk. *Indian Heart Journal*. 2020;72:333-336.
27. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X and Lu Z. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiology*. 2020;5:811.
28. Ruan Q, Yang K, Wang W, Jiang L and Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Medicine*. 2020;46:846-848.
29. Manolis AS, Manolis TA, Manolis AA, Papatheou D and Melita H. COVID-19 Infection: Viral Macro- and Micro-Vascular Coagulopathy and Thromboembolism/Prophylactic and Therapeutic Management. *Journal of Cardiovascular Pharmacology and Therapeutics*. 2020;26:12-24.
30. Que Y, Hu C, Wan K, Hu P, Wang R, Luo J, Li T, Ping R, Hu Q, Sun Y, Wu X, Tu L, Du Y, Chang C and Xu G. Cytokine release syndrome in COVID-19: a major mechanism of morbidity and mortality. *Int Rev Immunol*. 2021:1-14.
31. Mengozzi A, Georgiopoulos G, Falcone M, Tiseo G, Pugliese NR, Dimopoulos MA, Ghiadoni L, Barbieri G, Forfori F, Carrozzi L, Santini M, Monzani F, De Marco S, Menichetti F, Virdis A and Masi S. The relationship between cardiac injury, inflammation and coagulation in predicting COVID-19 outcome. *Scientific Reports*. 2021;11.
32. Wichmann D, Sperhake J-P, Lütgehetmann M, Steurer S, Edler C, Heinemann A, Heinrich F, Mushumba H, Kniep I, Schröder AS, Burdelski C, de Heer G, Nierhaus A, Frings D, Pfefferle S, Becker H, Bredereke-Wiedling H, de Weerth A, Paschen H-R, Sheikhzadeh-Eggers S, Stang A, Schmiedel S, Bokemeyer C, Addo MM, Aepfelbacher M, Püschel K and Kluge S. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. *Ann Intern Med*. 2020;173:268-277.

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Frameworks for Global Health Collaboration in Pandemic Disease

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ABSTRACT

Novel disease emergence with associated outbreaks and pandemics have become increasingly common in the last several decades. For centuries, people have utilized various forms of collaboration to control outbreaks. Modern global health frameworks now play a central role in guiding a targeted and coordinated international disease response; recent pandemics have shown that such systems have both strengths and vulnerabilities. This report assesses the existing global health infrastructure for pandemic response and discusses how the World Health Organization (WHO) and global health infrastructure has responded to recent public health threats.

KEYWORDS: pandemic, health policy, World Health Organization, global health, COVID-19

INTRODUCTION

In the past two decades, there have been numerous infectious disease outbreaks of worldwide importance: several strains of influenza A (2009 H1N1, H5N1), a number of strains of coronavirus including severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, also known as the COVID-19 pandemic), as well as multiple independent viral hemorrhagic fevers. Zoonotic illnesses, such as those mentioned above, are transmitted from animal to human hosts; zoonoses account for 60% of all known infectious disease and make up approximately 75% of modern emerging and novel infectious disease threats.[1,2]

The early identification of infectious disease outbreaks is contingent on monitoring systems, which range from the local to the regional and global level. Systems such as the Pakistani Disease Early Warning System, the United States National Outbreak Reporting System, or the regional African REDISSE (renforcement du système régional de surveillance des maladies) can collate data to more efficiently identify a developing disease epidemic.[3–5] However, outbreak detection is complicated by the fact that many modern pandemic illnesses, including influenza, SARS, MERS, and SARS-CoV-2, have all had somewhat nonspecific clinical syndromes, and were initially detected due to geographic clustering.[6] This is in contrast to outbreaks of hemorrhagic fever which are often clinically quite distinct. A number of other factors, including accessible and highly trafficked international trade and travel networks, facilitate the dissemination of communicable disease among and between countries.[7–9] Recent experience has shown that collaborative responses to disease outbreaks come with unique challenges but stand to yield worldwide benefits.

GLOBAL FRAMEWORKS FOR COLLABORATION AROUND DISEASE CONTROL

History of collaboration

Disease control measures (namely quarantine) for leprosy and bubonic plague have been recognized throughout human history.[10] For the last several centuries, it has been known that infectious disease threats require collective action and coordinated intervention towards containment and disease control. Beginning in 1851, the International Sanitary Conventions were held in Paris in response to multiple European cholera epidemics, in order to address concerns of the ill effects of disease outbreak and the subsequent negative impacts of border closures.[11,12] At the 1874 conference, a permanent international health agency was first proposed, and was intended to focus on cholera but also "pay attention to other epidemic diseases."[10]

The Pan-American Sanitary Bureau was founded in 1902, based in Washington, DC, and served to coordinate health care among countries in North, Central and South America.[10,13] The third Sanitary Conference of the Pan-American Sanitary Bureau led to the establishment of a formal collaboration with the Office International d'Hygiène Publique, with the focus on exchange of information regarding "sanitary conditions" and disease quarantine measures in the ports of member states.[13] Both organizations distributed monthly bulletins that contained information for public health officials, including sanitation measures, statistics, and understanding of the spread of disease.[10,13]

The World Health Organization (WHO) was founded in 1948, shortly after the founding of the United Nations, and brought together existing global and regional health entities.[14] In 1951, WHO member-states adopted the International Sanitary Regulations which were revised in 1969 to create the International Health Regulations (IHR), which initially covered six specific diseases.[12] The IHR were revised

several times and eventually pared down to three diseases: yellow fever, cholera and plague.

In the late 1990s and early 2000s, WHO member-states devised a new legal framework with the same name, the International Health Regulations. This new iteration of the IHR has the stated purpose "to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks."[15] Such aims are achieved through individual member-states building up a core public health capacity, obligations to avoid actions which impart negative economic effects or impede the rights of travelers, and through member obligations around notification to the WHO of potential public health emergencies.[15] Under the 2005 IHR, members are to notify the WHO about any public health event which could be of concern to the other nation-states. While the formal designation of a public health emergency of international concern (PHEIC) can only be declared by the WHO secretary-general, under the terms of the IHR member-states must notify the WHO of any potential such emergency. PHEICs are defined as events which pose a risk to other countries due to the risk of international spread, and may require a systematic international response.[12,15]

The IHR & PHEICs

The 2005 IHR represented a distinct shift from a rigid, disease-specific approach to an open-ended collaborative approach, and the IHR has since been described as "the sole and indispensable legal framework for global health security."[16] The 2005 iteration of the IHR does not focus on a specific disease or mode of transmission, but instead lays out an agreed upon paradigm for disease identification and control. Under the IHR, countries shifted towards a more comprehensive public health system capacity approach that is not focused on specific diseases or entry/exit-points.[16] Additionally, member-states are obligated to notify the WHO about any domestic public health event which potentially poses a risk to other countries, and members are to respond to WHO requests for further details and information.[12]

IHR Compliance and Dispute Mechanism

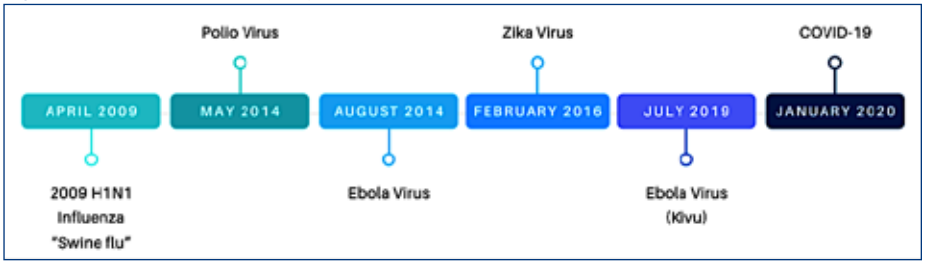
The IHR does not have an enforcement mechanism built into its regulations, though geo-political pressure and international standing are considered forces that encourage compliance.[12] Notably, the IHR has no funding for monitoring and there are no concrete consequences for IHR non-compliance.[16,17] There has been almost no prior work evaluating member-state compliance with the WHO IHR in the acute phase of an epidemic/pandemic public health emergency.[17]

WHO member-states are meant to collaborate through the WHO around infectious disease outbreaks. The 2015 United Nations Sustainable Development Goals (SDGs) emphasize the particular vulnerability of developing nations to infectious outbreaks and epidemic disease. SDG 3D highlights the need for all countries, and "in particular developing countries," to "strengthen capacity for early warning, risk reduction and management of national and global health risks."[18] This SDG ties in directly with the IHR and reinforces the notion that development is reliant on health system capacity and infrastructure at the local and global level.

PHEICs and Emergency Committee

Six PHEICs have been declared between 2009 and 2021. The action to declare a given event as a PHEIC has been critiqued as subjective and prone to inconsistencies and geopolitical considerations.[16] The six PHEICs to date are outlined in **Figure 1**. Across events, the WHO has not recommended travel restrictions in regards to a PEHIC, except in very limited situations such as pregnant women traveling to Zika endemic areas.[19]

Figure 1. Public Health Emergency of International Concern (PHEIC) Declarations to Date[20]



Though the decision to declare a PHEIC lies with the WHO director-general, advice and recommendations are offered by way of an advisory panel titled the Emergency Committee. An emergency committee has been convened by the WHO with each major public health threat; the emergency committee meets in private, and until recently the membership lists were not available, and outcome reports have been limited in their explanation around decision-making.[16,21] The emergency committees are convened only as needed and membership is pulled from a list of pre-approved subject matter technical experts who are recommended by member-state governments.[21] The emergency committee works to assess all available data to make an informed recommendation to the WHO director-general, and if conditions for a PHEIC are satisfied the committee then puts forth recommendations for actions to the director-general and member-states.[21]

Member-State Autonomy and Self-Interest

When a disease outbreak occurs, individual countries may act in insular and self-interested ways that run counter to obligations under the IHR. This can impede a robust and coordinated international response, and in many ways runs

counter to the collaborative aims of the WHO and global multilateral frameworks.[22] It has been suggested that nation-states that are heavily engaged in trade may be incentivized to conceal an outbreak early on in an attempt to control the disease without outside knowledge or assistance. Similarly, concealment may help temporarily protect against the risk of loss of domestic and international public opinion and confidence.[23] Interestingly, some countries that obtain significant revenues from tourism have been more apt to quickly report infectious threats (for example, Vietnam in the 2003 SARS epidemic), and such decisions have seemingly been rewarded through sustained confidence in government transparency.[23]

Beyond government actors, large corporations and multi-national businesses play a major role in politics and global decision making in the face of a disease outbreak or formal PHEIC. Private corporations may make decisions regarding trade and travel outside of the recommendations or purview of national governments or the WHO.[23] Even if member-states do not restrict travel, it is common for private corporations to make autonomous decisions regarding extracting employees from hot-spots, or canceling trade and travel routes to affected areas.[16,21,23] Such corporate decisions are subject to political and economic considerations, but lie well outside of the purview of the IHR or any other legally-binding multilateral agreement.

Novel Approaches to Novel Diseases

The 2005 IHR made a distinctive shift towards capacity building and generalized disease control preparedness. This shift has generated innovative thinking around how to expand capacity and prepare for novel and dynamic infectious disease outbreaks. Unique solutions to disease control preparedness and monitoring have included regional surveillance networks, which have been set up outside of the formal WHO networks, by national governments to self-organize an optimal sub-regional surveillance system (such as the above mentioned African REDISSE).[1,5] Individual countries have also taken steps towards domestic disease control mechanisms; for example, the United States maintains a "Do Not Board" list for individuals with known infectious risks to disallow certain travel at high risk of spreading targeted communicable diseases.[24]

Recent outbreaks affecting low-income countries have stimulated discussion around the creation of funding mechanisms to quickly assist in mobilization and disease containment in such settings.[25] In response, the World Bank launched the Pandemic Emergency Financing Facility (PEF) to provide the world's poorest countries with rapid funding in times of disease outbreaks.[26] As a response to the difficulty in financing the response to the 2014 Ebola crisis, the PEF was launched in 2016. This financing mechanism is funded through over 50 donor countries (many of whom are members of the International Development Association, or IDA) and the private sector, not through potential recipient countries.[26] Functionally, certain criteria for a pandemic emergency must be met in order for funds to be available for disbursement, and can go to governments of low-income countries and pre-approved frontline organizations such as the WHO and the United Nations Children's Fund.[26]

WHO/IHR and COVID-19

The WHO declared the SARS-CoV-2 outbreak a PHEIC on Jan 30, 2020.[27,28] The COVID-19 pandemic led to the creation of a disease-specific emergency committee, which consists of: one chairman, 18 members, and 13 advisors.[29] After each meeting the emergency committee releases a set of recommendations to both the WHO secretariat and member-states. After their most recent (ninth) meeting on 22 October 2021, the emergency committee for COVID-19 reiterated that they believe the pandemic continues to constitute a PHEIC.[30] The emergency committee for COVID-19 continues to recommend the WHO secretariat lead as a global coordinator and collaborator, particularly through the lens of global and regional multilateral organizations and member-states.[31]

In response to the COVID-19 outbreak, which met PEF pandemic emergency criteria, more than USD$195 million has been earmarked for the world's 64 poorest countries through the PEF mechanism.[26,32] The creation and utilization of relief funds like these are, theoretically, of the largest potential benefit to lower income countries who are the least resilient towards and most significantly affected by the downstream effects of travel and/or trade restrictions due to a disease outbreak.[11] As of July 2020, $146.5 million had been transferred to 48 countries.[32] This is a substantial disbursement in support of a pandemic disease response, though not nearly adequate to ameliorate the needs that have come up for treatment and control of the COVID-19, nor to offset wide-ranging deleterious economic impacts.

Interestingly, other components of the global health and development sphere have come together to lend aid to COVID-19 response efforts. The World Food Programme (WFP) has been able to respond to large reductions to international air travel and resultant gaps in supply chains to leverage its preexisting logistics capacity. WFP has utilized its logistics network to develop an air bridge system with several global and regional hubs.[33,34] The WFP air bridge network has worked to ferry humanitarian aid and crucial supplies where they are needed, though funding for the network is not yet adequate for the forecasted need/demand.[35] While COVID-19 has shown how some global actors may choose to act in self-interested ways, others have found new and innovative ways to respond.

DISCUSSION

With COVID-19 we have seen nations neglecting the agreed-to international legal obligations; the WHO plays a

key role in creating and implementing global health law.[36] People have been coordinating around infectious disease management on an international level for centuries. Infectious outbreaks seen throughout the last few decades, including the ongoing COVID-19 pandemic, have shown the importance of global collaboration and coordination. Several socio-demographic and biological risk factors indicate that future infectious pandemics are likely; the world is closely interconnected, the global population is still growing and urbanizing, and epidemic/pandemic disease outbreaks strain local and national health systems.

The IHR create a framework for globally coordinated preparedness and response despite these evolving challenges. The IHR has both strengths and shortcomings in augmenting the response to an infectious disease outbreak. Though WHO plays the leading role through the IHR, many different stakeholders, including: member states, multilateral organizations, non-profit and civil society organizations, and private businesses all are impacted by and have a role to play in infectious disease outbreaks and epidemics/pandemics of global concern. The WHO has developed a system for declaring and responding to public health emergencies of international concern.

The response to COVID-19 has shown that the existing global health framework for pandemic response has benefits and drawbacks. Novel approaches continue to be developed and can work to augment the IHR. There has been success in providing accelerated funding to LMICs in early pandemic response, as well as national, regional, and global programmatic efforts. Looking forward, there will continue to be future infectious disease outbreaks of global concern. With each new outbreak there needs to be ever-evolving ways of coordinating and responding within and complementary to existing and future iterations of global health frameworks.

References

1. Bond KC, Macfarlane SB, Burke C, Ungchusak K, Wibulpolprasert S. The Evolution and Expansion of Regional Disease Surveillance Networks and Their Role in Mitigating the Threat of Infectious Disease Outbreaks. Emerg Health Threats J [Internet]. 2013 Jan 25 [cited 2020 Jul 30];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3557911/
2. Zoonotic Diseases | One Health | CDC [Internet]. 2021 [cited 2021 Aug 24]. Available from: https://www.cdc.gov/onehealth/basics/zoonotic-diseases.html
3. Rahim M, Kazi BM, Bile KM, Munir M, Khan AR. The impact of the disease early warning system in responding to natural disasters and conflict crises in Pakistan. East Mediterr Health J Rev Sante Mediterr Orient Al-Majallah Al-Sihhiyah Li-Sharq Al-Mutawassit. 2010;16 Suppl:S114-121.
4. Rainey JJ, Phelps T, Shi J. Mass Gatherings and Respiratory Disease Outbreaks in the United States - Should We Be Worried? Results from a Systematic Literature Review and Analysis of the National Outbreak Reporting System. PloS One. 2016;11(8):e0160378.
5. Agbo S, Gbaguidi L, Biliyar C, Sylla S, Fahnbulleh M, Dogba J, et al. Establishing National Multisectoral Coordination and collaboration mechanisms to prevent, detect, and respond to public health threats in Guinea, Liberia, and Sierra Leone 2016-2018. One Health Outlook. 2019;1:4.
6. Perl TM, Price CS. Managing Emerging Infectious Diseases: Should Travel Be the Fifth Vital Sign? Ann Intern Med [Internet]. 2020 Mar 3 [cited 2020 Jul 25]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7081174/
7. Brownstein JS, Wolfe CJ, Mandl KD. Empirical Evidence for the Effect of Airline Travel on Inter-Regional Influenza Spread in the United States. PLOS Med. 2006 Sep 12;3(10):e401.
8. Colizza V, Barrat A, Barthélemy M, Vespignani A. The role of the airline transportation network in the prediction and predictability of global epidemics. Proc Natl Acad Sci. 2006 Feb 14;103(7):2015–20.
9. Hollingsworth TD, Ferguson NM, Anderson RM. Frequent Travelers and Rate of Spread of Epidemics. Emerg Infect Dis. 2007 Sep;13(9):1288–94.
10. Howard-Jones N. Origins of international health work. Br Med J. 1950 May 6;1(4661):1032–7.
11. Tigerstrom B von, Wilson K. COVID-19 travel restrictions and the International Health Regulations (2005). BMJ Glob Health. 2020 May 1;5(5):e002629.
12. World Health Organization. Frequently asked questions about the International Health Regulations (2005) [Internet]. Geneva: World Health Organization; 2009 [cited 2020 Jul 28] p. 6. Available from: https://www.who.int/ihr/about/FAQ2009.pdf
13. Lloyd BJ. The Pan American Sanitary Bureau. Am J Public Health Nations Health. 1930 Sep;20(9):925–9.
14. Lidén J. The World Health Organization and Global Health Governance: post-1990. Public Health. 2014 Feb 1;128(2):141–7.
15. WHO. International Health Regulations (2005) [Internet]. World Health Organization. World Health Organization; 2005 [cited 2020 Jul 25]. Available from: http://www.who.int/ihr/about/en/
16. Luca Burci G. The Outbreak of COVID-19 Coronavirus: are the International Health Regulations fit for purpose? [Internet]. EJIL: Talk! 2020 [cited 2020 Jul 28]. Available from: https://www.ejiltalk.org/the-outbreak-of-covid-19-coronavirus-are-the-international-health-regulations-fit-for-purpose/
17. Rhymer W, Speare R. Countries' response to WHO's travel recommendations during the 2013–2016 Ebola outbreak. Bull World Health Organ. 2017 Jan 1;95(1):10–7.
18. World Health Organization. SDG 3: Ensure healthy lives and promote wellbeing for all at all ages [Internet]. WHO. World Health Organization; 2016 [cited 2020 Aug 28]. Available from: http://www.who.int/sdg/targets/en/
19. World Health Organization. Information for travellers visiting countries with Zika virus transmission [Internet]. WHO. World Health Organization; 2019 [cited 2020 Aug 28]. Available from: http://www.who.int/csr/disease/zika/information-for-travelers/en/
20. World Health Organization. Disease Outbreaks [Internet]. WHO. World Health Organization; 2020 [cited 2020 Aug 14]. Available from: http://www.who.int/emergencies/diseases/en/
21. Eccleston-Turner M, Kamradt-Scott A. Transparency in IHR emergency committee decision making: the case for reform. BMJ Glob Health. 2019 Apr 1;4(2):e001618.
22. Commission on a Global Health Risk Framework, National Academy of Medicine, Secretariat. The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises [Internet]. Washington (DC): National Academies Press (US); 2016 [cited 2020 Jul 25]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK368394/
23. Worsnop CZ. Concealing Disease: Trade and Travel Barriers and the Timeliness of Outbreak Reporting. Int Stud Perspect. 2019 Nov;20(4):344–72.
24. Jungerman MR, Vonnahme LA, Washburn F, Alvarado-Ramy F. Federal travel restrictions to prevent disease transmission in the United States: An analysis of requested travel restrictions. Travel Med Infect Dis. 2017 Jul 1;18:30–5.

