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# Non-convulsive Seizures Mimicking Creutzfeldt-Jakob Disease with Rapid Resolution and Recurrence of MRI Abnormalities

Kohei Hasebe MD; Ryota Sato MD; Leimomi Kanagusuku MD; Huidy Shu MD, PhD

## Abstract

An 88-year-old man presented with acute altered mental status. Brain magnetic resonance imaging (MRI) demonstrated “cortical ribboning,” which is classically associated with Creutzfeldt-Jakob disease. His rapid clinical improvement prompted a follow-up MRI three days after presentation, which showed resolution of the acute abnormal signals. The patient was eventually diagnosed with non-convulsive seizure. Five months later, he returned with a similar clinical presentation and MRI findings after self-discontinuation of anticonvulsant. It is important for clinicians to be aware that neurological changes associated with non-convulsive seizures can acutely mimic Creutzfeldt-Jakob disease, and to consider a short interval follow-up MRI for diagnostic challenges in acute settings.

## Keywords

Non-convulsive seizure, Creutzfeldt-Jakob disease, mimic, MRI, transient

## Abbreviations and Acronyms

CJD = Creutzfeldt-Jakob disease

CSF = cerebrospinal fluid

DWI = diffusion-weighted imaging

EEG = electroencephalogram

FLAIR = fluid-attenuated inversion recovery

MRI = magnetic resonance imaging

RT-QuIC = real-time quaking-induced conversion assay

sCJD = sporadic Creutzfeldt-Jakob disease

SITMA = seizure-induced transient MRI abnormalities

## Introduction

Creutzfeldt-Jakob disease (CJD) is a non-curable, rapidly progressive neurodegenerative disease for which MRI may assist in the diagnosis. Non-convulsive seizure epilepticus refers to prolonged seizures that may manifest primarily as an impaired level of consciousness or behavioral changes rather than movements of extremities. A variety of conditions are reported as CJD mimics, including seizure-induced transient MRI abnormalities (SITMA). SITMA may pose particular clinical challenges in cases where the clinical history is unhelpful or unavailable. This paper discusses a patient who presented with convincing CJD-like symptoms, who clinically and radiographically improved over 3 days, and experienced a recurrent episode with clinical symptoms and MRI abnormalities 5 months later.

## Case Report

An 88-year-old man presented to the emergency department with acute confusion, altered vision, and gait instability. He

had a past medical history of non-Hodgkin’s lymphoma in remission, right posterior parietal meningioma, and progressive memory loss over a few years with rapid deterioration over a few months. The patient’s proxy reported that he woke up at 3 am on the day of admission complaining of lightheadedness. He woke up again at 5 am exhibiting confusion, repeatedly dropping and picking up an object on the floor, and inability to leave his bathroom. Additionally, he complained that his vision was altered.

In the emergency department, he was not in acute distress, with a body temperature of 36.6 °C, heart rate 59 beats/min, blood pressure 146/72 mmHg, respiratory rate 13/min, and oxygen saturation 99% on room air. He was alert and oriented to person and place, but not to time. Neurological exam revealed impaired attention span and concentration, left visuospatial neglect, and mildly increased muscle tone throughout. There was no obvious myoclonus. The remainder of the neurological exam was unremarkable.

Laboratory studies revealed a white blood cell count of 7,600 / $\mu$ L with 76% neutrophils. His hemoglobin was 10.7 g/dL and platelets were 242,000 / $\mu$ L. Electrolyte, liver, and renal panels were unremarkable. Urinalysis had no major findings. MRI of the brain without contrast demonstrated diffusion-weighted imaging (DWI) lesions in the posterior right thalamus extending in the right hypothalamic region and right parietal-occipital-temporal and occipital lobes with cortical ribboning, in addition to an unchanged 3.2 cm right posterior parietal extra-axial mass, consistent with meningioma (Figure 1). Meanwhile, T2 fluid-attenuated inversion recovery (FLAIR) remained without acute changes as seen on DWI (Figure 2).