25. Stein F, Sridhar D. Health as a "global public good": creating a market for pandemic risk. BMJ [Internet]. 2017 Aug 31 [cited 2020 Jul 30];358. Available from: https://www.bmj.com/content/358/bmj.j3397
26. World Bank. Pandemic Emergency Financing Facility [Internet]. World Bank. 2019 [cited 2020 Aug 14]. Available from: https://www.worldbank.org/en/topic/pandemics/brief/pandemic-emergency-financing-facility
27. Adhanom T. IHR Emergency Committee on Novel Coronavirus (2019-nCoV) [Internet]. 2020 [cited 2020 Jul 25]. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-statement-on-ihr-emergency-committee-on-novel-coronavirus-(2019-ncov)
28. Lee K, Worsnop CZ, Grépin KA, Kamradt-Scott A. Global coordination on cross-border travel and trade measures crucial to COVID-19 response. Lancet Lond Engl. 2020 23;395(10237):1593–5.
29. World Health Organization. List of members and advisers to International Health Regulations (IHR) 3rd Emergency Committee for COVID-19 [Internet]. WHO. World Health Organization; 2020 [cited 2020 Jul 30]. Available from: http://www.who.int/ihr/procedures/novel-coronavirus-2019/ec-30042020-members/en/
30. World Health Organization. Statement on the ninth meeting of the International Health Regulations (2005) Emergency Committee regarding the coronavirus disease (COVID-19) pandemic [Internet]. [cited 2021 Nov 18]. Available from: https://www.who.int/news/item/26-10-2021-statement-on-the-ninth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic
31. World Health Organization. Statement on the fourth meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of coronavirus disease (COVID-19) [Internet]. 2020 [cited 2020 Oct 4]. Available from: https://www.who.int/news-room/detail/01-08-2020-statement-on-the-fourth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-coronavirus-disease-(covid-19)
32. World Bank. Fact Sheet: Pandemic Emergency Financing Facility [Internet]. World Bank. 2020 [cited 2020 Aug 14]. Available from: https://www.worldbank.org/en/topic/pandemics/brief/fact-sheet-pandemic-emergency-financing-facility
33. Devi S. Travel restrictions hampering COVID-19 response. Lancet Lond Engl. 2020;395(10233):1331–2.
34. World Health Organization. First UN solidarity flight departs Addis Ababa carrying vital COVID-19 medical supplies to all African nations [Internet]. 2020 [cited 2020 Jul 25]. Available from: https://www.who.int/news-room/detail/14-04-2020-first-un-solidarity-flight-departs-addis-ababa-carrying-vital-covid-19-medical-supplies-to-all-african-nations
35. World Food Program. WFP launches international passenger air service for humanitarian and health workers in Tanzania | World Food Programme [Internet]. 2020 [cited 2020 Jul 25]. Available from: https://www.wfp.org/news/wfp-launches-international-passenger-air-service-humanitarian-and-health-workers-tanzania
36. Meier BM, Habibi R, Yang YT. Travel restrictions violate international law. Science. 2020 Mar 27;367(6485):1436–1436.

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Eliminating Disparities in Young Adult Tobacco Use: The Need for Integrated Behavioral Healthcare

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(***Editor's Note: Part 3 of a series***)

ABSTRACT

OBJECTIVES: There is limited data available specific to young adult tobacco use in Rhode Island. This study examines whether young adult cigarette and e-cigarette use varies by sociodemographics, mental health, and use of other substances.

METHODS: This cross-sectional web-based survey was administered during the COVID-19 pandemic, from May to October 2020.

RESULTS: A total of 12.9% of young adults reported current cigarette or e-cigarette use. Young adults who currently used cigarettes or e-cigarettes were more likely to be white, non-Hispanic, younger, and have depressive symptoms, a depression diagnosis, suicide ideation, engage in harmful drinking, alcohol dependence, current marijuana use, and frequent marijuana use.

CONCLUSIONS: To address the needs of disproportionately affected young adults, steps must be taken to integrate comprehensive, barrier-free, widely promoted coverage of tobacco cessation treatment in all behavioral healthcare settings.

KEYWORDS: young adults, tobacco, behavioral health, Rhode Island

INTRODUCTION

Tobacco use is the leading cause of premature death worldwide, with 6 million deaths per year attributed to tobacco use.[1] Many users started in their youth or young adult years, and they are at high risk for adverse health outcomes. In Rhode Island, an estimated 16,000 children under the age of 18 will prematurely die from smoking.[2] While the hazards of tobacco smoking are well-established,[3] the body of evidence on the health consequence of using e-cigarettes, otherwise known as vaping, is still evolving due to their novelty. Among important early findings include reports that e-cigarettes can cause similar effects on the body as traditional cigarettes, such as scarring of the lung tissue, respiratory disease, dangerous ingestion levels of heavy metals, and oxidative stress at the molecular level.[4,5]

In 2015, youth tobacco use rates declined to historical lows while e-cigarette use accelerated. While only 10.8% of U.S. high school students were using traditional tobacco products, 24% reported past 30-day e-cigarette use.[6] After 2015, rates of use for tobacco products, including e-cigarettes, continued to rise for four consecutive years, reaching a peak in 2019. That year, 53.3% of high school students had ever used a tobacco product; 31.2% had used a tobacco product within the past 30 days; and e-cigarettes were the most common product used. Rhode Island saw similar trends; in 2019, 33.3% of high school students were using any tobacco product, and e-cigarettes were the most commonly used product.[7]

Due to a combination of the COVID-19 and legislation that raised the minimum legal purchase age for tobacco products to 21 and banned the sale of flavored e-cigarettes, national prevalence rates in teens slightly declined.[8] However, due to the lack of data on the Rhode Island young adult population, little is known on the baseline rates of cigarette or e-cigarette use, or which subpopulations are disproportionately affected. Understanding who is disproportionately affected and common comorbidities of cigarette and e-cigarette use can help inform more targeted interventions for high-risk populations. To address this need, we used data from 2020 Rhode Island Young Adult Survey to determine whether characteristics of cigarette and e-cigarette use vary by sociodemographics, mental health, and use of other substances.

METHODS

Sample

The Rhode Island Young Adult Survey (RIYAS) is a behavioral health survey of young adults aged 18–25 years who resided in Rhode Island for at least part of the year and spoke English or Spanish. This self-reported, cross-sectional, web-based survey was administered in 2020 from May through October. Recruitment was primarily through paid Instagram ads and was supplemented by posts to Facebook community groups and email to three institutions of higher education. Surveys took 15 minutes on average and respondents received $10 electronic Amazon gift cards. Of the 546 completed surveys, 528 (97%) provided valid race/ethnicity data and were included in the analytic sample. This study was approved by the Johnson & Wales Institutional Review Board.

Measures

The primary outcome, current cigarette or e-cigarette use, was assessed based on two survey questions. Anyone who responded "yes, in the past month" to either of the following questions was defined as engaging in current cigarette or e-cigarette use, respectively: "Have you ever smoked all or part of a cigarette?" or "Have you ever used E-cigarettes such as JUUL or other brands?"

Mental health measures included anxiety symptoms, depressive symptoms, depression diagnosis, and suicide ideation. Anxiety symptoms were assessed via the validated Generalized Anxiety Disorder-7, a screening tool for past two-week anxiety among the general adult population.[9] A continuous score was generated based on 7 items with responses on a 4-point Likert scale. A cut-off score of 10 or higher was used to identify those with likely anxiety disorder.[10] Past week depressive symptoms were assessed via the validated Center for Epidemiologic Studies Short Depression Scale,[11] which is used to create a continuous score based on 10 items with responses on a 4-point Likert scale. A cut-off score of 10 or more was considered depressive disorder.[12] Depression diagnosis was operationalized by positive responses to the question, "During the past 12 months, has a medical professional told you that you have depression?" Suicide ideation was measured by "yes" or "no" response to the survey question, "During the past 12 months, did you ever seriously consider attempting suicide?"

Substance use measures included harmful drinking, alcohol dependence, current marijuana use, and frequent marijuana use. Harmful drinking and alcohol dependence were assessed by the validated AUDIT score generated from 10 items.[13] Scores of 8 or more were considered harmful drinking and scores of 15 or more were considered alcohol dependence.[14] Current marijuana use was defined as those who responded "yes, in the past month" to the question "Have you ever used marijuana (weed, pot, mary jane, grass)?" Frequent marijuana users were those who reported use for 15 or more days of the past 30.

Important covariates were sexual and gender identity, race/ethnicity, age, and social status. Social status was assessed via the MacArthur Scale of Subjective Social Status, which assesses perceived social status relative to others in their community, where 1 indicates "worst off" and 10 indicates "best off".[15]

Statistical Analysis

Descriptive and bivariate statistics were assessed by the outcome, current cigarette or e-cigarette use (**Table 1; Table 2**). Bivariate tests included chi-square tests for categorical variables and t-tests for continuous variables. Adjusted odds of current cigarette or e-cigarette use were calculated using multivariable logistic regression for each mental health measure and each substance use measure while controlling for covariates – sexual and gender identity, race/ethnicity, age, and social status (**Figure 1**). Statistical significance was assumed at a threshold of $p<0.05$ and all analyses were conducted using Stata version 15.[16]

Table 1. Sociodemographic and Behavioral Health Characteristics of 2020 Rhode Island Young Adult Survey and Current Cigarette or E-cigarette Users

Characteristics	RIYAS n = 528 (%)	Current Cigarette or E-cigarette Use n = 68 (%)	P-value
Heterosexual Male	106 (20.1)	20 (29.4)	0.082
Heterosexual Female	280 (53.0)	29 (42.7)	
Sexual or Gender Minority	142 (26.9)	19 (27.9)	
White, non-Hispanic	361 (68.4)	56 (82.4)	**0.008**
Non-white or Hispanic	167 (31.6)	12 (17.7)	
Social Ladder (mean; SD)	6.30 (1.69)	5.99 (163)	0.094
Age (mean; SD)	20.54 (2.24)	19.72 (1.88)	**0.001**
Anxiety Symptoms	165 (31.3)	28 (41.2)	0.058
Depressive Symptoms	233 (44.1)	41 (60.3)	**0.004**
Depression Diagnosis	115 (21.8)	22 (32.4)	**0.024**
Suicide Ideation	64 (12.1)	15 (22.1)	**0.007**
Harmful Drinking	88 (16.7)	27 (39.7)	**<0.001**
Alcohol Dependence	19 (3.6)	8 (11.8)	**<0.001**
Current Marijuana Use	151 (28.6)	38 (55.9)	**<0.001**
Frequent Marijuana Use	66 (12.5)	23 (33.8)	**<0.001**

Note: P-values were calculated using chi-square tests for categorical characteristics and t-tests for continuous characteristics.

Table 2. Current Cigarette and E-cigarette Use in the 2020 Rhode Island Young Adult Survey

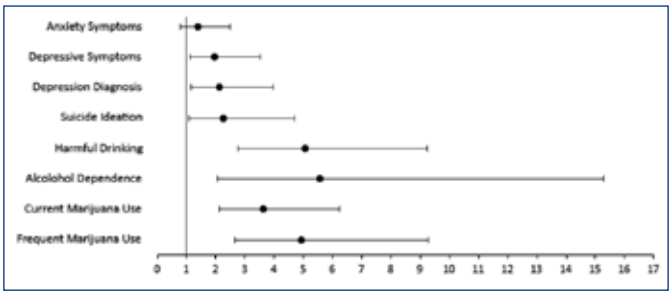
Nicotine Use Behavior	n (%)
Current Cigarette Use Only	9 (1.7)
Current E-cigarette Use Only	44 (8.3)
Current Cigarette and E-cigarette Use	15 (2.8)
Current Cigarette or E-cigarette Use	68 (12.9)

RESULTS

The RIYAS sample was predominantly heterosexual female (53.0%), white, non-Hispanic (68.4%), and had a mean age of 20.5 (**Table 1**). Among the sample, 68 (12.9%) currently used cigarettes or e-cigarettes, with 4.6% reporting current cigarette use and 11.2% reporting current e-cigarette use (**Table 2**). Among current cigarette users, 62.5% also currently used e-cigarettes, while among current e-cigarette users, 25.4% also currently used cigarettes.

Bivariate results suggest those who currently used cigarettes or e-cigarettes were more likely to be white,

Figure 1. Adjusted Odds of Young Adult Current Cigarette or E-cigarette Use by Behavioral Health Outcomes



Note: Multivariable logistic regressions were used to calculate adjusted odds while controlling for sexual and gender identity, race/ethnicity, age, and social ladder.

non-Hispanic (p = 0.008), younger (p = 0.001), and have depressive symptoms (p = 0.004), a depression diagnosis (p = 0.024), suicide ideation (p = 0.007), engage in harmful drinking (p < 0.001), alcohol dependence (p < 0.001), current marijuana use (p < 0.001), and frequent marijuana use (p < 0001).

After adjustment for covariates, all mental health measures (except anxiety symptoms) and substance use measures were significantly associated with increased odds of current cigarette or e-cigarette use. Odds of cigarette or e-cigarette use increased with anxiety symptoms [1.41 (95%CI: 0.79, 2.50)], depressive symptoms [1.98 (95%CI: 1.11, 3.54)], depression diagnosis [2.15 (95%CI: 1.16, 3.97)], suicide ideation [2.27 (95%CI: 1.10, 4.68)], harmful drinking [5.06 (95%CI: 277, 9.23)], alcohol dependence [5.58 (95%CI: 2.04, 15.30)], current marijuana use [3.63 (95%CI: 2.11, 6.24)], and frequent marijuana use [4.94 (95%CI: 2.64, 9.28)].

DISCUSSION

The goal of these analyses was to establish baseline characteristics of young adult nicotine users in Rhode Island by sociodemographics and other behavioral health outcomes. Current cigarette and e-cigarette use was prevalent among young adults, with 12.9% using e-cigarettes or cigarettes. However, e-cigarette use was far more common with 11.2% reporting current use. Current cigarette or e-cigarette use disproportionately occurred in those who were younger, white, non-Hispanic, and who had co-morbid mental illness, such as depression and suicidal ideation. Similarly, users of nicotine products, in general, were far more likely to engage in other substance use and abuse including harmful drinking and frequent marijuana use. In fact, the odds of alcohol dependence were 5.6 times greater in those who used cigarettes or e-cigarettes.

Young Adult Cigarette and E-Cigarette Use

Young adult-specific data for Rhode Island is typically not available from other surveillance systems, which is a distinct novelty and benefit of the RIYAS. For example, current cigarette and e-cigarette use prevalence among young adults (aged 18–24 years) in the 2020 Rhode Island Behavioral Risk Factor Surveillance System (BRFSS) are unavailable due to small sample size and lack of assessment, respectively.[17] However, findings from the 2019 Rhode Island Youth Risk Behavior Surveillance Survey (YRBSS) suggest a higher prevalence of current e-cigarette use among high school students (30.1%) than among this young adult sample (11.2%), although current cigarette use among high school students was comparable (4.2% versus 4.6%).[18] Further, Rhode Island high school students who currently used e-cigarettes did not differ by sex, but white students were more likely to use than other race/ethnicities, which is similar to RIYAS participants. Higher prevalence of e-cigarette use in high school students is also consistent with our findings that younger young adults were more likely to use cigarettes or e-cigarettes. E-cigarette use in high school students may be higher due to increased availability to minors relative to other substances like marijuana and alcohol, appealing flavors, low costs, and discrete designs, while older young adults may transition from e-cigarettes to other substances as they reach the legal minimum purchase age and the substances become more accessible.[19]

Findings herein also suggest that young adults suffering from poor mental health or engaging in other substance use or abuse are significantly more likely to also engage in cigarette or e-cigarette use. This finding is consistent with other research in the general population[20] and among young adults.[21] To reach those at high risk, tobacco treatment for young adults must be integrated into behavioral healthcare. Studies suggest that smoking cessation does not interfere with behavioral health treatments and, in fact, can improve mental health[22,23] and make substance relapses less likely.[20,24]

Interventions to Address Disproportionately Affected Young Adults

Current treatments and interventions for young adult tobacco use in Rhode Island includes the Rhode Island Nicotine Helpline, or "My Life, My Quit," an independently run, free service that connects young people with one-on-one cessation support.[25,26] Tailored mental health quitline programs, which include additional calls, longer duration of combination nicotine-replacement therapy, and specific attention to mental health issues, are a novel and important way to address the dual needs of this population.[27]

Another effective intervention is Screening, Brief Intervention, and Referral to Treatment (SBIRT) at the point-of-care.[28] When used as part of an evidence-based approach, SBIRT is effective in prevention and early intervention of tobacco use in young adults, but barriers to implementation must be addressed and it must be targeted to young adults with symptoms of poor mental health and substance use disorders. Additionally, SBIRT is not consistently implemented in practice settings, nor is it necessarily covered by insurance or provider reimbursements.

Under the Affordable Care Act, insurance companies must cover some level of tobacco cessation treatment, but coverage varies dramatically between plans. Some policies cover pharmacotherapy, counseling services, and/or quitlines,[29] but coverage may be limited to specific cessation medications, the number of weeks on a specific pharmacotherapy, sessions of individual counseling per year, the number of quit attempts per year, or impose yearly or lifetime dollar limits. Similarly, insurance coverage for step therapy,[30] one approach to tobacco cessation, often requires that a patient try and fail cheaper treatments before receiving coverage for more expensive medications, which makes it more likely that participants become discouraged or run out of coverage. These barriers to sustained treatment affect the success of those attempting to quit nicotine products, especially among those already struggling with mental health or substance abuse. Research strongly suggests that comprehensive, barrier-free, widely promoted coverage of these treatments increases treatment utilization and quit rates.[31]

Eliminating barriers to tobacco cessation services, such as integrating tobacco cessation programming into all behavioral health services, is essential to effectively address nicotine use in young adults.[32] Important steps include implementing tobacco-free policies inside and on the campuses of behavioral health settings,[33] increasing tobacco use and dependence screenings in mental health and substance use treatment settings,[34] and engaging health professions outside the behavioral health field, such as pharmacists, for the implementation of cessation treatment.[35]

Limitations

While this study provides novel findings specific to young adult cigarette and e-cigarette use in Rhode Island, it is not without limitations. This study is comprised of a convenience sample of young adults and may not be representative of the young adult population in Rhode Island. However, to our knowledge, this is the largest young adult-specific surveillance study in Rhode Island to date. All measures were self-reported and therefore could be influenced by social desirability and recall bias. Though valid and reliable assessments for anxiety symptoms, depressive symptoms, harmful drinking, and alcohol dependence were used, these should not be considered synonymous with a diagnosis. Also of note, this study specifically assessed current cigarette or e-cigarette use, but did not assess the use of other tobacco products such as cigars, pipes, or smokeless tobacco. Despite these limitations, this study highlights the subpopulations of young adults in Rhode Island most likely engaged in cigarette and e-cigarette use, as well as the significant co-occurrence of this use with poor mental health and other substance use.

CONCLUSIONS

Young adults in Rhode Island are a high-risk population for cigarette and e-cigarette use, particularly those with mental health conditions and/or substance use disorders. To strive for health equity, steps must be taken to integrate comprehensive, barrier-free, widely promoted coverage of cessation treatment in all behavioral healthcare settings.

References

1. Tobacco. *World Health Organization.* 2014 https://www.who.int/news-room/fact-sheets/detail/tobacco
2. The Health Consequences of Smoking: 50 Years of Progress. *A Report of the Surgeon General*, 2014.
3. U.S. Department of Health and Human Services. Smoking Cessation. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2020.
4. Tobore TO. On the potential harmful effects of E-Cigarettes (EC) on the developing brain: The relationship between vaping-induced oxidative stress and adolescent/young adults social maladjustment. *J Adolesc*. 2019;76:202-209. doi:10.1016/j.adolescence.2019.09.004.
5. Hamberger ES, Halpern-Felsher B. Vaping in adolescents: epidemiology and respiratory harm. *Curr Opin Pediatr*. 2020;32(3):378-383. doi:10.1097/MOP.0000000000000896
6. Centers for Disease Control and Prevention. 2015 Youth Risk Behavior Survey Data. Available at: www.cdc.gov/yrbs.
7. Wang TW, Gentzke AS, Creamer MR, et al. Tobacco Product Use and Associated Factors Among Middle and High School Students - United States, 2019. *MMWR Surveill Summ*. 2019;68(12):1-22. Published 2019 Nov 6. doi:10.15585/mmwr.ss6812a1
8. Gentzke AS, Wang TW, Jamal A, et al. Tobacco Product Use Among Middle and High School Students - United States, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(50):1881-1888. Published 2020 Dec 18. doi:10.15585/mmwr.mm6950a1
9. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097. doi:10.1001/archinte.166.10.1092
10. Löwe B, Decker O, Müller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care*. 2008;46(3):266-274. doi:10.1097/MLR.0b013e318160d093
11. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement*. 1977;1(3):385-401. doi:10.1177/014662167700100306
12. Bradley KL, Bagnell AL, Brannen CL. Factorial validity of the Center for Epidemiological Studies Depression 10 in adolescents. *Issues Ment Health Nurs*. 2010;31(6):408-412. doi:10.3109/01612840903484105
13. Conigrave KM, Hall WD, Saunders JB. The AUDIT questionnaire: choosing a cut-off score. *Addiction*. 1995;90:1349-1356.
14. Bohn MJ, Babor TF, Kranzler HR.The Alcohol Use Disorders Identification Test (AUDIT): Validation of a screening instrument for use in medical settings. *Journal of Studies on Alcohol*, Volume 56, Issue 4, 1995, Pages 423-432
15. Vidal C, Brown W, Lilly F. The Impact of Subjective and Objective Social Status on Depression in a Cohort of Graduate-Level Students. *Open Journal of Social Sciences*. 2018;6:287-301. doi: 10.4236/jss.2018.65021
16. StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.

17. Centers for Disease Control and Prevention (CDC). Behavioral Risk Factor Surveillance System Survey Data. Atlanta, Georgia: *U.S. Department of Health and Human Services, Centers for Disease Control and Prevention*, 2020.
18. Centers for Disease Control and Prevention. 2019 Youth Risk Behavior Survey Data. Available at: www.cdc.gov/yrbs.
19. Chadi N, Hadland SE, Harris SK. Understanding the implications of the "vaping epidemic" among adolescents and young adults: A call for action. *Subst Abus*. 2019;40(1):7-10. doi:10.1080/08897077.2019.1580241
20. Schroeder S A, Morris CD. Confronting a neglected epidemic: tobacco cessation for persons with mental illnesses and substance abuse problems. *Annual Review of Public Health*, 2010;31:297–314.
21. Becker TD, Arnold MK, Ro V, Martin L, Rice TR. Systematic Review of Electronic Cigarette Use (Vaping) and Mental Health Comorbidity Among Adolescents and Young Adults. *Nicotine Tob Res*. 2021;23(3):415-425. doi:10.1093/ntr/ntaa171
22. Prochaska JJ, Das S, Young-Wolff KC. Smoking, Mental Illness, and Public Health. *Annu Rev Public Health*. 2017;38:165–185. doi: 10.1146/annurev-publhealth-031816-044618.
23. Compton W. The need to incorporate smoking cessation into behavioral health treatment. *The American Journal on Addictions*.2018;27(1):42–43.
24. Taylor G, McNeill A, Girling A, Farley A, Lindson-Hawley N, Aveyard P. Change in mental health after smoking cessation: systematic review and meta-analysis. *BMJ*. 2014;348:1151.
25. Prochaska JJ, Delucchi K, Hall SM. A Meta-Analysis of Smoking Cessation Interventions With Individuals in Substance Abuse Treatment or Recovery. *Journal of Consulting and Clinical Psychology*. 2004;72(6):1144-1156.
26. Tobacco Control Program. *State of Rhode Island Department of Health*. https://health.ri.gov/programs/detail.php?pgm_id=33
27. Morris CD, Lukowski AV, Vargas-Belcher RA, Ylioja TE, Nash CM, Bailey LA. Quitline Programs Tailored for Mental Health: Initial Outcomes and Feasibility. *Am J Prev Med*. 2021;60(3 Suppl 2):S163-S171. doi:10.1016/j.amepre.2020.02.025.
28. Agerwala SM, McCance-Katz EF. Integrating screening, brief intervention, and referral to treatment (SBIRT) into clinical practice settings: a brief review. *J Psychoactive Drugs*. 2012;44(4):307-317. doi:10.1080/02791072.2012.720169
29. Rhode Island Medicaid Insurance Tobacco Cessation Benefits. *State of Rhode Island Department of Health*. 2019. https://health.ri.gov/publications/quickreferenceguides/201803RIMedicaidInsuranceTobaccoCessationBenefits.pdf
30. Ebbert JO, Little MA, Klesges RC, et al. Step Care treatment for smoking cessation. *Health Educ Res*. 2017;32(1):1-11. doi:10.1093/her/cyw051
31. DiGiulio A, Jump Z, Babb S, et al. State Medicaid Coverage for Tobacco Cessation Treatments and Barriers to Accessing Treatments - United States, 2008-2018. *MMWR Morb Mortal Wkly Rep*. 2020;69(6):155-160. Published 2020 Feb 14. doi:10.15585/mmwr.mm6906a2
32. Hall SM, Prochaska JJ. Treatment of smokers with co-occurring disorders: emphasis on integration in mental health and addiction treatment settings. *Annu Rev Clin Psychol*. 2009;5:409-431. doi:10.1146/annurev.clinpsy.032408.153614.
33. Centers for Disease Control and Prevention. Smokefree policies improve health, 2018. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/secondhand_smoke/protection/improve_health/index.htm. Accessed June 25, 2020.
34. Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. *Public Health Service*. May 2008.
35. Dent LA, Harris KJ, Noonan CW. Randomized Trial Assessing the Effectiveness of a Pharmacist-Delivered Program for Smoking Cessation. *Annals of Pharmacotherapy*. 2009;43(2):194-201. doi:10.1345/aph.1L556

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Predictors of Price Transparency for Cataract Surgery and Laser Posterior Capsulotomy at Academic Hospitals in the United States

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ABSTRACT

PURPOSE: To describe the characteristics of United States (US) academic hospitals that predict transparency of cash and commercial payer-negotiated prices for cataract surgery (CS) and laser posterior capsulotomy (LPC).

METHODS: A systematic review of websites for hospitals affiliated with ophthalmology residency programs was conducted to determine price transparency. Hospital characteristics were extracted from the American Hospital Association Annual Survey and Turquoise Health. Descriptive statistics, t-tests, χ^2 tests, and logistic regression analyses were used to compare hospitals based on price transparency for CS and LPC.

RESULTS: There were no differences in price transparency for CS and LPC based on net income, urban-rural classification, region, hospital beds, or surgical operations. Having more full-time personnel was associated with cash price transparency. No differences were identified between hospitals based on payer-negotiated price transparency.

CONCLUSIONS: Academic hospitals for ophthalmology with more full-time personnel had greater cash price transparency for CS and LPC. However, price transparency did not vary for other characteristics.

KEYWORDS: price transparency, cost, cataract surgery, laser posterior capsulotomy

INTRODUCTION

Price transparency is one focus in efforts to reduce healthcare costs. Many hospitals are not in compliance with Centers for Medicare and Medicaid Services (CMS) requirements to disclose cash and payer-negotiated prices for seventy inpatient and outpatient services, including cataract surgery (CS) and laser posterior capsulotomy (LPC).[1] This study identified predictors of price transparency for CS and LPC among United States (US) academic hospitals for ophthalmology.

METHODS

The Rhode Island Hospital Institutional Review Board determined this research did not involve human subjects or require further review.

Academic hospitals were defined as primary hospital affiliates of Accreditation Council for Graduate Medical Education-accredited ophthalmology residency programs. US Department of Veterans Affairs and Department of Defense hospitals were not included, given their different payment models. Each hospital's website was reviewed in September 2021 to determine cash and payer-negotiated prices for CS (Current Procedural Terminology [CPT] code: 66984) and LPC (CPT code: 66821).

Price-disclosing competitors for CS or LPC within 10 miles were identified using Turquoise Health, a public database of hospital prices. Hospital ownership was categorized as nonprofit, for profit, or state/local government. Number of hospital beds, surgical operations, and full-time personnel and net income were extracted from the American Hospital Association (AHA) Annual Survey. The number of full-time personnel included all full-time employees, including licensed providers, nurses, and housekeeping staff. Urban-rural classification was based on US Department of Agriculture Rural-Urban Commuting Area codes; region was based on US Census Bureau designations.

Descriptive statistics, student t-tests, and χ^2 tests were used to analyze differences between hospitals based on price transparency for CS and LPC. Logistic regression was used to calculate odds ratios associated with price transparency. Statistical analyses were conducted using Stata with alpha=0.05.

RESULTS

One hundred eighteen academic hospitals for ophthalmology were included; most were nonprofits (65%; 77/118) and in metropolitan areas (98%; 116/118). Most hospitals disclosed cash prices for CS and LPC (54%; 64/118) but not commercial payer-negotiated prices (13%; 15/118).

Hospitals with more full-time personnel were more likely to disclose cash prices for CS and LPC (**Table 1**); no significant differences were identified between hospitals for payer-negotiated price transparency (**Table 2).** Hospitals that did not disclose prices for CS were less likely to disclose prices for LPC (18% vs 59%; p<0.001), and hospitals that did not disclose prices for LPC were less likely to disclose prices for CS (20% vs 62%; p<0.001).

In logistic regression, having ≥6,000 full-time personnel [OR=2.13, 95% CI=1.01–4.50] was associated with cash price transparency; no variables were significantly associated with payer-negotiated price transparency (**Table 3**).

Table 1. Characteristics of academic hospitals that do or do not report cash prices for CS and LPC

Characteristics	Hospitals disclosing both cash prices (n=64)	Hospitals not disclosing both cash prices (n=54)	Test statistic, p-value
Urban–rural classification, n (%) [a]			
Metropolitan	62 (97)	54 (100)	χ^2=1.72,
Micropolitan	2 (3)	0 (0)	p=0.190
Small town	0 (0)	0 (0)	
Rural	0 (0)	0 (0)	
Competitors within 10 miles, mean (SD) [b]	3.41 (4.34)	2.20 (2.59)	t=-1.78, p=0.077
0–4, n (%)	42 (66)	42 (78)	χ^2=2.11,
5+	22 (34)	12 (22)	p=0.146
Ownership, n (%)			
Nonprofit	42 (66)	36 (67)	**χ^2=5.43,**
For profit	0 (0)	4 (7)	**p=0.066**
Public	22 (34)	14 (26)	
Region, n (%)			
Northeast	20 (31)	13 (24)	**χ^2=7.60,**
West	9 (14)	5 (9)	**p=0.107**
South	16 (25)	25 (46)	
Midwest	19 (30)	10 (19)	
Other (Puerto Rico)	0 (0)	1 (2)	
Hospital beds, mean (SD)	694.81 (410.97)	633.74 (411.12)	t=-0.80, p=0.423
0–649, n (%)	35 (55)	31 (57)	χ^2 =0.09,
650+	29 (45)	23 (43)	p=0.767
Surgical operations, mean (SD)	34393.86 (29491.65)	26724.96 (29913.34)	t=-1.40, p=0.165
0–29999, n (%)	39 (61)	38 (70)	χ^2=1.15,
30000+	25 (39)	16 (30)	p=0.284
Full–time personnel, mean (SD)	7660.11 (6080.14)	4917.83 (4202.08)	**t=-2.80, p=0.006**
0–5999, n (%)	30 (47)	36 (67)	**χ^2=4.65,**
6000+	34 (53)	18 (33)	**p=0.031**
Net income, mean (SD)	85807483.95 (258030204.10)	106624568.90 (319670283.90)	t=0.49, p=0.627
$0 to$–1,654,754, n (%)	20 (31)	10 (18)	**χ^2=3.39,**
$–1,654,754 to $2.97e7	14 (22)	15 (28)	**p=0.336**
$2.97e7 to $1.09e8	13 (20)	16 (30)	
$1.09e8+	17 (27)	13 (24)	

CS, cataract surgery; LPC, laser posterior capsulotomy; SD, standard deviation. Statistically significant relationships are bolded.

[a] Based on Rural-Urban Commuting Area codes provided by the United States Department of Agriculture

[b] Provided by Turquoise Health, a publicly available database of hospital prices for services and items

[c] Provided by the American Hospital Association Annual Survey

[d] Provided by the American Hospital Association Financial Database

Table 2. Characteristics of academic hospitals that do or do not report payer-negotiated prices for CS and LPC

Characteristics	Hospitals disclosing both insurance prices (n = 26)	Hospitals not disclosing both insurance prices (n = 92)	Test statistic, p-value
Urban–rural classification, n (%) [a]			
Metropolitan	25 (96)	91 (99)	χ^2=0.93,
Micropolitan	1 (4)	1 (1)	p=0.336
Small town	0 (0)	0 (0)	
Rural	0 (0)	0 (0)	
Competitors within 10 miles, mean (SD) [b]	4.08 (4.40)	2.51 (3.40)	t=-1.94, p=0.055
0–4, n (%)	15 (58)	69 (75)	χ^2=2.96,
5+	11 (42)	23 (25)	p=0.085
Ownership, n (%)			
Nonprofit	20 (77)	58 (63)	**χ^2=2.32,**
For profit	0 (0)	4 (4)	**p=0.313**
Public	6 (23)	30 (33)	
Region, n (%)			
Northeast	7 (27)	26 (28)	**χ^2=4.22,**
West	3 (12)	11 (12)	**p=0.377**
South	6 (23)	35 (38)	
Midwest	10 (38)	19 (21)	
Other (Puerto Rico)	0 (0)	1 (1)	
Hospital beds, mean (SD)	542.81 (333.73)	701.92 (424.65)	t=1.76, p=0.081
0–499, n (%)	14 (54)	38 (41)	χ^2=1.29,
500+	12 (46)	54 (59)	p=0.255
Surgical operations, mean (SD)	25397.08 (25320.04)	32435.12 (30904.02)	t=1.06, p=0.290
0–24999, n (%)	18 (69)	47 (51)	χ^2=2.70,
25000+	8 (31)	45 (49)	p=0.101
Full–time personnel, mean (SD)	5520.92 (4332.94)	6655.07 (5731.78)	t=0.94, p=0.352
0–5999, n (%)	17 (65)	49 (53)	χ^2=1.21,
6000+	9 (35)	43 (47)	p=0.272
Net income, mean (SD)	16367180.92 (119746058.60)	117650641.20 (315476285.50)	t=1.60, p=0.112
$0 to $–1,654,754, n (%)	8 (31)	15 (16)	χ^2=3.57,
$–1,654,754 to $2.97e7	7 (27)	21 (23)	p=0.312
$2.97e7 to $1.09e8	5 (19)	24 (26)	
$1.09e8+	6 (23)	32 (35)	

CS, cataract surgery; LPC, laser posterior capsulotomy; SD, standard deviation. Statistically significant relationships are bolded.

[a] Based on Rural-Urban Commuting Area codes provided by the United States Department of Agriculture

[b] Provided by Turquoise Health, a publicly available database of hospital prices for services and items

[c] Provided by the American Hospital Association Annual Survey

[d] Provided by the American Hospital Association Financial Database

Table 3. Predictors of academic hospital transparency for cash and payer-negotiated prices for CS and LPC

Characteristics	Cash prices OR [95% CI]	Payer-negotiated prices OR [95% CI]
Urban–rural classification		
Metropolitan	1 [reference]	1 [reference]
Micropolitan	1 [omitted] [a]	3.64 [0.22–60.27]
Small town		
Rural		
Competitors within 10 miles		
0–4	1 [reference]	1 [reference]
5+	1.83 [0.80–4.18]	2.20 [0.89–5.47]
Ownership		
Nonprofit	1 [reference]	1 [reference]
For profit	1 [omitted] [b]	1 [omitted] [b]
Public	1.35 [0.60–3.01]	0.58 [0.21–1.60]
Region		
Northeast	1 [reference]	1 [reference]
West	1.17 [0.32–4.28]	1.01 [0.22–4.66]
South	0.42 [0.16–1.06]	0.64 [0.19–2.12]
Midwest	1.24 [0.44–3.48]	1.95 [0.63–6.07]
Other (Puerto Rico)	1 [omitted] [b]	1 [omitted] [b]
Hospital beds		
0–499, n (%)	1 [reference]	1 [reference]
500+	1.36 [0.65–2.82]	0.60 [0.25–1.45]
Surgical operations		
0–24999, n (%)	1 [reference]	1 [reference]
25000+	1.81 [0.86–3.79]	0.46 [0.18–1.17]
Full–time personnel		
0–5999, n (%)	1 [reference]	1 [reference]
6000+	**2.27 [1.07–4.79]**	0.60 [0.24–1.49]
Net income		
$0 to $–1,654,754, n (%)	1 [reference]	1 [reference]
$–1,654,754 to $2.97e7	0.67 [0.22–2.02]	0.63 [0.19–2.10]
$2.97e7 to $1.09e8	0.63 [0.21–1.88]	0.39 [0.11–1.42]
$1.09e8+	1.48 [0.51–4.28]	0.35 [0.10–1.19]

CS, cataract surgery; LPC, laser posterior capsulotomy; CI, confidence interval; OR, odds ratio. Statistically significant relationships are bolded.
[a] Omitted due to collinearity
[b] Omitted due to perfect prediction

DISCUSSION

Academic hospitals with more full-time personnel disclosed cash prices for CS and LPC more often, possibly due to more personnel working on chargemasters or a threshold effect of market dominance. They may also be in areas with more physicians and healthcare workers, lowering physician fees and prices for services, contributing to a greater willingness to disclose prices.[2,3]

Differences were not identified between hospitals based on payer-negotiated price transparency. Previous research demonstrated that insurers with stronger market power, such as national insurers, negotiate lower prices,[2,3] possibly standardizing price transparency among hospitals.

Cost of healthcare is a key barrier to healthcare access, especially for people of color who tend to be uninsured and have less disposable income.[4] Price transparency reform may be a means of reducing the high cost of care in the US and addressing health disparities. Non-disclosure for CS and for LPC were associated with each other, underscoring the importance of assessing price transparency for other procedures at academic hospitals.

Opponents of price transparency reform have cited the burden of maintaining a chargemaster. In response, CMS developed a sliding scale of penalties for noncompliance based on hospital size, measured by hospital beds. However, consistent with previous research outside of ophthalmology,[5] our study finds that cash and payer-negotiated price transparency for CS and LPC did not differ based on number of hospital beds or surgical volume.

Limitations of this study include limited generalizability to non-academic hospitals and non-cataract procedures. Additionally, many hospitals imposed barriers to accessing price data such as anti-automation software, which we adjusted for with multiple chargemaster searches.

References

1. Berkowitz ST, Siktberg J, Hamdan SA, Triana AJ, Patel SN. Health care price transparency in ophthalmology. *JAMA Ophthalmol.* 2021 Nov 1;139(11):1210-1216.
2. Laugesen MJ, Glied SA. Higher fees paid to US physicians drive higher spending for physician services compared to other countries. *Health Aff (Millwood).* 2011;30(9):1647-1656.
3. Scheffler RM, Arnold DR. Insurer market power lowers prices in numerous concentrated provider markets. *Health Aff (Millwood).* 2017;36(9):1539-1546.
4. Richardson LD, Norris M. Access to health and health care: how race and ethnicity matter. *Mt Sinai J Med.* 2010;77(2):166-177.
5. Haque W, Ahmadzada M, Allahrakha H, Haque E, Hsiehchen D. Transparency, accessibility, and variability of US hospital price data. *JAMA Netw Open.* 2021;4(5):e2110109.

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Adequacy Rate of Magnesium Citrate Bowel Preparation in a Large Retrospective Cohort

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ABSTRACT

INTRODUCTION: Magnesium Citrate (MC) is not FDA approved as a colonoscopy preparation. Advantages include low cost, small volume and accessibility without prescription. We retrospectively evaluated bowel preparations used in a private gastroenterology practice. The sample size is the largest for any similar studies (n =19,173).

METHODS: Electronic Medical Records were queried for colonoscopies between 2010-2016. Bowel preps, indications (screening vs. other) and preparation adequacy were all recorded. Adequacy rates were calculated and compared using generalized linear modeling. Data were analyzed using SAS.

RESULTS: The most common prep used was MC 2 bottles; screening (n=6,064, with 98.94% adequacy) and non-screening (n=3,251, with 99.29% adequacy), followed by MC 3 bottles; screening (n=2,757 with 90.35% adequacy), and non-screening (n=1,925 with 92.92% adequacy).

CONCLUSION: MC bowel preparation is adequate, well tolerated, and inexpensive. In a large retrospective analysis, it compares favorably to other preparations.

KEYWORDS: bowel preparations, colonoscopy, magnesium citrate

INTRODUCTION

Adequate bowel preparation is vital for high quality colonoscopy. Optimal bowel cleansing shortens the time of the procedure and increases polyp detection rate. Conversely, suboptimal bowel preparation may lead to inadequate visualization of the colon, missing polyps and repeat procedures with its associated financial and time burdens on patients and the healthcare system.[1,2,3] According to both American and European societies of gastrointestinal endoscopy, cost, safety and tolerability are important attributes of an optimal bowel prep.[4,5]

Concern about bowel preparation was the most common reason cited by people older than age 50 years for not having a colonoscopy.[6] Magnesium citrate (MC) is an osmotic agent that achieves bowel cleansing by increasing intraluminal fluid volume and stimulating bowel motility.[7,8] MC has the advantage of being of low volume which increases tolerability, and it is inexpensive, costing around $2 for a two bottle prep. Both factors are important concerns to patients. Brand name bowel preparations can cost at least 10 times and up to 100 times the price of MC.

Few published studies compared tolerability and efficacy of magnesium citrate to polyethylene glycol (PEG). Rapier et al compared two different MC preps to PEG; although bowel cleansing rates were lower in MC arms, it did not reach statistical significance and there was no evidence of a difference in tolerability between groups.[9] Aurora et al found that PEG and oral sodium phosphate were superior to MC.[10] In a more recent study by Gu et al, MC showed significantly higher tolerability compared to PEG (P = 0.014) and a higher adequate bowel cleansing rate 90.6% vs 48%.[11]

Several studies have evaluated the safety and efficacy of MC demonstrating no evidence of a difference or higher tolerability and bowel cleansing compared with PEG. However, small sample size is an important limitation common among these studies. We evaluated bowel preparations including MC used in an endoscopy center of a community gastroenterology private practice. We hypothesized that MC bowel preparations would be at least as effective as other available bowel preparations and have the advantage of substantial reduction of cost.