Given the scant history and characteristic findings on MRI, CJD and encephalitis were considered in the differential diagnosis. The patient was admitted for further investigation including: extensive laboratory testing (Vitamin B12, methylmalonic acid, folate, thyroid stimulating hormone, ammonia, erythrocyte sedimentation rate, C-reactive protein, lactic dehydrogenase, HIV antibody/antigen, rapid plasma reagin (RPR), paraneoplastic autoantibody panel, cerebrospinal fluid (CSF) analysis (cell count, protein, glucose, bacterial culture and gram stain, herpes simplex virus 1 and 2 PCR, venereal disease research laboratory test (VDRL), 14-3-3 protein, real-time quaking-induced conversion (RT-QuIC) assay), electroencephalogram (EEG), and repeat brain MRI.

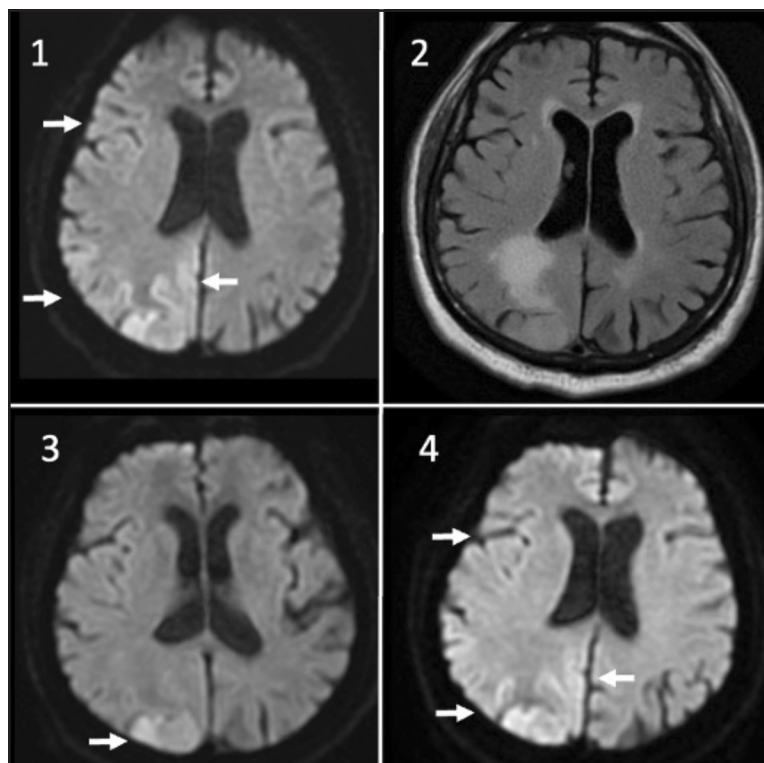


On the second day of admission, the patient began to clinically improve. Upon neurological exam, he was alert and oriented to person, place, and time. He still exhibited mild visuospatial neglect on the left, as well as ideomotor apraxia, which was not evaluated on admission. Additional work up was unremarkable, except for CSF total protein 91 mg/dL, ESR 75 mm/hr, and ammonia 88  $\mu\text{mol/L}$ . EEG revealed diffuse slowing, with focal slowing over the right parietal area. CJD, autoimmune encephalitis, and non-convulsive seizures with prolonged post-ictal state remained as differential diagnoses.

On the third day, the patient reported improvements of his subjective symptoms. He remained alert and fully oriented. His ideomotor apraxia and left-sided visuospatial neglect had completely resolved. Ammonia level was normalized to 29  $\mu\text{mol/L}$ . This clinical improvement argued against a diagnosis of CJD. On the fourth day, repeat brain MRI with and without

contrast demonstrated near-complete resolution of the right thalamic and right parietal-occipital-temporal cortical lesions, suggesting SITMA (Figure 3). All of the other tests returned normal, including the RT-QuIC. Based on the resolution of the MRI abnormalities, the diagnosis of SITMA was established. The patient was discharged with newly started lacosamide, an anti-epileptic medication, to prevent subclinical seizures thought to be provoked by his meningioma, which he subsequently self-discontinued due to insomnia.

Five months later, the patient returned with left-sided neglect, left-sided weakness, and acute confusion. MRI (Figure 4) and EEG were similar to the previous findings. The patient was discharged home on second day of admission with levetiracetam, a different anti-epileptic medication. Since the discharge, the patient has not had any recurrence of seizures.