METHODS

Design and sample

Bowel preparations data were documented along with adequacy of the prep in a private, community-based, single specialty gastroenterology practice in Providence, RI. IRB approval was obtained. The Electronic Medical Records using the endoscopic report writer (MDReports) was queried for patients who underwent colonoscopies between 2010 to 2016. Colonoscopies were performed by eight different board-certified gastroenterologists in the group. The bowel prep used, indication for the colonoscopy (screening vs. other indications) and preparation adequacy were queried for analysis retrospectively. Cases where the prep type or quality of the prep was not recorded were excluded. At our endoscopy center no patient navigator or phone applications were

utilized; however, both verbal and printed instructions were provided to the patient by nurses and medical assistants. The majority of our patients spoke English. For the minority who spoke either Spanish or Portuguese, an interpreter was utilized along with instructions in Spanish.

Adequacy was documented based on a numeric grade, [0 = excellent (equals 9 on Boston Bowel Preparation Scale (BBPS)), 1= good (equals 7,8 on BBPS), 2 = fair (equals 6 on BBPS), and 3 = poor (less than 6 on BBPS)]. Excellent, good and fair were considered adequate and poor was not. During the time of study, BBPS was not being used/recorded but now is and hence the translation to the equivalent BPPS score. All bowel preparations were given in a split dose fashion. An adequate prep resulted in following guidelines for next interval colonoscopy. On the other hand, inadequate preparation resulted in an earlier repeat of colonoscopy (less than a year).

Table 1. Adequacy rates of different preparations both screening and non-screening

Screening				Non-Screening			
Prep (n)	Mean	Lower Mean	Upper Mean	Prep (n)	Mean	Lower Mean	Upper Mean
Combo (n= 2613)	99.08%	98.65%	99.38%	Combo (n= 1347)	99.48%	98.92%	99.75%
Golytely 4L (n= 98)	95.92%	89.66%	98.45%	Golytely 4L (n= 39)	92.31%	78.75%	97.49%
Mg C 2 (n= 6064)	98.94%	98.67%	99.16%	Mg C 2 (n= 3251)	99.29%	98.95%	99.53%
Mg C 3 (n= 2757)	90.35%	89.51%	91.13%	Mg C 3 (n= 1925)	92.99%	91.92%	93.92%
Miralax (n= 142)	93.08%	62.02%	99.35%	Miralax (n= 51)	100.00%	0.00%	100.00%
Moviprep (n= 132)	100.00%	0.00%	100.00%	Moviprep (n= 21)	100.00%	0.00%	100.00%
Nuletely 4L (n= 117)	100.00%	0.00%	100.00%	Nuletely 4L (28)	100.00%	0.00%	100.00%
Suprep (n=160)	99.38%	95.71%	99.91%	Suprep (n= 48)	100.00%	0.00%	100.00%

Statistical Methods

Adequacy was modeled using a binomial distribution (numeric grade: 0 = excellent, 1 = good, 2 = fair, and 3 = poor) and a binary distribution (adequate (0, 1, and 2) vs. inadequate (3)) between Preparation groups (combination-which was a 4 liter PEG + MC 2, Golytely, MC 2 – 2 bottles of MC + 2 Dulcolax, MC 3 – 3 bottle of magnesium citrate, Miralax (including Miralax with Dulcolax and 1 bottle MC), Moviprep, Nulytely, Suprep) by screening and non-screening colonoscopy using generalized linear modeling (GLM). An adequate prep resulted in following guidelines for next interval colonoscopy. We considered an adequacy threshold rate of 90% (at least 90% of all colonoscopies in any group had at least fair or better test) to be clinically useful. All modeling was accomplished using SAS Software 9.4 (SAS Inc., Cary, NC) with the GLIMMIX procedure. Bonferroni adjustments were used when comparing preparation types. All interval estimates were calculated using 95% confidence.

RESULTS

As shown in **Table 1**, the most common prep used was MC 2 for both screening (n=6,064, with 98.94% adequacy rate) and non-screening (n=3,251, with 99.29% adequacy rate), followed by MC 3 (n=2,757 with 90.35% adequacy rate, and n=1,925 with 92.92% adequacy rate) and then combination prep (n=2,613 with 99.08% adequacy rate and n=1,347 with 99.28% adequacy rate). All other preps occurred in fewer than 160 screening patients and 51 non-screening patients, respectively; Golytely 4L (n=98 for screening, with 95.92% adequacy AND n=39 for non-screening, with 92.31% adequacy rate), Miralax (n=142 for screening, with 93.08% adequacy rate AND n=51 for non-screening, with 100% adequacy rate), Moviprep (n=132 for screening, AND n=28 for non-screening, with 100% adequacy rate for both groups), Nulytely (n=117 for screening AND n=28 for non-screening, with 100% adequacy rate for both groups), and Suprep (n=160 for screening with 99.28% adequacy rate AND n=48 for non-screening with 100% adequacy rate). The total number of patients who received these preps and had adequate grades was n=18,793.

In addition, no grade for each bowel preparation fell under 2 or "fair," as illustrated in **Figure 1**. As seen in **Table 2**, exploratory comparisons revealed combination was better than Golytely for non-screening, and combination was better

Figure 1. Graph showing all the preparations we evaluated to be adequate. It also shows that MgC 2 performed better than MgC 3. This applies for both screening and non-screening groups.
MgC 2: Magnesium Citrate 2 bottles with Dulcolax.
MgC 3: Magnesium Citrate 3 bottles.

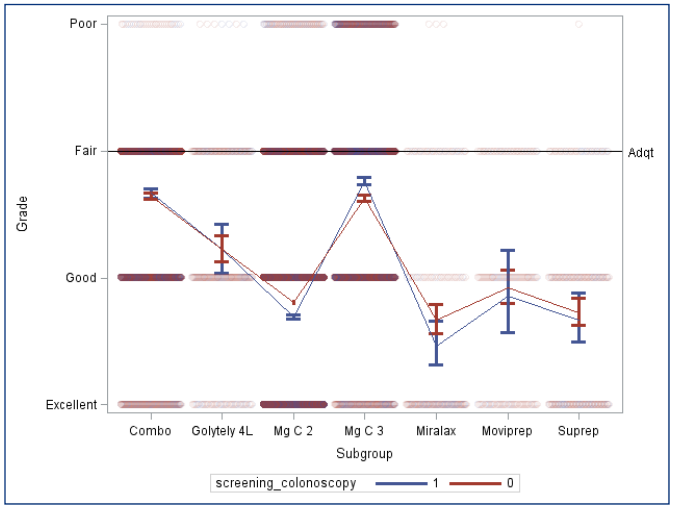

Table 2. Comparing Mg C 2 and Mg C 3 to other preparations, in screening and non-screening groups

Prep 1 (Screening)	Prep 2	P Value
Mg C 2	Mg C 3	**<.0001**
	Golytely 4L	**0.0085**
	Miralax	0.0192
	Moviprep	0.9393
	Nuletely 4L	0.9428
	Combo	0.5595
	Suprep	0.6006
Mg C 3	Golytely 4L	**0.0738**
	Miralax	**0.095**
	Moviprep	0.9255
	Nuletely 4L	0.9299
	Osmoprep	0.1945
	Combo	1.65
Prep 1 (Non- Screening)	**Prep 2**	**P Value**
Mg C 2	Mg C 3	**<.0001**
	Golytely 4L	**0.0001**
	Miralax	0.9636
	Moviprep	0.9763
Mg C 3	Golytely 4L	0.8695
	Miralax	0.9547
	Moviprep	0.9705
	Nuletely 4L	0.9659
	Combo	**<.0001**
	Suprep	0.9545

than MC 3 for both screening and non-screening. In addition, MC 2 was better than Golytely for non-screenings and higher than MC 3 for both screenings and non-screenings.

DISCUSSION

Our retrospective study shows that MC is adequate as a bowel preparation for screening, surveillance and diagnostic colonoscopies. PEG preparations have historically been the standard of care for bowel cleansing and FDA-approved preparations have usually been compared to 4L PEG. We summarize the available bowel preparations that are FDA approved. In addition, we included data that are used by the FDA, as well as data from large trials, reviews, and meta-analysis evaluating different bowel preparation in **Table 3**.

In our outpatient endoscopy center, all bowel preparations used met the mean adequacy threshold of > 90% effectiveness. This high rate of effective bowel preparations for various preparations may suggest selection bias in terms of patients booked as outpatients in a private practice ASC, staff and physician education of patients for effective bowel preparations, or possible other factors.

During the period of the study, we were not routinely using a validated bowel preparation such as the Boston Bowel Preparations Score (BBPS). Over the last few years, we have used the BBPS as a validated measure. Thus, we can translate our scale as follows: excellent= BBPS 9, good= BBP 8, fair= BBPS 6-7, poor/inadequate= BBPS < 6.

Adenoma detection rates (ADR) were monitored by individual physicians and the practice as a whole beginning in 2008. Since 2015, there was data available from the groups' formal participation in GIQuIC, a nationally recognized quality benchmarking initiative. From the beginning of 2015 through the end of 2016, the endoscopy center's overall ADR rate for screening colonoscopies including serrated lesions was 51.09% (1550/3034) with a gender breakdown of 57.85% in males (825/1426) and 45.09% in females (725/1608). This significantly is above quality benchmark thresholds and suggests an overall high quality exam regardless of preparation used.

Interestingly, we found that 2 bottles of MC with 2 Dulcolax tablets was better than 3 bottles, and we hypothesized that this could be due to intolerance to larger volume of MC, possible selection bias in choosing MC 3 for selected patients, and that a subset of patients who received the 3 bottles prep likely did not finish it entirely (many patients would report anecdotally that they were nauseated by the time they were scheduled to take the third dose and were not able to take the entire third dose). Nonetheless, despite that caveat, MC 3 still appeared to be adequate. Furthermore, it is likely that the same bowel prep was chosen for a follow-up procedure if it previously gave an adequate prep, whereas if the prep was inadequate, a more vigorous prep such as a combination prep might have been selected for the follow-up procedure. This may result in a "stacking effect" for the MC 2 or other preps, making them appear better in the time period studied.

Combination preparation, which is a combination of Golytely or Nulytely with MC, did worse in terms of adequacy than 2 bottles of MC preparation. However, this could be due to selection bias as a probable factor as typically combination preps were given to patients who had failed other preps previously or were known to have chronic constipation.

MC is significantly less expensive than other available bowel preparations–and has better tolerability due to low volume. Several studies have shown that MC has great tolerability as high as 100% in a prospective trial by Gu et al.[11] Also, studies have shown that high- and low-volume preparations are equally effective.[12]

Limitations of our study include the retrospective design and comparison of preparations that have varying numbers and that are not randomized. Specifically, these estimates and observed differences (and even lack of differences) should be interpreted with caution as the type of bowel preparation patients received was due to clinical judgment, not randomization. As such, observed differences (and lack of differences) could be due to the bowel preparation itself, the selection mechanism as to who received which bowel preparation, or the combination of the two. Also, no

Table 3.

	4L PEG/4L Nulytely	Moviprep	Miralax	Suprep	Mag Citrate	Suclear	Prepopik	Osmoprep (48g)	Osmoprep (60g)	Plenvu
FDA	N/A	(n=153) 88.9% (CI 9.8, 1.3)	N/A	(n=180) 97% (CI -2%, 5%)	N/A	*Study 1* (n=176) 90% (CI 84%, 94%) *Study 2* (n=185) 94% (CI 89%, 97%)	*Study 1* (n=304) 84.2% (CI 3.4%, 16.2%) *Study 2* (n=284) 83.0% (CI -2.9%, 9.6%)	(n=236) 95%	(n=233) 97%	(n=275) 92% (CI 4.5%, -4.0%)
Metanalysis (1)	(n=458) 90.8% (CI 0.43,0.98)	N/A	(n=738) 89.7% (CI 0.43,0.98)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Metanalysis (2)	(n=934) 83% (CI 0.78, 0.89)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Metanalysis (3)	(n= 1049) 81% (CI 2.45 ,4.89)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Metanalysis (4)	(n=6593), 87.4% (84.1,90.7)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (5)	(n=430) 84 % (CI Reference)	(n=267) 91.1% (CI 0.85,2.44)	(n=2,499) 92.5% (CI 1.24,2.49)	(n=426) 90.6% (CI 0.86, 2.16)	(n=48) 90.6% (CI 0.57,4.17)	N/A	N/A	N/A	N/A	N/A
RCT (6)	N/A	N/A	N/A	N/A	[MC alone]; (n=160) 67% VS [MC with Senna] (n=182) 95%	N/A	N/A	N/A	N/A	N/A
RCT (7)	(n=191) 90% (0.68, 3.00)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (8)	(n=93) 92% (0.21, 1.46)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (9)	(n=76) 81% (0.14, 0.61)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (10)	(n=210) 81% (0.69, 1.87)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
RCT (11)	(n=59) 78% (0.66, 5.42)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

1: Am J Gastroenterol. 2014 Oct;109(10):1566-74. doi: 10.1038/ajg.2014.238. https://www.ncbi.nlm.nih.gov/pubmed/25135007 (all RCTs were screening)

2: Gastrointest Endosc. 2014 Oct;80(4):566-576.e2. doi: 10.1016/j.gie.2014.05.320 https://www.ncbi.nlm.nih.gov/pubmed/25053529 (all indications)

3: Clin Gastroenterol Hepatol. 2012 Nov;10(11):1225-31. doi: 10.1016/j.cgh.2012.08.029 https://www.ncbi.nlm.nih.gov/pubmed/22940741

4: Clin Gastroenterol Hepatol. 2019 Nov 1. pii: S1542-3565(19)31246-7. doi: 10.1016/j.cgh.2019.10.044. https://www.ncbi.nlm.nih.gov/pubmed/31683057

5: Am J Gastroenterol. 2019 Feb;114(2):305-314. doi: 10.14309/ajg.0000000000000057. https://www.ncbi.nlm.nih.gov/pubmed/30730859 (all indications)

6: World J Gastroenterol. 2009 Apr 14; 15(14): 1759–1763. doi: 10.3748/wjg.15.1759. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2668782 (all indications) (no confidence interval reported)

7: Dis Colon Rectum. 1994 Mar;37(3):229-33; discussion 233-4. https://www.ncbi.nlm.nih.gov/pubmed/8137669

8: Am J Gastroenterol. 2003 Oct;98(10):2187-91. https://www.ncbi.nlm.nih.gov/pubmed/14572566

9: Endoscopy. 2005 Jun;37(6):537-41. https://www.ncbi.nlm.nih.gov/pubmed/15933926

10: Can J Gastroenterol. 2011 Dec;25(12):657-62. https://www.ncbi.nlm.nih.gov/pubmed/22175055

11: Gastrointest Endosc. 1998 Feb;47(2):167-71. https://www.ncbi.nlm.nih.gov/pubmed/9512283

patient satisfaction surveys in terms of individual preps were conducted. Overall facility satisfaction surveys consistently demonstrated high performance with scores over 95% in terms of the facility, scheduling, communication, staff and care received. Data were collected previously but then time constraints prevented analysis until later, when the project was taken up by Dr. AlSamman. Strengths of our study includes prospective documentation and a very large sample size – much larger than previously reported studies examining MC preparations. Although no formal power analysis was conducted to compare the differences between bowel preparations, the primary outcome – estimation of the adequacy rates of MC – were calculated using large sample sizes. Our experience supports the conclusion that MC preparations are adequate for both screening and diagnostic colonoscopies. In addition, MC is the least expensive preparation available. Though not FDA approved in the USA as a bowel preparation, given our experience and previous data, we feel MC should be considered a viable option for bowel preparation. Nonetheless, we should continue to exercise caution for patients who have chronic kidney disease, cirrhosis, and congestive heart failure. Despite the large sample size of our study, nonetheless, confidently generalize our findings given the retrospective nature of our analysis and nonrandomized design. Given its low cost, it is unlikely that any company would perform the prospective trial needed to obtain FDA approval. Hence, future guidelines should consider our experience and other published data on MC when updating bowel preparation guidelines.

References

1. Chokshi RV, Hovis CE, Hollander T, Early DS, Wang JS. Prevalence of missed adenomas in patients with inadequate bowel preparation on screening colonoscopy. *Gastrointest. Endosc.* **75**, 1197–1203 (2012).
2. Bechtold ML, Mir F, Puli SR, Nguyen DL. Optimizing bowel preparation for colonoscopy: a guide to enhance quality of visualization. *Ann. Gastroenterol. Hepatol.* **29**, 137–146 (2016).
3. Kluge MA, et al. Inadequate Boston Bowel Preparation Scale scores predict the risk of missed neoplasia on the next colonoscopy. *Gastrointest. Endosc.* **87**, 744–751 (2018).
4. Hassan C, et al. Bowel preparation for colonoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. *Endoscopy* **51**, 775–794 (2019).
5. Johnson DA, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US multi-society task force on colorectal cancer. *Gastroenterology* **147**, 903–924 (2014).
6. Harewood GC, Wiersema MJ, Melton LJ., 3rd. A prospective, controlled assessment of factors influencing acceptance of screening colonoscopy. *Am. J. Gastroenterol.* **97**, 3186–3194 (2002).
7. Binder HJ. Pharmacology of laxatives. *Annu. Rev. Pharmacol. Toxicol.* **17**, 355–367 (1977).
8. Vradelis S, et al. Addition of senna improves quality of colonoscopy preparation with magnesium citrate. *World J. Gastroenterol.* **15**, 1759–1763 (2009).
9. Rapier R, Houston C. A prospective study to assess the efficacy and patient tolerance of three bowel preparations for colonoscopy. *Gastroenterol. Nurs.* **29**, 305–308 (2006).
10. Arora M, et al. A critical evaluation and a search for the ideal colonoscopic preparation. *Clin. Res. Hepatol. Gastroenterol.* **37**, 200–206 (2013).
11. Gu P, et al. Comparing the Real-World Effectiveness of Competing Colonoscopy Preparations: Results of a Prospective Trial. *Am. J. Gastroenterol.* **114**, 305–314 (2019).
12. Spadaccini M, et al. Efficacy and Tolerability of High- vs Low-Volume Split-Dose Bowel Cleansing Regimens for Colonoscopy: a Systematic Review and Meta-analysis. *Clin. Gastroenterol. Hepatol.* (2019) doi:10.1016/j.cgh.2019.10.044.

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Epidemiology of Birth Defects in Rhode Island, 2018–2020

KRISTEN ST. JOHN, MPH; SAMARA VINER-BROWN, MS

In Rhode Island, approximately 375 infants are born with a birth defect every year.[1] A birth defect is a structural abnormality present at birth that affects the development of organs and tissues of an infant. It may be identified during pregnancy, at birth, or following birth. Although not all birth defects can be prevented, common causes include environmental pollutants, certain medical conditions and medications, infections, personal behaviors, and genetics.[1,2] Depending on the severity of the birth defect, there may be serious consequences for the infant, requiring medical, educational, or developmental interventions.[2] Infants with birth defects account for approximately 20% of infant deaths each year both nationally[3] and in Rhode Island.[4] Having a birth defects surveillance system is important in the early identification of infants and children with birth defects to prevent more serious effects throughout their life.

Rhode Island's birth defects surveillance system, located in the Rhode Island Department of Health's (RIDOH) Birth Defects Program (RIBDP), tracks birth defects, identifies children who may require additional support services, and assists in developing policies to reduce birth defects and infant mortality. Providers are mandated by regulation (216-RICR-10-10-3) to report birth defects in children up to the age of five who are diagnosed with a birth defect. Reporting occurs mainly through automated discharge reporting from birth hospitals and from provider reports.

The RIBDP routinely analyzes its surveillance data to examine trends and risk factors for birth defects. The results of these analyses are used to inform Rhode Island prevention efforts and policy. From 2015 to 2019, the prevalence rate of birth defects in Rhode Island increased by 27%.[1] Prevalence remained stable from 2015 to 2017, with the largest increase (20%) occurring from 2017 to 2018 and remaining elevated from 2018 to 2019.[1] More recent Rhode Island data for 2020 are now available. The RIBDP examined the epidemiology of birth defects cases from 2018 to 2020 to determine overall prevalence, prevalence of maternal characteristics of cases, and frequently impacted body systems to better characterize populations affected by birth defects in Rhode Island.

METHODS

All RI maternity hospitals report newborns diagnosed with a 10th Clinical Modification of the International Classification of Diseases (ICD-10) 'Q' code at discharge from the birth hospital to the RIBDP on a regular basis. The RIBDP staff confirm the accuracy of reported birth defects diagnoses through chart review of reported cases. A birth defects case is a newborn diagnosed with a birth defect ICD-10 'Q' code after chart review and had a Rhode Island maternal residence at time of birth. Minor birth defects were excluded from our case definition to focus on more relevant conditions for data analysis (case definition is available at https://health.ri.gov/publications/databooks/2018BirthDefects.pdf). Prevalence rates were calculated for 2016 to 2020 to examine overall prevalence trends over time. Cases were limited to newborns born from 2018 to 2020, which is the most recent full year of data available and the period of recent increases in prevalence rates.

To obtain infant and maternal information, birth defects cases were linked to birth certificate data from RIDOH's Center for Vital Records. Maternal characteristics used in analyses included city/town of residence, education, insurance, education level, pre-pregnancy weight and height, and race/ethnicity. These characteristics were known to be generally associated with birth defects in Rhode Island from previous analyses[1,5,6] and were self-reported by the mother on the birth certificate. To calculate the overall prevalence rate, birth certificate data for live births were used as the denominator for each birth year in the cohort. Birth certificate data were then stratified by maternal characteristic to provide denominators to calculate prevalence rates for birth defects by these characteristics.

City/town of residence was defined as core or non-core. A core city (Central Falls, Pawtucket, Providence, and Woonsocket) had a poverty level higher than 25%. Combined race and ethnicity categories were classified as follows: non-Hispanic White, non-Hispanic Black or African American, non-Hispanic Asian, and Hispanic (all races). Those with unknown ethnicity and who were non-Hispanic with an unknown or other race were not included in race/ethnicity rates. Additionally, American Indian/Alaskan Native and Native Hawaiian/Pacific Islander race categories were not included due to RIDPH's small numbers policy.[7] Body mass index (BMI) was calculated using pre-pregnancy height (inches) and weight (pounds) from birth certificate data ($BMI=weight/height^2 \times 703$). Obesity was defined as having a BMI greater than or equal to 30 kg/cm^2.

To determine prevalence rates by body system, birth defects were also grouped into major body systems using ICD-10 'Q' codes. Some newborns had multiple birth defects and as these birth defects often affected different body systems, this analysis used all birth defects reported when determining counts by body system.

SAS Version 9.4 software was used for data cleaning and frequency calculations (SAS Institute, Cary, NC). Prevalence rates were calculated using Microsoft Excel (Microsoft Office 365, Version 2008).

RESULTS

Birth defects prevalence increased 24% from 2016 to 2020 in Rhode Island (**Figure 1**). From 2018 to 2020, there were 1,247 birth defects cases reported to the RIBDP and 30,755 Rhode Island resident births. The overall prevalence rate of birth defects from 2018 to 2020 was 405 cases per 10,000 live births (**Table 1**). Two percent of birth defects cases were unable to be linked with the birth certificate file to obtain maternal characteristic information. **Table 1** shows the overall prevalence of birth defects by year, along with prevalence rates per 10,000 live births by selected maternal characteristics. Prevalence rates were highest for each respective maternal characteristic in cases with a maternal age at delivery of 35 years of age and older, maternal residence in a core city, maternal non-Hispanic black race/ethnicity, public insurance, and a maternal education level of less than 12th grade completed. Prevalence rates were similar when stratifying cases by maternal marital status and obesity status.

Twenty-six percent of newborns (n=324) had more than one birth defect diagnosed (range: 1 to 9 birth defects). **Table 2** shows the prevalence rates of birth defects grouped by body system. Cardiovascular system birth defects were the most prevalent among cases (171 cases per 10,000 live births), followed by the genitourinary (157 cases per 10,000 live births) and musculoskeletal systems (123 cases per 10,000 live births). Birth defects affecting the orofacial and respiratory body systems were least frequently seen.

Figure 1. Birth Defects Prevalence Rates, Rhode Island, 2016–2020

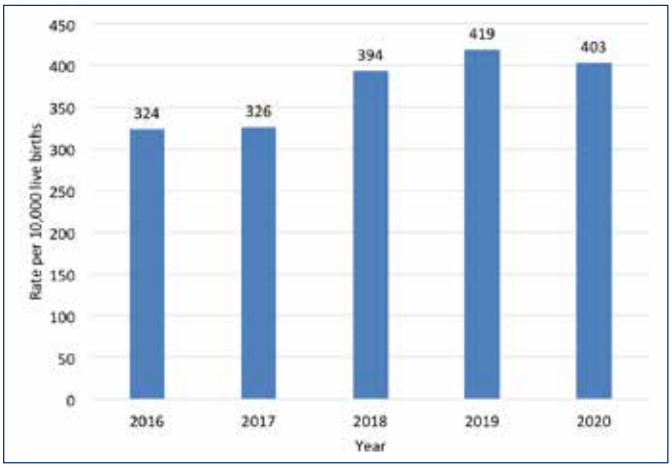

Table 1. Birth Defect Prevalence Rates by Maternal Characteristics, Rhode Island, 2018–2020

	Counts	Prevalence rate per 10,000 live births
Overall	**1247**	**405**
Maternal Age		
<25	231	402
25-34	701	380
35 and older	284	432
City/Town		
Core*	486	393
Non-Core	691	376
Race/Ethnicity		
Non-Hispanic White	612	358
Non-Hispanic Black	136	496
Non-Hispanic Asian	53	364
Hispanic	368	430
Marital Status		
Single	533	396
Married	674	393
Insurance		
Public	721	418
Private	487	390
Education		
<12th grade	185	527
12th grade	271	434
>12th grade	722	372
Obese (BMI greater than or equal to 30)		
Yes	310	403
No	844	394

*A core city (Central Falls, Pawtucket, Providence, and Woonsocket) has a poverty level higher than 25%.

Table 2. Birth Defect Prevalence Rates by Body System, Rhode Island, 2018–2020

Birth Defect	ICD-10 'Q' Codes	Counts (n)	Rate per 10,000 live births
Cardiovascular	Q20-Q28	526	171
Genitourinary	Q50-Q64	484	157
Musculoskeletal	Q65-Q79	380	123
Central Nervous System	Q00-Q07	103	33
Chromosomal	Q90-Q99	83	27
Gastrointestinal	Q38-Q45	62	20
Eye/Ear/Face/Neck	Q10-Q18	56	18
Orofacial	Q35-Q37	35	11
Respiratory	Q30-Q34	19	6

DISCUSSION

Rhode Island birth defects prevalence rates began to increase in 2018. It is uncertain if this increase is seen nationally or in other states, as there are many factors complicating this comparison. Birth defects reporting to the Centers for Disease Control and Prevention (CDC) is not required. The National Birth Defects Prevention Network (NBDPN) has surveillance guidelines that only include 47 major birth defects, while Rhode Island's case definition is inclusive of most birth defects. Additionally, there is variation in the surveillance methods used by states and variations in maternal characteristics by state, which would affect the rates produced. The NBDPN only publishes state-level, not national, prevalence estimates for the 47 birth defects with 2014 to 2018 being the most recent years available, by race/ethnicity, maternal age, and infant sex. Because of Rhode Island's size and case counts, the RIBDP can conduct statewide birth defects surveillance and have more current data, which is important to identify trends over time.

Consistent with previous years, newborns born to mothers residing in a core city, having a maternal education level less than 12th grade, identifying with a non-Hispanic Black or African American race/ethnicity, and having public insurance had higher birth defects prevalence rates. Rhode Island is beginning to see shifts in the most prevalent maternal characteristics of newborns diagnosed with birth defects. Our current prevalence rates are similar when looking at marital status and are now highest in the maternal age group of 35 years of age and older. The most recent five-year period (2013–2017) not including the birth cohorts in our analyses suggested birth defects prevalence for each respective characteristic was highest in maternal age groups of under 25 and newborns born to women with a marital status of single.[8] Based on our findings, RIBDP will continue to monitor trends in prevalence rates to assist in informing our outreach efforts and existing birth defects-related policies. It is possible that shifts in maternal characteristics trends are related to the decreasing birth population size over time and changes in the characteristics of the birth population. The RIBDP will also work with partners in RIDOH's Health Equity Institute to determine if there are any different outreach strategies that can be used to reach these populations in outreach and prevention efforts.

Additionally, previous Rhode Island case control studies suggested that Rhode Island women who were obese prior to pregnancy had an increased risk of having a baby with a birth defect[5,6], while the prevalence rates for 2018 to 2020 did not vary when examining by maternal obesity status. The RIBDP plans to conduct an updated case control study with these more recent data to determine if the trends observed previously for maternal obesity still hold for recent years.

Compared to previous years, the cardiovascular system continues to have the highest prevalence rate among body systems.[8] Although the genitourinary and musculoskeletal systems have also had higher rates than other body systems in previous years, the genitourinary system has the second highest prevalence from 2018 to 2020, whereas from 2013 to 2017, it was the third highest prevalence.[8] The RIBDP will work with its Birth Defects Advisory Council to determine if there is a true increase in prevalence in the genitourinary body system which should be explored or if it could be due to any changing diagnostic practices in recent years.

With an increase in the prevalence rate of birth defects in Rhode Island in recent years, it is important to more frequently analyze data to examine trends in prevalence over time. In addition to the typical five-year timeframes, the RIBDP will also conduct analyses by two- or three-year timeframes to help better identify changes in prevalence rates by maternal characteristics. Future analyses will focus on prevalence rates for certain maternal characteristics by body systems to further focus birth defects awareness efforts, as was previously done with maternal obesity.[5,6]

It is possible the recent increase in birth defects prevalence is due to an unknown risk factor, as not all birth defects have known causes or can be prevented.[1,2] There are some modifiable risk factors, such as pre-pregnancy weight, the RIBDP can focus on to help reduce birth defects prevalence in Rhode Island. As pre-term birth and low birthweight have also been tied to birth defects[4], the RIBP will study how these are related to receipt of prenatal care. Additionally, there may be environmental risk factors, which are not included in birth certificate data, that are contributing to increasing prevalence. The RIBDP will continue to examine prevalence of maternal characteristics in its birth defects case data to help focus future outreach and prevention efforts in Rhode Island.

LIMITATIONS

All maternal characteristics were self-reported on the birth certificate, which may over- or underestimate some characteristics, such as BMI, in the birth population and birth defects cases.

References

1. Rhode Island Birth Defects Data Book 2021, Rhode Island Department of Health (https://health.ri.gov/publications/databooks/2021BirthDefects.pdf).
2. Centers for Disease Control and Prevention (CDC). Facts about Birth Defects. https://www.cdc.gov/ncbddd/birthdefects/facts.html Accessed January 21, 2022.
3. Almli LM, Ely DM, Ailes AC, et al. Infant Mortality Attributable to Birth Defects – United States, 2003-2017. MMWR Morb Mortal Wkly Rep 2020;62:25-29.
4. Rhode Island Birth Defects Data Book 2018, Rhode Island Department of Health (https://health.ri.gov/publications/databooks/2018BirthDefects.pdf).
5. Arias W, Viner-Brown S. Pre-pregnancy Obesity and Birth Defects in Rhode Island. Rhode Island Medical Journal. 2010;93:10:321-322.
6. St John K, Viner-Brown S. Maternal Obesity and Birth Defects in Rhode Island. Rhode Island Medical Journal. 2019;101:9:50-52.
7. Rhode Island Department of Health. Rhode Island Small Numbers Reporting Policy. Accessed January 24, 2022. https://health.ri.gov/publications/policies/SmallNumbersReporting.pdf
8. Rhode Island Birth Defects Data Book 2019, Rhode Island Department of Health, (https://health.ri.gov/publications/databooks/2019BirthDefects.pdf).

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Hospital Community Benefits in a Changing Health Care System

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The recent decision by Attorney General Peter Neronha and the Federal Trade Commission (FTC) to challenge the proposed merger between the state's two largest hospital networks leaves Rhode Island's health care market in a state of flux. Despite support from key stakeholders, including Brown University, health care unions, and the Rhode Island Foundation, the creation of a locally controlled, non-profit integrated academic health care system (IAHS) appears unlikely in the near term. After more than a decade of on-again, off-again merger talks, Lifespan and Care New England will need to seek alternative paths to shore up their financial positions. The prospect of new entrants into the Rhode Island health care market, however, raises significant questions for state regulators in the coming years. While much attention will be paid to the impact of future merger proposals on the price of hospital care, the state's review process should also foster greater transparency about the level and distribution of hospital community benefits in Rhode Island.

Hospital Community Benefits

No clear federal standards govern the provision of community benefits by hospitals. In 2021, the American Hospital Association warned the fiscal stress of the COVID-19 pandemic could limit hospitals' ability to invest in community services in the near term.[1] The proposed IAHS would have created a "market dominant" hospital network in Rhode Island, commanding more than 50% market share.[2] In exchange, the benefits of any future proposed merger to patients and taxpayers must be clearly articulated in advance of final approval to promote accountability and transparency.

The term "community benefit" was first coined in 1969 to describe spending that fulfills the requirements for tax exempt status under the Internal Revenue Code.[3] Hospitals, however, are free to define both the nature and level of their community benefits. Non-profit hospitals report these benefits annually to the Internal Revenue Service on Schedule H of Form 990.[4]

Rhode Island requires all hospitals to meet a 'community standard' for the provision of hospital care, community benefits, and uncompensated care.[5] To maintain its license, each hospital must report its charity care costs, bad debt expenses, and Medicaid shortfalls to the Department of Health by March 1 each year.[6] The state requires hospitals to provide free care to uninsured patients with earnings up to 200% of the Federal Poverty Line (FPL) and to charge patients with incomes between 200–300 percent of the FPL on a sliding scale. Hospitals remain free to determine their own fee structure.[6] The state does not currently specify a minimum threshold or target for community benefits.

Most community benefits reported by hospitals take the form of 'shortfalls' or 'underpayment' by public payers such as Medicare and Medicaid. Payment shortfalls, however, remain a hotly contested measure of hospital community benefits. Hospitals routinely negotiate discounts with private insurers that pay less than their posted charges in exchange for patient volume. As a result, some critics question why Medicaid shortfalls count as 'community benefits' while negotiated discounts with third-party payers do not.[7] In 2020, the Lown Institute – a nonpartisan health policy thinktank focused on promoting health equity – developed an index that ranked hospitals based on their commitment to social responsibility that excluded shortfalls for publicly insured patients from its calculations.[8] In 2021, the Lown Index also computed a 'fair share deficit' for non-profit hospitals that compared each hospital's community benefit spending to the value of its tax exemption (estimated at 5.9 percent of overall expenditures).[9] Establishing a floor for community benefit spending, however, is potentially problematic. While a fixed target could force lagging hospitals to increase their expenditures, such regulations could discourage other institutions from exceeding the minimum threshold.[10]

Comparative Lesson Drawing

No New England state requires hospitals to provide a minimum level of community benefits, even though all require some form of community benefit reporting.[6] In Connecticut, the House Public Health Committee passed HB 6550 in 2021, which proposed to "establish a minimum community benefit and community building spending threshold" over a two-year period.[11,12] In Massachusetts, hospitals must "maintain or increase the percentage of gross patient service revenues allocated to free care" as a condition of licensure.[13] The Attorney General's Community Benefits Guidelines emphasize collaboration with community groups, but do not set requirements for specific programs or a minimum level of investment.[14]

In 2019, Oregon emerged as a national leader in setting standards for hospital community benefits after the passage of House Bill 3076, which established a community benefit spending floor for hospitals and hospital systems.[10] Institutions that do not meet the community benefit spending floor over a 12-month period face the potential loss of their tax exemption for the next twenty-four months.[15] Non-compliant hospitals must increase their spending to meet the community benefit spending floor to "the maximum amount possible while retaining sufficient days cash on hand" to maintain their credit rating.[15] This threatened loss of non-profit status provides a compelling rationale for hospitals to comply with the new community benefit requirements.

Costs and Benefits of Hospital Mergers

State hospital community benefit policies take on renewed importance in the context of growing consolidation within the U.S. hospital industry. Proponents of hospital mergers often cite studies commissioned by the American Hospital Association that found mergers can lower costs through greater economies of scale, consolidated purchasing, and organizational efficiencies.[16] Numerous empirical studies found that after a merger, prices tend to rise, as larger hospitals systems command higher reimbursement rates from third-party purchasers.[17,18] Leemore Dafny, a health economist at Harvard Business School argued that "absent any change to the status quo, health care businesses and their boards, even not-for-profit entities, cannot be relied upon to avoid transactions that might reduce net benefits to society."[19] In this context, the provision of hospital community benefits serve can serve as a key 'vital sign' for policymakers and regulators to evaluate the impact of mergers on patients and their communities. As Dr. Vikas Saini, the president of the Lown Institute noted, "It's not enough for hospitals to say they're committed to social responsibility. They need to put their commitment into action."[20]

This approach is also consistent with the position of the FTC in evaluating proposed hospital mergers. Stakeholders in proposed mergers must provide evidence of "cognizable, merger-specific efficiencies" that consolidation will yield tangible benefits for consumers and patients.[21] In November 2020, the FTC challenged a proposed merger in Memphis because "it would have eliminated competition between two of only four hospital providers."[22] In December 2020, the FTC argued that a proposed hospital merger in Bergen County, New Jersey "would control three of the six inpatient general acute care hospitals in Bergen County" and "leave insurers with few alternatives for inpatient general acute care services."[23] In February 2022, the FTC unanimously voted to challenge the proposed merger between Lifespan and Care New England by filing an administrative complaint in federal court. As the Director of the FTC's Bureau of Competition noted, "By eliminating competition between Lifespan and Care New England, this merger would create a new healthcare conglomerate with outsized power over the entire continuum of healthcare services. As this country struggles to recover from a devastating pandemic, we can't afford to allow this kind of concentrated control over critical healthcare services."[24]

Policy Implications

In evaluating future hospital mergers or acquisitions in Rhode Island, state officials should adopt former President Ronald Reagan's maxim regarding arms control negotiations to "trust, but verify."[25] Any proposed transaction must establish clear guidelines for *how* the new system will benefit the community. The Office of the Attorney General and the Department of Health should require a minimum threshold for community investment – separate and distinct from 'shortfalls' related to care provided to publicly insured and uninsured patients – as an important element of creating a health care system that meets the needs of all Rhode Islanders. It is up to policymakers to decide what constitutes a 'fair share' contribution for hospital systems. Rather than specifying a fixed percentage of revenues for all institutions, as part of the review process regulators should require parties to a merger to negotiate public commitments to fund specific organizations and programs throughout Rhode Island.

In evaluating new partners for either Care New England or Lifespan, state regulators should exercise their leverage to re-envision how hospitals can best meet the needs of their communities. Since the state provides non-profit hospitals with exemptions from income, property, and sales taxes, policymakers have a legitimate interest in assessing the societal return on investment from these foregone revenues. In exchange for their tax-exempt status, public officials can – and should – negotiate public commitments from any potential merger partners to ensure that hospitals provide cognizable benefits to their communities.

References

1. Kaufman, Hall & Associates. National Hospital Flash Report Summary: June 2021. Report prepared for the American Hospital Association. 2021, Mar 22. https://www.aha.org/system/files/media/file/2021/03/Kaufman-Hall-2021-Margins-Report-final.pdf.
2. Kocher RP, Shah S, Navathe AS. Overcoming the Market Dominance of Hospitals. *JAMA*. 2021, Mar 9;325(10):929-30.
3. James J. Non-profit Hospitals' Community Benefit Requirements. *Health Aff*. 2016; Feb 25. https://www.healthaffairs.org/do/10.1377/hpb20160225.954803/full/.
4. RTI International. Community Benefit Spending 101. 2021. http://www.communitybenefitinsight.org/?page=info.cb101.
5. Community Catalyst. 2021. Rhode Island. https://www.communitycatalyst.org/initiatives-and-issues/initiatives/hospital-accountability-project/free-care/states/rhode-island.
6. National Association for State Health Policy. Hospital Community Benefits Comparison Table for Six New England States. 2018, May 3. https://www.nashp.org/wp-content/uploads/2018/05/Hospital-community-benefits-chart-final-5_3_2018.pdf.

7. Lown Institute. Winning Hospitals 2021 – Community Benefit. 2021; https://lownhospitalsindex.org/2021-winning-hospitals-community-benefit/.
8. Saini V, Brownlee S, Gopinath V, Smith P, Chalmers K, Garber J. 2021 Methodology of the Lown Institute Hospitals Index for Social Responsibility. Needham, MA: The Lown Institute. 2021, Sep 21. https://lownhospitalsindex.org/wp-content/uploads/2021/09/2021_Methodology_9-21-21.pdf.
9. Toleos A. Most U.S. Non-profit Hospitals Neglect Community Investment Obligation, Analysis Reveals. Needham, MA: The Lown Institute. 2021, Jul 11. https://lowninstitute.org/press-release-most-us-non-profit-hospitals-neglect-community-investment-obligation-analysis-reveals/.
10. Kacik A. Oregon Sets Floor for Community Benefit Spending; Other States May Follow Suit. *Modern Healthcare*. 2021, Feb 8;6-7.
11. HB 6550. An Act Concerning the Office of Health Strategy's Recommendations Regarding Various Revisions to Community Benefits Programs Administered by Hospitals. https://legiscan.com/CT/text/HB06550/id/2352877/Connecticut-2021-HB06550-Comm_Sub.pdf.
12. Roll Call - CT HB06550 | 2021 | General Assembly. https://legiscan.com/CT/rollcall/HB06550/id/1029042.
13. Massachusetts General Law Section 51G(3), https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXVI/Chapter111/Section51G.
14. Commonwealth of Massachusetts, Office of the Attorney General. "The Attorney General's Community Benefits Guidelines for Non-Profit Hospitals." https://www.mass.gov/doc/community-benefits-guidelines-for-non-profit-hospitals/download.
15. Oregon House of Representatives. HB 3076. 2019 Regular Session. https://olis.oregonlegislature.gov/liz/2019R1/Downloads/MeasureDocument/HB3076/Introduced.
16. May S, Noether M, Stearns B. Hospital Merger Benefits: An Econometric Analysis Revisited. Chicago: American Hospital Association. 2021, Aug. https://www.aha.org/system/files/media/file/2021/08/cra-merger-benefits-revisited-0821.pdf.
17. Schwartz K, Lopez E, Rae M, Neuman T. What We Know About Provider Consolidation. Kaiser Family Foundation. 2020, Sep 2. https://www.kff.org/health-costs/issue-brief/what-we-know-about-provider-consolidation/.
18. Dafny L, Lee TH. The Good Merger. *N Engl J Med.* 2015, May 28;372(22):2077-2079.
19. Dafny L. Addressing Consolidation in Health Care Markets. *JAMA.* 2021, Mar 9;325(10): 927-928.
20. Toleos A. Equity is the missing piece for elite hospitals to be truly socially responsible. Needham, MA: The Lown Institute. 2021, Sep 21. https://lowninstitute.org/press-release-equity-is-the-missing-piece-for-elite-hospitals-to-be-truly-socially-responsible/.
21. Federal Trade Commission. Administrative Part 3 Complaint. Docket No. 9399. In the Matter of Hackensack Meridian Health, Inc. and Englewood Healthcare Foundation.2020, Dec 3. https://www.ftc.gov/system/files/documents/cases/d09399_administrative_part_3_complaint_-_public.pdf.
22. Federal Trade Commission. Statement of Daniel Francis, Deputy Director of the FTC's Bureau of Competition, Regarding the Announcement that Methodist LeBonheur Healthcare has Abandoned Its Proposed Acquisition of Two Memphis-area Hospitals from Tenet Healthcare. 2020, Dec 23. https://www.ftc.gov/news-events/press-releases/2020/12/statement-daniel-francis-deputy-director-ftcs-bureau-competition.
23. Federal Trade Commission. FTC Challenges Hackensack Meridian Health, Inc.'s Proposed Acquisition of Competitor Englewood Healthcare Foundation. 2020, Dec 3. https://www.ftc.gov/news-events/press-releases/2020/12/ftc-challenges-hackensack-meridian-health-incs-proposed.
24. Federal Trade Commission. FTC and Rhode Island Attorney General Step in to Block Merger of Rhode Island's Two Largest Healthcare Providers. 2022, Feb 17. https://www.ftc.gov/news-events/press-releases/2022/02/ftc-rhode-island-attorney-general-step-block-merger-rhode-islands.
25. Reagan R. Remarks on Signing the Intermediate-Range Nuclear Forces Treaty. Simi Valley, CA: Reagan Presidential Library. 1987, Dec 8. https://www.reaganlibrary.gov/archives/speech/remarks-signing-intermediate-range-nuclear-forces-treaty.

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What America's Struggle with Abortion Access Means for Reproductive Healthcare in Rhode Island

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The Texas Heartbeat Act and the Current State of US Abortion Legislation

On September 1, 2021, Texas legislators passed the Texas Heartbeat Act, also known as Senate Bill 8 or "SB8," and in doing so changed the landscape of abortion care overnight. Whereas other "heartbeat bills" have failed to be enacted due to the historic Roe v. Wade ruling, SB8 has thus far evaded repeal by way of deeming "aiding and abetting" abortion after 6 weeks as a civil infraction to be enforced by private citizens rather than by government agencies. This law has resulted in a near total halt to abortion provision in Texas due to fears of overwhelming litigation for anyone involved in assisting in an abortion in any way, from providers and clinic staff to Uber drivers and family members. In a region like Texas' Rio Grande Valley, there is only one abortion clinic to meet the needs of millions of people, and the most severe effects have disproportionately landed on those with already limited resources and barriers to accessing healthcare.[1] Texans seeking abortion after 6 weeks of pregnancy have had to find care in neighboring states, across international borders, self-manage their abortions, or – if no care is able to be arranged – default into carrying undesired pregnancies. The SB8 legislation has coincided with a groundswell of other anti-abortion bills throughout the country. In 2021, states enacted 106 abortion restrictions, the most ever in a single year since the passage of Roe v. Wade.[2] According to the Guttmacher Institute, 58% of people who identify as women aged 13–44 currently live in a state considered "hostile" towards abortion access.[3] The Coastal US is not necessarily insulated from such hostility. In fact, despite the landmark 2019 passage of the Rhode Island Reproductive Privacy Act, which codified the right to abortion into our state legislature, restrictions still exist. In addition to a requirement for parental consent for persons under 18, Rhode Island state policy excludes insurance coverage for abortion for state employees and Medicaid patients, representing one in three Rhode Islanders. These laws disproportionately restrict abortion access for young, low-income persons and people of color who are overrepresented in the Medicaid program, restricting private medical decisions about their bodies and reproductive futures, and further entrenching minorities into disadvantaged positions.

A Persistent Connection Between Discrimination and Restricting Abortions

In the pre-Civil War era, abortion before "quickening" was a common practice. At the time, most reproductive care, including birthing and abortion, was provided by midwives – many of whom were women of color, immigrants, and slaves.[4] Following the Civil War, the American birth rate was falling as women sought more freedom over their roles in society; this decline was especially striking among middle and upper class white families.[5] Subsequently, anti-abortion propoganda and moral panic regarding the decline of the white birth rate was on the rise. The medical community became highly involved in these cultural and political discussions. Horatio Storer, known as the father of American gynecology, lobbied the AMA shortly after its formation in 1857 to start a committee on "criminal abortion.[5] Their concerted efforts resulted in the AMA successfully delegitimizing midwifery while simultaneously lobbying state legislatures to outlaw abortion.[6] As this was at a time when women and people of color were excluded from the "legitimate" practice of medicine, essentially all reproductive care was relegated to white male physicians.

Even though all states had abortion bans on their books by 1910, affluent mostly white women who could afford to travel and pay private physician fees continued to access abortions.[7] Those who could not make these accommodations suffered the consequences. One study done in New York City in the 1960s showed that one in four childbirth-related deaths among white women was due to abortion, compared to one in two childbirth-related deaths among nonwhite women.[7] When Roe v. Wade was ultimately decided in 1973, the mortality rate from abortions sharply declined to the point that death from abortion is now exceedingly rare.[7] The increased access to abortion that followed Roe's passage lead to fewer delays in care; simultaneously, the proportion of abortions performed in the earlier stages of pregnancy, when complications are rare, rose.[7] This retrospective highlights the outsized effect that abortion laws have on autonomy, safety, and the long-standing, disproportionate, and potentially deadly burden these laws place on communities of color and socioeconomically disadvantaged communities.

Where do we go from here?

Since Roe's passage, there have been continuous attempts to challenge and reverse it. Though many of these efforts have been unsuccessful, the recent Supreme Court hearings of United States v. Texas (regarding SB8) and Dobbs v. Jackson Women's Health represent the most serious legal threats to the constitutional right to abortion. Combined with the lack of state-level protections to abortion in a majority of states (only 15 have codified this right in their legislatures; 12 have "trigger laws" which would automatically ban all abortions if Roe was reversed)[8], we face the possibility of returning to a scarcity of accessible abortions as seen in the pre-Roe era and the subsequent harms associated with this lack of access. As physicians, we often see these harms strictly through the lens of physical health; but it is worth noting also the social harms inflicted on patients. Well over half of all persons seeking abortion are poor or low- income, and well over half are either already parents allocating their limited resources to their current children or otherwise cite that they do not have the resources to carry and subsequently care for a child.[9] The UCSF Turnaway Study found that 72% of people who sought an abortion but ultimately did not receive one ended up living in poverty, compared to 55% of those who were able to obtain an abortion, providing further evidence that restricting access to needed healthcare services like abortion perpetuates cycles of poverty.[10]

As we await Supreme Court decisions and look ahead to a new legislative session in Rhode Island, we as a healthcare community must prioritize reproductive autonomy, equity, and access for our patients and fellow Rhode Islanders. The pace of anti-abortion efforts is unlikely to let up; if unchallenged, these efforts will likely be successful in severely limiting abortion access for all, with the most significant burden falling on already historically and systematically disadvantaged communities. The medical community played an important role hundreds of years ago in suppressing reproductive choice with deleterious consequences, but we now have the opportunity to call for reproductive justice. In fact, the Rhode Island legislature is considering the Equality in Abortion Coverage Act this session, which would remove the discriminatory legislation prohibiting Medicaid and government insurance from covering abortion services. We should continue to support abortion clinicians in the state and the organizations that employ them. We need to advocate within our professional organizations for improved training for residents in abortion care, bolster this education in the primary care specialties, and support primary care offices seeking to provide abortions. Ultimately, without strong and clear effort to protect abortion access, we may quickly run out of time to stand up for reproductive justice.

References

1. Undocumented women face shrinking options for reproductive health care under Texas abortion law. The World from PRX. Accessed November 10, 2021. https://theworld.org/stories/2021-09-02/undocumented-women-face-shrinking-options-reproductive-health-care-under-texas
2. Nash E. For the first time ever, U.S. states enacted more than 100 abortion restrictions in a single year. Guttmacher Institute. Published September 30, 2021. Accessed November 10, 2021. https://www.guttmacher.org/article/2021/10/first-time-ever-us-states-enacted-more-100-abortion-restrictions-single-year
3. Nash E. State abortion policy landscape: From hostile to supportive. Guttmacher Institute. Published December 10, 2018. Accessed November 10, 2021. https://www.guttmacher.org/article/2019/08/state-abortion-policy-landscape-hostile-supportive
4. Reagan LJ. Linking midwives and abortion in the Progressive Era. Bull Hist Med. 1995;69(4):569-598. PMID: 8563453.
5. Digital History. Digitalhistory.uh.edu. Accessed November 26, 2021. http://www.digitalhistory.uh.edu/topic.cfm?topicID=17'
6. Tone A, ed. Controlling Reproduction: An American History. Rowman & Littlefield; 1996.
7. Gold RB. Lessons from Before Roe: Will Past be Prologue? Guttmacher Institute. Published September 22, 2004. Accessed November 28, 2021. https://www.guttmacher.org/gpr/2003/03/lessons-roe-will-past-be-prologue
8. Abortion policy in the absence of roe. Guttmacher Institute. Published March 14, 2016. Accessed November 10, 2021. https://www.guttmacher.org/state-policy/explore/abortion-policy-absence-roe
9. Jerman J, Jones RK, Onda T. Characteristics of U.S. abortion patients in 2014 and changes since 2008. Published online 2016. Accessed November 10, 2021. https://www.guttmacher.org/report/characteristics-us-abortion-patients-2014
10. Foster DG, Farber ON, Gilbert Welch H, et al. When women are denied an abortion, their children fare worse than peers. STAT. Published December 5, 2018. Accessed November 10, 2021. https://www.statnews.com/2018/12/05/how-abortion-denial-affects-children-well-being/

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The Role, Importance of Timely Rehabilitation During the COVID-19 Pandemic

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The Food and Agriculture Organization of the UN[1] and World Health Organization (WHO)[2] recently published guidelines offering nutrition advice for adults during the COVID-19 outbreak.[3,4] We write to support and share these efforts promoting good health and strong immunity with the Rhode Island medical community as we collectively battle the fourth wave of the COVID-19 pandemic. These publications are nicely summarized in an article by Phillipou et al, highlighting the importance of healthy body weight, hydration, balanced diet, and limiting ultra-processed foods, fats, sugars, salt, and alcohol to boost immunity.[5]

Despite widespread public health and vaccination efforts, the COVID-19 pandemic persists with staggering effects on human suffering, healthcare, population dynamics, and economics in Rhode Island. With waning vaccine efficacy and emergence of variants including Delta and Omicron, we must consider all options to strengthen immunity as vaccination efforts continue. Due to medical compromise, limited mobility in communal settings, and reduced function, our patients are vulnerable to COVID-19 and resultant sequelae. As such, we humbly assert the importance and timeliness of promoting rehabilitation to further combat this disease.

As provider encouragement strongly predicts patient adherence to healthy lifestyle and exercise, we must educate our patients on these strategies to protect themselves.

The immune system fights the novel coronavirus with two lines of defense: innate (general) and adaptive (specialized) immunity.[6] New vaccines against SARS-CoV-2 are novel in triggering innate immunity, complimenting evidence-based public health measures including physical distancing, facial masks, and handwashing.[7] Recognition of pathogens and immune strength trigger adaptive immunity.[8-13] There's a compelling link between physical activity and the body's defense system to strengthen immunity.

Physical activity is defined as movement involving muscle contraction. Most activities of daily living (ADLs), allowing patients to care for themselves, and some instrumental activities of daily living (IADLs), which are more complex tasks, require physical activity. Exercise is a focused form of physical activity intended to acquire and enhance fitness or other health benefits. Exercise enhances immunosurveillance by increasing leukocytes, granulocytes, circulating levels of interleukin (IL)-6, and natural killer (NK). Furthermore, exercise in water augments leukocyte, granulocyte, and monocyte responses with immune-stimulating effects.[14] As exercise is an important component of multidisciplinary and multimodal rehabilitation, improving survival, accelerating recovery, reducing re-injury, preventing chronic disease,[15-17] rehabilitation professionals are key to immune defense.

It has been shown that Long-Haul Syndrome, including mood disorders, fatigue, and perceived cognitive impairment, has severe negative impact on function.[18,19] The significant influence of persistent symptoms on ADLs and quality of life, notwithstanding severity of acute infection, validate the need for acute rehabilitation[18] after acute medical management. Although no direct link has been identified, lifestyle measures including restorative sleep, smoking cessation, stress management, psychological well-being, and healthy social connections play an important role in primary, secondary, and tertiary pre-vention of COVID-19.[19,20] As provider encouragement strongly predicts patient adherence to healthy lifestyle and exercise, we must educate our patients on these strategies to protect themselves. Any member of the interdisciplinary rehabilitation team has an opportunity to educate their patients as part of a comprehensive preventive treatment adjunct.

Fortunately, there are many rehabilitation options within Rhode Island and the surrounding medical community. These include inpatient acute rehabilitation as well as outpatient therapies, all of which use an interdisciplinary treatment paradigm to improve the lives of patients. Furthermore, there are specific programs that combine land therapy with water therapy to optimize positive effects on immune function. Although many models prevail, in our experience and focus on rehabilitation, conditioning, and training in both land and water environments, we resolutely acknowledge and support the work of the UN and WHO. We stand alongside our rehabilitation family to assert a pivotal role in maintaining immune health. Through rehabilitative science and technology in conjunction with our focus on lifestyle measures and exercise, we play an important role in strengthening immunity throughout the rehabilitation care continuum.[5] Together, we will forestall the scourge of COVID-19 to limit impairment, disability, and handicap during this unprecedented public health crisis.

References

1. Food and Agriculture Organization of the United Nations. Maintaining a healthy diet during the COVID-19 pandemic. Available at: http://www.fao.org/3/ca8380en/CA8380EN. Pdf. Accesses November 18, 2021.
2. World Health Organization. Nutrition advice for adults during the COVID-19 outbreak. Available at: http://www.emro.who.int/nutrition/nutrition-infocus/nutrition-advice-for-adults-during-the-covi-19-outbreak.html. Accessed December 2, 2021.
3. Noun Project (creators: Tulphan, Econceptive, Creative Stall, Monkik, Simon, Lo, Royyan Razka,Andrei Yuskchenko, Vector Bakery, Sergei Shramko, Turkub, Carlo Pico, Eucalp, Ninejipjip, Georgiana Ionescu, Icons Producer). Available at https://thenounproject.com. Accessed November 28, 2021.
4. World Health Organization. Obesity and overweight. Available at: https://thenounproject.com. Accessed November 28, 2021.
5. Philippou E, Negm A, Heyn P. Ten dietary steps to strengthen your immune system - A guide for older individuals at risk of COVID-19. Arch Phys Med and Rehab 2021; 102:1865-1868.
6. Warrington R, Watson W, Kim H, Antonetti F. An introduction to immunology and immunopathology. Allergy Asthma Clin Immunol. 2011 Nov 10; 7 Suppl 1(Suppl 1): S1. Doi: 10.1186/1710-1492-S1-S1. PMID: 22165815; PMCID: PMC3245432.
7. Teijaro J, Farber D. COVID-19 vaccines: modes of immune activation and future challenges. Nature Reviews Immunology. 2021. 21, 195-197.
8. Monye I, Adelowo B. Strengthening immunity through healthy lifestyle practices: Recommendations for lifestyle interventions in the management of COVID-19. Lifestyle Medicine. 2020 Jul; 1(1): e7.
9. Childs C, Calder P, Miles E. Diet and immune function. Nutrients 2019, 11, 1933; doi:10.3390/nu11081933.
10. Woods J, Davis J, Smith J, Nieman D. Exercise and cellular innate immune function. Med Sci Sports Exerc. 1999: 31: 57-66.
11. Davison G, Kehaya C, Jones A. Nutrtional and physical activity interventions to improve immunity. Am J Lifestyl Med. 2016.
12. Maidens C, Childs C, Przemska A, Dayel IB, Yaqoob P. Modulation of vaccine response by concomitant probiotic administration. Br J Clin Pharmacol. 2013; 75:663-670.
13. Goldspink DF. Ageing and activity: their effects on the functional reserve capacities of the heart and vascular smooth and skeletal muscles. *Ergonomics.* 2005;48(11–14):1334–1351.
14. Nieman D, Wentz L. The compelling link between physical activity and the bodys defence system. J Sport Health Sci 2019 May; 8(3): 201-217.
15. Westerterp KR. Daily physical activity and ageing. *Curr Opin Clin Nutr Metab Care.* 2000;3(6):485–488.
16. Hurley BF, Roth SM. Strength training in the elderly: effects on risk factors for age-related diseases. *Sports Med.* 2000;30(4):249–268
17. Hornbrook MC, Stevens VJ, Wingfield DJ, Hollis JF, Greenlick MR, Ory MG. Preventing falls among community-dwelling older persons: results from a randomized trial. *Gerontologist.* 1994;34(1):16–23
18. Vanichkachorn G. Post-COVID-19 syndrome (long haul syndrome): Description of a multidisciplinary clinic at mayo clinic and characteristics of the initial patient cohort. Mayo Clinc Proc. 2021 Jul.
19. Albu S, Rivas Zozaya N, Murillo N, Garcia-Molina A, Chacon C, Kumru H. What's going on following acute covid-19? Clinical characteristics of patients in an out-patient rehabilitation program. NeuroRehabilitation. 2021; 48 (4): 469-480.
20. Thakur A, Joshi V, Thakur H. Immunology and its relation with food components: An overview. Intl J Food Ferment Technol. 2019; 9 (1):01-16.

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In RIMJ 50-plus years ago: 'One and Two Sentence Essays'

MARY KORR
RIMJ MANAGING EDITOR

In addition to reading the scientific and medical contributions of physicians and members of the healthcare community in Rhode Island 50 years ago with very interesting images, X-rays, and charts of yesteryear, archival editions of the *Rhode Island Medical Journal* published during the 1970s included a regular, succinct feature titled "One Sentence Essay" and "Two Sentence Essay." Occasionally there was a rare one labeled "Three Sentence Essay." The essays were displayed on the page by three anchors above and below them.

While most editors today would hyphenate the compound modifier to one-sentence essay, etc., I will leave it in its original rendition. And, of course, one could argue that a single or two sentences does not fit into the essay genre – but perhaps **SEEBERT GOLDOWSKY, MD**, then editor-in-chief, or **JOHN FARRELL, ScD**, managing editor, would offer a counterpoint to that argument.

In any event, the cryptic and often wry comments offer reflective and amusing reading on wintry days, ie:

The cover image of the *Rhode Island Medical Journal* of January 1972 shows the Royal C. Taft Building for Out Patients at Rhode Island Hospital, from the hospital's 27th annual report of 1890. The building was featured on the cover to accompany an article on the delivery of ambulatory care.

We can see farther because we stand on the shoulders of giants.
— *Sir Isaac Newton*

That is a well-known fact, so well known that it may not be true at all.
— *The Red Queen to Alice*

In addition to philosophical and literary topics, observations in the essays offered opinions on patient care, scientific research, history, current events, medical writing and editing, and politics, as shown in the following samples.

One Sentence Essays

The secret of caring for the patient is caring for the patient.
— *Francis Peabody, MD*

System, or as I shall term it, the virtue of method, is the harness without which only the horses of genius travel.
— *Sir William Osler*

We have to defend the country against mediocrity: mediocrity of soul, mediocrity of ideas, and mediocrity of action.
— *Abraham Flexner, expressing his philosophy of education*

There is no good writing, only good rewriting.
— *Joseph Garland, MD, late editor of The New England Journal of Medicine*

Illustration of Sir Isaac Newton
[Source Wikimedia, Creative Commons: https://commons.wikimedia.org/wiki/File:Seeman_Newton_1726.jpg]

Illustration by John Tenniel of the Red Queen lecturing Alice for Lewis Carroll's "Through The Looking Glass".
John Tenniel, Public domain, via Wikimedia Commons
https://commons.wikimedia.org/wiki/File:Tenniel_red_queen_with_alice.jpg

If you steal from one author, it is plagiarism; if you steal from two it is research.
— *Anon.*

Pardee's Law: There is an inverse relationship between the uniqueness of an observation and the number of investigators who report it simultaneously.

One surgeon to another: "It was a tough operation – ten minutes in the operating room and eight hours filling out the insurance forms."
— *Anon.*

The effectiveness of a politician is inversely proportional to his commitment to principle.
– *Sam Shaffer, political writer*

All great occasions have an element of crowding.
— *Winston Churchill*

Solutions to problems create problems.
— *Loren Eiseley, anthropologist*

There was a recent joke in Europe to the effect that in January scientists in the United States announced a new fundamental invention; in February the Russians announced that they had invented it ten years before; and in March the Japanese commenced large scale commercial shipping of the device into the United States.
— *Joseph S. Wright,*
Chairman of the Board, Zenith Radio Corp.

Infections of the ear with pathogenic fungi have something in common with the snakes of Ireland; there are none.
— *Kingerty FAJ,*
The Myth of Otomycosis,
JAMA, 191:129. Jan. 1965.

Two Sentence Essays

Only a few years ago, three open-heart procedures a week were considered an active schedule. Today, we often have five procedures requiring use of the pump oxygenator under way simultaneously in one operating suite; throughout our medical center 50 open-heart procedures are often performed in one week.
— *Michael E. DeBakey, MD,*
The Year Book of General Surgery, 1970

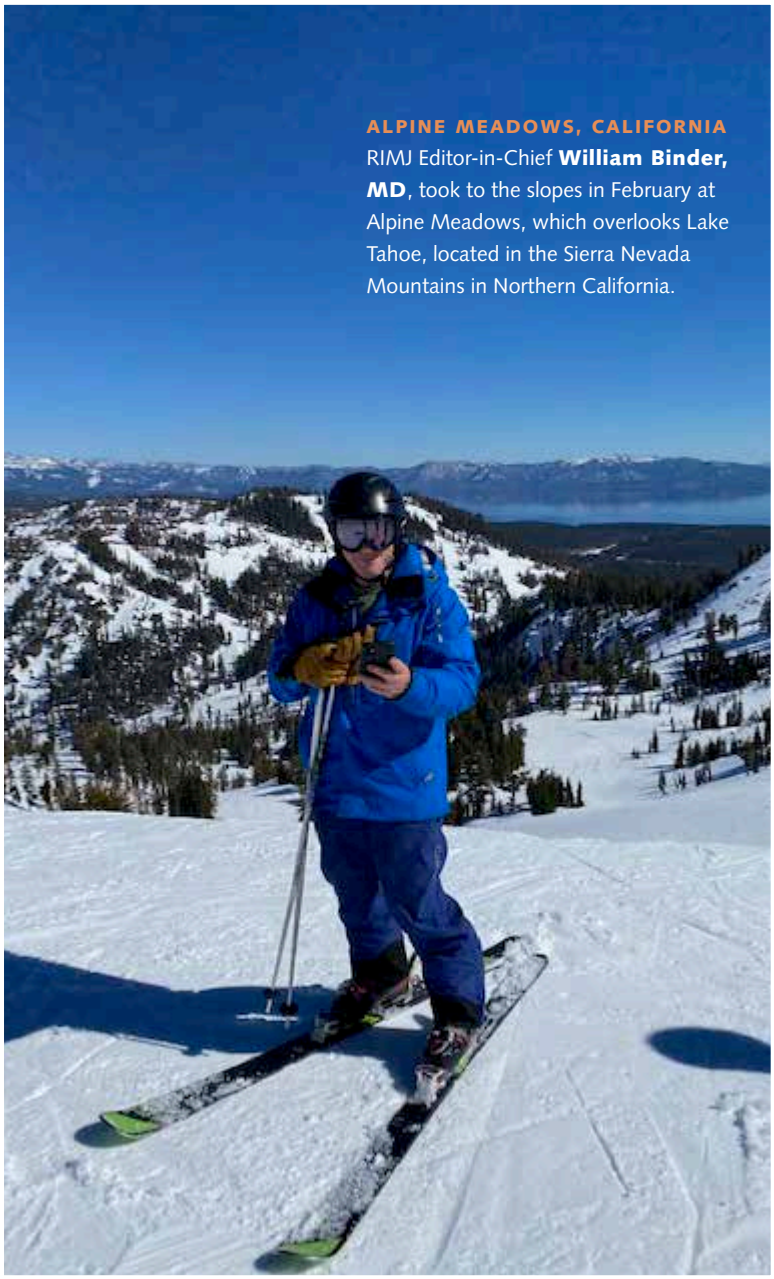
A few hundred years ago, if you had daily talks with the Blessed Virgin, you were St. Bernadette. If you do it today, you are put into an institution on a heavy diet of drugs.
— *Ann Morrissey, mental health advocate and independent candidate for Congress from Rhode Island* ❖

We are read everywhere

In the past year, more than **55,000** unique viewers from **121** countries have read articles in the *Rhode Island Medical Journal* or researched topics in its archives.

Top 10 countries in 2022

1. US
2. Canada
3. UK
4. India
5. China
6. Netherlands
7. Germany
8. Italy
9. Philippines
10. Australia



ALPINE MEADOWS, CALIFORNIA
RIMJ Editor-in-Chief **William Binder, MD**, took to the slopes in February at Alpine Meadows, which overlooks Lake Tahoe, located in the Sierra Nevada Mountains in Northern California.

PALISADES TAHOE, CALIFORNIA
Alexandre Rajbhandari, from Paris, France, a reporter for Bloomberg News, who usually skies in the Alps, checked out a recent themed issue of RIMJ on climate change while skiing in Tahoe National Forest in California, on a February trip to visit family. Situated in the west hills of Lake Tahoe, Palisades Tahoe is located in the Olympic Valley, where the Winter Olympics was held in 1960.

Wherever you may be, or wherever your travels may take you, check the Journal on your mobile device, and send us a photo: mkorr@rimed.org.


Adventures
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Working for You: RIMS advocacy activities

February 1

RIMS Physician Health Committee (PHC): **Herbert Rakatansky, MD**, Chair

American Medical Association (AMA) Advocacy Resource Center conference call to discuss legislative efforts that threaten Public Health Authorities

Legislative Committee hearings

February 2

American Medical Political Action Committee (AMPAC): regional political directors' call

Hospital Capacity Workgroup meeting: **Elizabeth Lange, MD**, President; **Catherine A. Cummings, MD**, Past President; **Thomas Bledsoe, MD,** President Elect; **Bradley Collins, MD**, RIMS Past President; **Nadine Himelfarb, MD**, President RI-ACEP

Legislative Committee hearings

February 3

Meeting with Blue Cross & Blue Shield of Rhode Island (BCBSRI): **Elizabeth Lange, MD**, President; **Thomas A. Bledsoe, MD,** President-elect

Diabetes Prevention Program Stakeholder Network

Legislative Committee hearings

February 7

RIMS Council meeting: **Elizabeth Lange, MD**, President

February 8

Meeting with Senator DiMario regarding prior authorization legislation

February 9

RI Department of Health (RIDOH) Board of Medical Licensure and Discipline (BMLD)

Governor's Overdose Intervention and Prevention Task Force: **Sarah Fessler, MD**, RIMS Past President

February 10

Annual Healthcare lobbyist pre-session discussion

February 11

RIMS Finance Committee: **Kwame Dapaah-Afriyie, MD,** Chair

Health Information Technology Steering Committee

February 14

Legislative Committee hearing

February 15

AMA National Advocacy conference virtual Capital Hill visits: Senator Reed; Congressman Langevin; Congressman Cicilline; **Thomas Bledsoe, MD,** President Elect; **Heather A. Smith, MD,** Vice President, AMA Council on Legislation, Vice Chair; **Stacy Paterno**, RIMS CEO

Legislative Committee hearings

February 16

Legislative Committee hearings

February 17

Office of the Health Insurance Commissioner (OHIC) HIT Steering Committee: **Peter Hollmann, MD**

Legislative Committee hearings

February 18

Meeting regarding Ambulance Service Coordinating Advisory Board (ASCAB): **Elizabeth Lange, MD**, President; **Elizabeth Cummings, MD**, Past President

February 21

State House Update: **Michael E. Migliori, MD**, RIMS Public Laws Committee Chair; and **Peter Karczmar, MD,** RI Medical Political Action Committee (RIMPAC) Chair

February 22

Meeting with Alkermes, Inc. regarding RIMS legislation to codify MAT/MOUD at Department of Corrections

Interstate licensure compacts strategy discussion

February 23

Addressing the Opioid Crisis: Sage Consumption and Federal Preemption – What's Next?: Yale University Webinar

February 24

Governor's Overdose Task Force: Racial Equity Work Group

RIMS Physician Health Program Governance Committee: **Jerry Fingerut, MD**, Chair

RIMS NOTES: *News You Can Use*

Our biweekly e-newsletter is published on alternate Fridays exclusively for RIMS members. Contact Dulce Cosme if you've missed an issue, dcosme@rimed.org.

RIMS CORPORATE AFFILIATES

The Rhode Island Medical Society continues to drive forward into the future with the implementation of various new programs. As such, RIMS is expanded its Affinity Program to allow for more of our colleagues in healthcare and related business to work with our membership. RIMS thanks these participants for their support of our membership.

Contact Ali Walz for more information: 401-331-3207 or awalz@rimed.org

www.nhpri.org

Neighborhood Health Plan of Rhode Island is a non-profit HMO founded in 1993 in partnership with Rhode Island's Community Health Centers. Serving over 185,000 members, Neighborhood has doubled in membership, revenue and staff since November 2013. In January 2014, Neighborhood extended its service, benefits and value through the HealthSource RI health insurance exchange, serving 49% the RI exchange market. Neighborhood has been rated by National Committee for Quality Assurance (NCQA) as one of the Top 10 Medicaid health plans in America, every year since ratings began twelve years ago.

www.ripcpc.com

RIPCPC is an independent practice association (IPA) of primary care physicians located throughout the state of Rhode Island. The IPA, originally formed in 1994, represent 150 physicians from Family Practice, Internal Medicine and Pediatrics. RIPCPC also has an affiliation with over 200 specialty-care member physicians. Our PCP's act as primary care providers for over 340,000 patients throughout the state of Rhode Island. The IPA was formed to provide a venue for the smaller independent practices to work together with the ultimate goal of improving quality of care for our patients.

RIMS gratefully acknowledges the practices who participate in our discounted Group Membership Program

ANCHOR MEDICAL ASSOCIATES

Block Island Medical Center

BROWN SURGICAL ASSOCIATES
BROWN PHYSICIANS, INC.

COASTAL MEDICAL
LEADERS IN HEALTHCARE

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PCHC
PROVIDENCE COMMUNITY HEALTH CENTERS

RI ENT

Rhode Island Eye INSTITUTE

SKIN PROS

The Providence CENTER

Thundermist HEALTH CENTER

Tri-County Community Action Agency
Helping people. Changing lives.

UNIVOTO
University Otolaryngology

WellOne
Primary Medical and Dental Care

Wood River Health Services
The Heart of South County since 1976

For more information about group rates, please contact Ali Walz, RIMS Director of Member Services

'BrainGate+SoftRobotics' team wins CERF ALS research prize

PROVIDENCE – The Cullen Education and Research Fund (CERF), a private philanthropy based in London, recently announced the first recipient of its CERF Medical Engineering Prize for ALS Research. **DR. LEIGH HOCHBERG**, **DR. CONOR WALSH**, and **DR. SABRINA PAGANONI** have been awarded the prize, which is accompanied by €500,000 (about $570,000).

The "BrainGate+SoftRobotics" team from Brown University, Harvard University and Massachusetts General Hospital (MGH) is creating a series of technologies intended to improve arm and hand function for people with muscle weakness and paralysis, including people with amyotrophic lateral sclerosis (ALS).

The prize was established to recognize outstanding research and to encourage the development of technologies that maintain or restore function of the arm and hand for people with ALS/Motor Neuron Disease (MND).

Leigh Hochberg, MD, PhD

Conor Walsh, PhD

Sabrina Paganoni, MD, PhD

"We received an exceptional number of excellent entries for this our first Medical Engineering prize," **DAVID T. CULLEN**, chairman and founder of CERF, said. "The combined entry from the Brown and Harvard Universities and MGH utilised innovative fresh thinking, using highly advanced technologies. We congratulate the team and would like to see them bring their innovations to the market place as soon as possible to greatly assist the day to day quality of life of people living with ALS and, indeed, patients of many other conditions."

The winning team is working together to create wearable soft robotics that maintain the function of the arm and hand, and can be controlled entirely by a person's intention to move. The soft robotic system, already in development, can detect subtle movements – for example, the partial flexion of an index finger

The BrainGate+SoftRobotics team is creating a series of technologies such as this soft robotic glove intended to improve arm and hand function for people with ALS, muscle weakness and paralysis. The system, already in development, is designed to be worn so it can sense subtle movements and translate them into full actions. [PHOTOS COURTESY CERF/HARVARD BIODESIGN LAB]

– and pneumatically actuate a glove that quietly and smoothly completes the closing of the hand to grasp a coffee cup.

The research team is working to combine the soft robotic technology with the investigational BrainGate system, a tiny array of electrodes that can sense and decode signals from the brain's motor cortex. The team aims to use signals from the brain to drive the soft robotics, restoring people's ability to reach and grasp.

"On behalf of our BrainGate team, I'm so grateful to the Cullen Family for their visionary and engaged support of research to help people with ALS," said Dr. Hochberg. "Brain-computer interfaces, including the system being developed by our BrainGate consortium, hold tremendous potential to restore communication and mobility for people with paralysis."

Dr. Hochberg is a critical care and vascular neurologist and Director of the MGH Center for Neurotechnology and Neurorecovery; Professor of Engineering in the School of Engineering and Carney Institute for Brain Science at Brown University; Director of the Dept. of Veterans Affairs Rehabilitation Research and Development Center for Neurorestoration and Neurotechnology in Providence, and senior lecturer on Neurology at Harvard Medical School. He also directs the BrainGate clinical trials, conducted by a team of clinical and basic neuroscience and neuroengineering researchers from across the nation.

Soft robotics

"Soft robotics can quietly, smoothly and unobtrusively provide for either rehabilitation or restorative function for people with ALS, stroke or spinal cord injury," said Dr. Walsh, the Paul A. Maeder Professor of Engineering and Applied Sciences at the Harvard John A. Paulson School of Engineering and Applied Sciences. "Watching and listening to end users evaluate our soft robotic systems is incredibly inspiring. Their ideas and feedback continue to push the technology further and faster with an unyielding focus on developing portable systems that restore highest priority functions for people with tetraplegia. Our work with the BrainGate team is leading to a palette of coordinated technologies that will provide the right amount of assistance at the right moment for people with ALS."

Dr. Walsh is also an associate faculty member at the Wyss Institute for Biologically Inspired Engineering and an Adjunct Associate Professor in the Department of Physical Therapy & Athletic Training at Boston University. He is the is the founder of the Harvard Biodesign Lab, which brings together researchers from the engineering, industrial design, apparel, biomechanics, physical therapy and business communities to develop and translate new disruptive robotic technologies for augmenting and restoring human performance.

"Many of us in the ALS community are working to develop therapies that will slow down, stop, or even reverse the loss of neurons. As new medications are developed that prolong life, it is imperative to also develop tools that can improve patient's independence," said Dr. Paganoni. "Seeing people with tetraplegia type on a computer screen or move a limb, simply by thinking about those movements, is remarkable. These are critical steps on the path to truly restored function for people with ALS. We are grateful to all people living with paralysis who choose to participate in these ongoing clinical trials: it's only through their generous efforts that we can discover and develop such revolutionary technologies."

Dr. Paganoni is physician-scientist at the Healey & AMG Center for ALS in the Department of Neurology at Massachusetts General Hospital, Co-Director of the MGH Neurological Clinical Research Institute, and Assistant Professor of Physical Medicine and Rehabilitation at Spaulding Rehabilitation Hospital/Harvard Medical School focuses on clinical trials and therapy development for ALS. ❖

[*CAUTION: Investigational Device. Limited by Federal law to investigational use.*]

Lifespan, CNE withdraw merger application

Align not to enter into litigation with FTC ruling to block the merger

PROVIDENCE – The Board of Directors for both Lifespan and Care New England met separately last week and have decided not to pursue litigation on the matter, and will withdraw their Hospital Conversions Act application from the Rhode Island Dept. of Health (RIDOH).

This decision follows the Federal Trade Commission (FTC) announcement on February 17, 2022, that it intended to file suit to block the Lifespan and Care New England merger, citing competition concerns. Rhode Island Attorney General Peter Neronha joined the FTC in challenging the merger on that same day.

Both boards also voted not to pursue a legislative solution, such as a Certificate of Public Advantage (COPA). Additionally, the parties have terminated the Definitive Agreement which included an exclusivity clause.

A statement from the organizations said both continue to believe the combination of the systems would have greatly enhanced the clinical, academic and research missions, reduced costs and improved the patient care environment.

It further stated that both organizations are committed to partner in ways that are appropriate from a legal perspective, and allow them to best serve the needs of the community and that leadership is focused on figuring out, with its academic partner, Brown University, the best path forward for the community in terms of cost, quality and access to healthcare in an extremely challenging environment. ❖

RI first in US for percentage of population fully vaccinated

PROVIDENCE – Rhode Island is now ranked as the leading state in the nation for percentage of its population that is fully vaccinated against COVID-19 at 80%. Rhode Island also currently ranks 3rd in the nation for COVID-19 boosters at over 37%.

"Severe illness from COVID-19 is now largely preventable because of the primary series vaccines and booster doses that we have available," said Interim Director of Health **JAMES McDONALD, MD, MPH**. "The success of Rhode Island's vaccination campaign is a main reason why our hospitalization rate per case in January did not reach the levels that we saw at prior points in the pandemic. However, COVID-19 is still with us. It is critical that we all remain up to date with our COVID-19 vaccinations."

Since COVID-19 cases peaked most recently in early January, Rhode Island has seen a 94% decrease in case rates. Hospitalizations have decreased by 52% since their peak in mid-January. Rhode Island is tied for 3rd in the nation for vaccinations among children ages 5 to 11. ❖

CDC releases new reports on health, well-being of children during COVID-19

WASHINGTON, DC – On Feb. 18th, the Centers for Disease Control (CDC) released two new reports in *MMWR* that provide important insights on the health and well-being of children and adolescents during the COVID-19 pandemic.

The first report looked at pediatric emergency department visits. The study found that overall pediatric emergency department visits decreased in 2020, 2021, and in January 2022 compared with visits in 2019, while COVID-19-related emergency department visits increased across all pandemic years and among pediatric age groups.

There were also increases in the weekly number and proportion of emergency department visits for certain types of injuries, some chronic diseases, and visits related to behavioral health concerns, especially among older children (5–11 years) and adolescents (12–17 years). Factors affecting caregivers during the pandemic, including unavailable or unpredictable childcare, illness, financial hardship, and mental health concerns, might increase a child's vulnerabilities. Loss of a parent or caregiver, increases in other challenges, and disruptions in daily routine due to the COVID-19 pandemic might have also increased a child's behavioral health concerns and unhealthy coping behaviors.

Mental health conditions

The second report examined changes in pediatric emergency department visits for mental health conditions and found that adolescent girls (12–17 years) accounted for the largest increases in the number and proportion of emergency department visits for mental health conditions in 2020, 2021, and in January 2022 compared with 2019. Weekly visits for eating and tic disorders increased for females, and particularly adolescent females (12–17 years), during 2020, 2021, and in January 2022.

The highly complex nature of individual experiences makes it difficult to identify a single reason for changes in mental health conditions during the pandemic. While extended time at home could increase familial support for some youth, it may have increased challenges and stressors among others. These factors, as well as other pandemic-related stressors that impact families (e.g., increases in parental mental health problems, parental substance use, financial strain, and loss of a parent or caregiver), could have created or increased the risk for mental health conditions.

Early identification and expanded evidence-based prevention and intervention strategies are critical to improving children's mental health, especially among adolescent females who might have increased need. CDC recommends increased awareness for health concerns among children and adolescents that could arise due to delayed medical care and heightened emotional distress. ❖

Innovative treatment for GERD marks first for RI

Dr. Jordan Hebert is first surgeon in RI to perform LINX® procedure as a surgical treatment for chronic heartburn caused by GERD

WAKEFIELD – On Jan. 31st, **DR. JORDAN F. HEBERT** of South County Medical Group successfully completed the first LINX® procedure in Rhode Island on a patient who suffered from gastroesophageal reflux disease (GERD).

This innovative procedure uses a magnetic implant to assist the weakened valve that separates the esophagus from the stomach.

"Being the first surgeon in Rhode Island to perform this treatment was made possible by South County Health bringing the latest generation of diagnostic and therapeutic technology all under one roof," Dr. Hebert said. "This procedure is a real game changer for patients suffering from GERD."

To perform the procedure, Dr. Hebert used da Vinci XI robotic-assisted surgical technology, an advanced, minimally invasive technique designed to help the patient heal quickly with minimal discomfort.

Because the procedure does not require changes to the stomach anatomy, patients can resume their normal diet immediately after surgery.

Dr. Jordan Hebert holds the LINX device used to surgically treat GERD.

Other surgical options for severe GERD include a procedure called fundoplication, which alters the anatomy of the stomach. While this option is suitable for some patients, there are side effects associated with fundoplication that many patients find chronically bothersome.

"I always strive to offer my patients the best surgical care options available, and that is why I decided to introduce this procedure to Rhode Island," Dr. Hebert said. "Many of the side effects that patients report with a traditional fundoplication are avoided with LINX."

The safety and effectiveness of the LINX® implant are well documented in the medical community.

"While this is the first time LINX has been used in Rhode Island, this is actually a time-tested treatment with a long track record of excellent results throughout the United States. LINX has been FDA approved for a decade now," he said. ❖

Dr. Jordan Hebert (seated left) manipulates the robotic arms of the daVinci XI from a console in the operating room to implant the LINX device. [PHOTOS COURTESY SOUTH COUNTY HEALTH]

$10M gift from Reed Hastings, Patty Quillin to bolster 58-year-old Brown-Tougaloo Partnership

TOUGALOO, MISS., PROVIDENCE [TOUGALOO COLLEGE AND BROWN UNIVERSITY] – A $10 million gift from Netflix CEO **REED HASTINGS** and documentary film producer **PATTY QUILLIN** will provide a major boost in scholarship support for students at Tougaloo College, a historically Black college in Tougaloo, Mississippi.

The gift will fund much-needed financial aid for Tougaloo students working toward careers in medicine, public health, the sciences, education, business and other fields and aspiring to make a positive impact on their communities after graduation. It will also support Tougaloo students participating in a unique and enduring 58-year-old partnership between Brown and Tougaloo, which has connected generations of students, faculty and staff from both institutions through academic exchanges, fellowships, research projects and other initiatives.

Hastings and Quillin, a California-based couple who are longtime champions of equity in education, have supported Historically Black Colleges and Universities (HBCUs) with multiple gifts over time, driven by the outsize role that HBCUs play in educating Black leaders who make a positive impact in a wide range of professions.

"HBCUs have been vastly undervalued for a long time," Hastings and Quillin said. "They have an incredible track record of graduating so many Black leaders across the U.S. – doctors, lawyers, engineers and more. By investing in the extraordinary students who attend Tougaloo and Brown, we're investing in America's future."

Of the total gift, $5 million will go to Tougaloo College to bolster the school's endowment and provide annual scholarship funding that directly supports high-achieving students with high financial need. Hastings joined Tougaloo President Carmen J. Walters and other college leaders in a visit to the Mississippi campus on Monday, Feb. 21, that included the opportunity to meet with students and faculty members.

Walters said the funds will provide crucial need-based scholarships to deserving and talented undergraduates, including many who continue to contend with the economic impact of the COVID-19 pandemic.

"The remarkable personal gift to the historic Brown-Tougaloo Partnership from philanthropists Reed Hastings and Patricia Quillin will transform the lives of Tougaloo College students," Walters said. "This donation, setting a new precedent as the largest gift to the Brown-Tougaloo Partnership, is a living testimony to their strong belief in the *value* of giving, the *value* of education and the *value* of HBCUs. This transformative gift is a life-changing opportunity for our students, and the impact will be far-reaching."

Scholarship fund at Brown

The remaining $5 million will establish the Brown-Tougaloo Partnership Scholarship Fund as part of Brown University's endowment. The fund will provide annual support for Tougaloo students who come to Brown as part of the partnership, whether to pursue a graduate or medical degree or an academic exchange program.

"Brown and Tougaloo share a deeply held commitment to preparing graduates to make a positive impact in their communities," said Brown President **CHRISTINA H. PAXSON**. "Our shared ideals serve as an unbreakable foundation for a 58-year-old partnership that has yielded important insights for students and scholars, infused both campuses with new perspectives and provided life-changing experiences for Tougaloo and Brown students. This generous gift from Reed Hastings and Patty Quillin ensures that this truly one-of-a-kind partnership will continue to expand for many decades to come."

Building on an enduring partnership

The gift from Hastings and Quillin is the largest philanthropic commitment to the longstanding Brown-Tougaloo Partnership, which began in 1964 during the Civil Rights Movement.

Patty Quillin and Reed Hastings
[PHOTO: DREW ALITZER PHOTOGRAPHY]

That year, as Tougaloo College became a known refuge for activists and a central meeting point for movement organizers, the Mississippi State Legislature introduced bills to revoke Tougaloo's charter and prevent its graduates from becoming teachers in the state. A group of concerned Providence citizens with ties to Mississippi approached then-Brown President Barnaby Keeney and asked for help to support Tougaloo. Months later, the two institutions had drawn up an agreement that began with a student exchange program funded by the Rockefeller and Ford foundations.

Fifty-eight years later, the agreement has grown into a strong, multifaceted partnership offering opportunities for student and faculty academic exchanges and collaborative research ventures. Since its inception, more than 760 Tougaloo and Brown students and faculty have participated in the program. Undergraduate participants spend time learning on the respective campuses, faculty build

research collaborations, and Tougaloo graduates pursuing medical careers come to Brown's Warren Alpert Medical School through an early-identification program. Most recently, Brown's School of Public Health created a Health Equity Scholars program, which each year admits an exceptional cohort of master of public health students from Tougaloo and other HBCUs.

The new Brown-Tougaloo Partnership Scholarship Fund enabled by the gift will ensure that participating Tougaloo students have access to myriad academic and fellowship opportunities at Brown. With an estimated initial annual payout between $200,000 and $250,000 (a number expected to grow over time) the fund will have the capacity to support a range of Tougaloo students with costs ranging from tuition for pursuing graduate or medical studies at Brown to undergraduate semester exchange programs.

Carey Williams, a senior biology major from Lexington, a small, rural town in the Mississippi Delta, is one student who will pursue an MD at Brown after graduating from Tougaloo. As a sophomore, Williams was admitted to an early-identification program (EIP) at Brown's Warren Alpert Medical School.

"For as long as I can remember, I wanted to be a medical doctor, and I want to serve my community by providing health care in underserved communities," Williams said. "The program afforded me opportunities to study at Brown for a semester, meet and experience people of different cultures, and gain an invaluable structured introduction to the elements of rigor and expectations toward the world of medical school. This program opened doors for me that I did not know existed."

Williams will graduate from Tougaloo College in May 2022 before heading to Providence for medical school.

"The scholarship made possible by Reed Hastings and Patricia Quillin will give me the financial freedom to accomplish my educational goals at Brown," Williams said. "The EIP program has allowed me to become more confident than ever in my pursuit of a career in medicine. The Brown-Tougaloo Partnership has changed my life for the better."

"HBCUs empower Black students to achieve their dreams, and that is a great thing to bring attention to," Hastings said. "Investing in the long-term health of these colleges and universities will help ensure a diverse and inclusive future for workplaces around the country."

He added that Brown's commitment to engaging with Tougaloo in the early 1960s – a time when many predominantly white institutions across the country, educational and otherwise, were reluctant to embrace the tenets of racial equality – inspired him to support the two institutions' unique partnership.

"The partnership between Tougaloo and Brown fascinates me, because it is truly exceptional," Hastings said. "This relationship has enriched so many lives over the last six decades. We wanted to make sure this special bond continues to prosper and thrive so that future generations of Tougaloo and Brown students can keep sharing new perspectives and generating new ideas." ❖

Brown researchers awarded Foundation for Opioid Response grant

NEW YORK, NY – The Foundation for Opioid Response Efforts (FORE), a private 501(c)(3) national grant-making foundation focused on ending the nation's opioid crisis, announced 11 new grants totaling $4.8 million to support innovative solutions to some of the opioid crisis' most challenging problems.


Alexandra Collins, PhD


Rachel Wightman, MD

"We are launching our Innovation Program to generate and support new approaches to some of the long-standing barriers to making real progress in addressing the opioid crisis – how to better tackle stigma, generate more timely and actionable data, and help for people transitioning from treatment to long-term recovery," says FORE President Dr. Karen A. Scott. "These projects have great potential to give us exciting new tools and lessons that will help communities around the country respond to the crisis more effectively, inform future policy decisions, and ultimately save lives."

"FORE prioritizes projects that reach high-risk populations with patient-centered solutions and a commitment to health equity," said Dr. Andrea Barthwell, Chair of FORE's Board of Directors. "Our new Innovation Program continues to show our commitment to funding diverse projects that contribute solutions to the crisis at national, state, and community levels."

FORE's Innovation Program is funding projects that combine approaches from diverse fields and engage multi-disciplinary teams to encourage work on some of the crisis' most intractable challenges:

Among the new grantees in the **Timely and Actionable Data** category is Brown University:

Understanding Drug Use Within a Rapidly Changing Supply: An Ethnographic and Toxicologic Investigation to Improve Overdose Prevention and Supply Surveillance Communication.

Principal Investigators: **ALEXANDRA COLLINS, PhD**, and **RACHEL WIGHTMAN, MD**, $564,319.

RI graded 'B' for gun safety laws

Giffords Law Center's Annual Gun Law Scorecard grades and ranks all 50 states on their gun laws; in 2021, 24 states received an F.

WASHINGTON, DC – In 2021, a number of state legislatures took the threat of gun violence seriously and passed 75 new laws in 27 states and Washington DC. In the latest edition of the **Annual Gun Law Scorecard, Giffords Law Center to Prevent Gun Violence** graded and ranked each state on the strength of its gun laws, showing that states with stronger gun laws have lower gun death rates and save more lives.

Rhode Island received a B for its gun safety laws. In 2020, the last year for which data is available, 54 people died from firearm injuries in Rhode Island, representing a 12% increase in the gun death rate in the state over the previous year. This increase was primarily driven by increases in gun homicides. The number of gun homicides rose from 12 in 2019 to 22 in 2020. Gun suicides fell slightly in the state. From 2019 to 2020, the gun suicide rate decreased by 7%.

In 2021, Rhode Island prohibited concealed carry permit holders from carrying guns on K-12 school grounds and passed legislation to curb gun trafficking. In order to improve its grade, Rhode Island should enact a firearm relinquishment law, invest in community violence intervention programs, strengthen protections for victims of domestic violence and hate crimes, and prohibit assault weapons and large-capacity magazines.

- **Website**: Learn more about Rhode Island's ranking by visiting this year's Scorecard.
- **Fact Sheet:** The State of Gun Violence in Rhode Island.

States with the strongest gun laws have continued taking significant steps to protect their residents from gun violence, including:

- **California (A)**: Enacted a law to improve efforts to identify gun dealers who engage in gun trafficking, committed $76 million for local community violence intervention and prevention programming, and made it easier for people who survive domestic abuse to obtain firearm-prohibiting protective orders.
- **New Jersey (A)**: Committed $10 million in funding for local community violence intervention and prevention programming.
- **New York (A-)**: Passed a first-of-its-kind law that allows people to sue gun dealers and manufacturers when they fail to act responsibly and created a state firearm violence research institute.
- **Maryland (A-):** Enacted a law requiring background checks on long gun purchases and committed significant funding for local community violence intervention and prevention programing.

States with the lowest grades are most responsible for the troubling export of guns used for crimes in other states. These states also put their residents at risk by pushing dangerous policies like "Stand Your Ground," which allows people to shoot first and ask questions later, and permitless carry, which allows untrained, unvetted people to carry hidden, loaded guns in public. Some of the worst legislation passed in the last year includes:

- **Iowa (F)**: Repealed its law requiring background checks on private sales of firearms and allowed people to carry concealed guns in public without safety training or a background check.
- **Missouri (F)**: Made law enforcement officers and agencies, public officials, and private individuals personally liable in civil court and subject to a $50,000 fine for enforcing federal gun laws.
- **Montana (F)**: Passed a law allowing guns on the campuses of colleges and universities that was later declared unconstitutional.

Visit the Annual Gun Law Scorecard at gunlawscorecard.org

"2021 was yet another year of crisis for our country. Too many communities had to reckon with the trauma and pain of surging gun violence, armed hate, and racial discrimination – all in the midst of the ongoing pandemic," said Robyn Thomas, executive director of Giffords Law Center to Prevent Gun Violence. "What our Scorecard shows, year after year is that it is possible to take action to end this senseless violence. States with strong gun safety laws have fewer gun deaths – but illegal trafficking leaves residents of these states vulnerable. This progress must extend to every single state across the nation. We hope the Gun Law Scorecard will continue to serve as a resource for our elected officials who understand that getting a passing grade can be a matter of life and death." ❖

Paul Edward Farmer, MD, PhD, passes away in Rwanda

Dr. Paul Farmer helped found Partners In Health, which now collaborates with governments across 12 countries to bring quality health care to those most in need. [PHOTO: JOHN RA / PARTNERS IN HEALTH]

BOSTON – Partners In Health announced that its co-founder, **PAUL EDWARD FARMER, MD, PhD**, 62, unexpectedly passed away Feb. 21st in Rwanda from an acute cardiac event while he was sleeping. He is survived by his wife, Didi Bertrand Farmer, and their three children.

Dr. Farmer was Kolokotrones University Professor and chair of the Department of Global Health and Social Medicine at Harvard Medical School, chief of the Division of Global Health Equity at Brigham and Women's Hospital in Boston, and co-founder and chief strategist of Partners In Health.

Farmer was a renowned humanitarian who worked hand in hand with local governments and organizations around the world, including those in many rural and underserved communities, to establish partnerships to help build hospitals, train medical workers, and establish community clinics in remote, impoverished areas where residents would otherwise have had little hope of any kind of health care.

He was the chief strategist and co-founder, with Jim Yong Kim, Ophelia Dahl, and Todd McCormack, of the social and health organization Partners In Health. Farmer also served as the United Nations Special Adviser to the Secretary-General on Community-based Medicine and Lessons from Haiti, a country where he first worked as a volunteer while still an undergraduate and where he spent much of his life.

Nobel Peace Prize laureate Archbishop Desmond Tutu called Farmer "one of the great advocates for the poorest and sickest of our planet."

Infectious disease specialist

Born in 1959 in North Adams, Massachusetts, Farmer grew up in Florida with his parents and five siblings, living at times in a school bus converted into a mobile home and on a boat. He attended Duke University on a Benjamin N. Duke Scholarship and received his MD in 1988 and his PhD in 1990 from Harvard University.

He specialized in infectious diseases and was the author of more than 200 scientific papers.

Farmer began his life's work as a college volunteer in Haiti in 1983, working with dispossessed farmers in the country's Central Plateau, where he was struck by the level of care available to impoverished residents. There, he served for 10 years as medical director of L'Hôpital Bon Sauveur, a charity hospital.

Farmer once told an interviewer, "There is nothing I like more than building a hospital – that's what I call a good pastime....That inspires me."

Farmer's work has become a model for health care delivery in underresourced communities worldwide; it laid the groundwork for developing the science of global health delivery implementation.

In 1987, Farmer co-founded Partners In Health, the Boston-based international non-profit that provides direct health care services, leading research, and advocacy on behalf of those who are sick and living in poverty.

Under Farmer's leadership, Partners In Health built a hospital in Haiti after an earthquake rocked the country in 2010, fought multidrug-resistant tuberculosis in Peru and around the globe, assisted Liberia and Sierra Leone in tackling Ebola, worked to stop the Zika virus, and is still dedicated to battling emerging new health threats.

Farmer's work with Partners In Health was described in a 2003 book by Pulitzer Prize-winning author Tracy Kidder, *Mountains Beyond Mountains: The Quest of Dr. Paul Farmer, a Man Who Would Cure the World.*

The book followed Farmer from Harvard to Haiti, Peru, Cuba, and Russia, describing, among other things, how he exported treatment for multidrug-resistant tuberculosis from Haiti to Peru and then to Siberia, achieving cure rates comparable to those in the United States.

Because of Farmer's efforts, Haiti saw higher rates of vaccination and lower rates of infant mortality and malnourishment in areas where PIH was active.

Farmer's work with his colleagues has also been chronicled in the *Bulletin of the World Health Organization*, *The Lancet*, the *New England Journal of Medicine*, *Clinical Infectious Diseases*, and *Social Science and Medicine.*

Farmer wrote extensively on health, human rights, and the consequences of social inequality. His books include *AIDS and Accusation*, *Haiti after the Earthquake, Infections and Inequalities*, *To Repair the World: Paul Farmer Speaks to the Next Generation*, and *A Path Out of Poverty*. In addition, Farmer was co-editor of *Women, Poverty, and AIDS, The Global Impact of Drug-Resistant Tuberculosis,* and *Global Health in Times of Violence.*

Farmer was a recipient of numerous honors, including the Margaret Mead Award from the American Anthropological Association, the American Medical Association's Outstanding International Physician (Nathan Davis) Award, a John D. and Catherine T. MacArthur Foundation Fellowship and, with his PIH colleagues, the Hilton Humanitarian Prize. He was a member of the Institute of Medicine of the National Academy of Sciences and of the American Academy of Arts and Sciences.

Harvard Medical School is planning a community memorial gathering via Zoom and will share details as soon as they are confirmed. ❖

Appointments

Ramin Ronald Tabaddor, MD, named Chief of Orthopedics for Kent Hospital

WARWICK – **RAMIN RONALD TABADDOR, MD**, has been appointed Chief of Orthopedics at Kent Hospital.

Dr. Tabaddor has been a practicing orthopedic surgeon at Kent Hospital since 2015. He received his medical degree from Boston University, completed the Harvard University's combined orthopedic residency program, as well as a Sports Medicine Fellowship from the University of Minnesota. He is currently the Director of the Hip Preservation Institute for University Orthopedics, and the Head Orthopedic Team Physician for the University of Rhode Island Athletics. He has also been awarded the Dean's Excellence in Teaching Award from the Warren Alpert Medical School of Brown University each of the last three years ❖

Kwame Dapaah-Afriyie, MD, named Governor-elect of RIACP

PROVIDENCE – **KWAME DAPAAH-AFRIYIE, MD, MBA, FAC**, Director of Hospital Medicine at The Miriam Hospital, has been designated Governor-elect Designee of the Rhode Island Chapter of the American College of Physicians.

His appointment kicks off a year of training before he commences a four-year term as governor that begins in spring 2023.

Dr. Dapaah-Afriyie founded the hospitalist program at The Miriam Hospital in 1997 and was named director of its division of hospitalist medicine in 2004. He was instrumental in the establishment of the hospitalist program at Newport Hospital, a Lifespan affiliate. He is a Senior Fellow in the Society of Hospital Medicine.

He completed his residency at The Miriam Hospital and earned his medical degree from the University of Science/Technology in Ghana. He is a Professor of Medicine (Clinical Educator) at the Warren Alpert Medical School of Brown University. ❖

Recognition

HopeHealth achieves SAGECare Platinum credential for serving LGBT elders

PROVIDENCE – HopeHealth has earned the highest national credential for cultural competency in serving and supporting older adults who identify as lesbian, gay, bisexual or transgender (LGBT).

Last year, more than 80% of HopeHealth staff completed one hour of SAGECare training covering an overview of the needs, concerns and unique history of LGBT older adults and how to improve the quality of care provided to them. The curriculum was developed by SAGE, the country's oldest and largest LGBT advocacy and services organization.

Additionally, at least 80% of HopeHealth's leadership team completed four hours of SAGECare training. By meeting the 80% benchmark, HopeHealth achieved platinum status.

"We have always prioritized person-centered support and care," HopeHealth President & CEO **DIANA FRANCHITTO** said. "Now by partnering with SAGECare, we are demonstrating our strong commitment to providing the best care possible while making each patient feel comfortable being who they are."

The 80% training standard has symbolic importance because an estimated 80% of the general population rely on legal or blood-related family members for caregiving. But LGBT people are twice as likely to live alone and four times less likely to have children, which can increase their risk of social isolation as they age. Loneliness and isolation have been shown to be associated with poor physical and mental health.

LGBT older adults may face challenges in seeking and receiving adequate and inclusive care or aging-related social services due to the inability to rely on traditional family supports. As a 2021 SAGECare Platinum credentialed provider, HopeHealth staff now have the communication tools and information needed to create a culture of dignity and respect for all their patients and their relationships in older age. ❖

Obituary

HENRY G. MAGENDANTZ, MD, 85, of Butler Avenue, passed away peacefully with his loving family by his side on January 27, 2022 at HopeHealth Hulitar Hospice Center, Providence. He was the husband of Kathy Jellison and the late Ann (Rotch) Magendantz.

Dr. Magendantz was an obstetrician/gynecologist for the Rhode Island Group Health Association and Harvard Pilgrim Health. He would later work for OB/GYN Associates, Providence, before entering private practice. Dr. Magendantz was a fertility specialist and was involved in the delivery of more than 3,000 infants over the course of his long career. He served as an attending at Miriam Hospital, Rhode Island Hospital, and Women & Infants Hospital. He was also a Clinical Associate Professor of Obstetrics and Gynecology at the Warren Alpert Medical School of Brown University.

A graduate of Phillips Exeter Academy, Class of 1954, Dr. Magendantz earned his bachelor's degree from Harvard College, Class of 1958, and his MD from the Duke University School of Medicine, Class of 1962.

From 1968-1970, he was a U.S. Army Major serving in the Army Medical Corps at Fort Campbell, Kentucky.

A longtime member of Central Congregational Church, he served as a deacon, and was a member of numerous committees. In addition, he was a member of the Nature Conservancy, the Audubon Society, the American Fertility Society and the American Civil Liberties Union.

Besides his wife, he is survived by one daughter, Elisa Barton of London, England; three sons, Eric Magendantz of Winter Park, Florida, Christopher Magendantz of West Hartford, Connecticut and Nicholas Magendantz of Barrington; one sister, Margaret Magendantz, PhD, of Cambridge, Massachusetts; three daughters-in-law, Sheila Tekavec, Kristin Magendantz and Kimberly Magendantz; one son-in-law, Samuel Barton and nine grandchildren.

A celebration of his life will be held later this year at Central Congregational Church, Providence. Private burial will be in Swan Point Cemetery, Providence. In lieu of flowers, contributions in his memory to Planned Parenthood–R.I. Chapter, 175 Broad Street, Providence, R.I. 02903, or to NARAL, 1725 Eye Street NW, Suite 900, Washington, D.C. 20006 would be appreciated. For the online guest book, please visit www.bellowsfuneralchapel.com. The family would like to thank Miriam Hospital and Wingate Residences for their outstanding care. ❖