**Figure 1.** MRI DWI at presentation with altered mental status, showing cortical restricted diffusion in the right parietal-temporal-occipital lobes (arrows).  
**Figure 2.** T2 FLAIR at presentation, showing unremarkable changes in the right parietal-temporal-occipital lobes.  
**Figure 3.** MRI DWI on day 3 of admission, showing near-complete resolution of right cortical restricted diffusion. Please note the unchanged 3.2 cm right posterior parietal extra-axial meningioma (arrow).  
**Figure 4.** MRI DWI after 5 months during another episode of altered mental status, showing recurrent restricted diffusion in the right parietal-temporal-occipital lobes (arrows).

## Discussion

CJD most commonly presents as a rapidly progressive dementia. Sporadic CJD (sCJD) accounts for 90% of human Prion diseases. Diagnostic criteria for probable sCJD proposed by the US Centers for Disease Control and Prevention (CDC) includes the following:<sup>1</sup>

(A) neuropsychiatric disorder plus positive RT-QuIC in CSF or other tissues, or (B) rapidly progressive dementia and at least 2 of the following 4 clinical features: myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, or akinetic mutism, with supportive findings on at least one of the following tests: typical EEG finding (eg, periodic sharp wave complexes), positive 14-3-3 CSF assay with a disease duration of less than two years, or an MRI showing hyperintensity in caudate/putamen or at least two cortical regions (temporal, parietal, and occipital) on DWI or FLAIR. There are reports of many conditions that can mimic CJD, such as encephalitis, hepatic failure, thyroid dysfunction, and the CNS manifestation of autoimmune disorders (eg, lupus, Sjögren syndrome, Hashimoto encephalitis).<sup>2-4</sup>

In the present case, declining memory with rapid deterioration, visual disturbance, increased muscle tone, and MRI abnormalities with ribboning on DWI were consistent with the diagnostic criteria of probable sCJD. Although seizure is rare in CJD, prior case studies have reported seizures and several cases of non-convulsive status epilepticus, as an initial manifestation.<sup>5</sup> Abnormal labs were retrospectively thought to be non-specific seizure-related changes, as elevated CSF protein, ammonia, and inflammatory changes have been reported with seizure activity.<sup>6-8</sup> Ammonia level improved to 29  $\mu\text{mol/L}$  in two days spontaneously, while other liver function tests remained normal. CJD was ruled out by hospital day 4 given clinical improvement without treatment, unremarkable labs, non-specific EEG, and resolution of MRI findings.

Seizure-induced transient MRI abnormality (SITMA) of the brain was first reported in 1987 by Kramer et al,<sup>9</sup> though the specific pathophysiology has remained elusive. Incidence of seizure-induced MRI abnormalities provoked by status epilepticus, a severe form of seizure, widely varies from 11.6% to 100% in the literature.<sup>10-11</sup> The recovery from SITMA also ranges from complete recovery, partial recovery, to persistent changes.<sup>12</sup> It is important to be aware that seizures can cause acute MRI changes, which often complicate clinical decision making.

In the present case, the SITMA closely approximated the typical MRI findings seen in CJD. However, the recovery in 3 days is more rapid than previously reported in the literature. Cianfoni et al reported reversibility of seizure-induced brain-MRI abnormalities between 15 and 150 days (average, 62 days) in an observation of 26 patients.<sup>13</sup> Yaffe et al reported a case of

normalized MRI in 5 days.<sup>14</sup> In addition, the SITMA mimicking CJD reappeared in 5 months, when the patient developed another episode of altered mental status. Although there are some reports of recurrence of seizure-induced MRI abnormalities,<sup>14-15</sup> it is not commonly documented in the literature. The patient's condition was thought to be postictal confusion after an unwitnessed non-convulsive seizure, given the focal slowing noted without epileptiform activity on EEG. Thus, it is important to consider a short interval follow-up MRI to avoid diagnostic ambiguity.

In conclusion, we report a case of a non-convulsive seizure mimicking CJD with a rapid SITMA recovery in 3 days and recurrence in 5 months. It is important for clinicians to be aware that confusion associated with non-convulsive seizures can acutely mimic CJD, and to consider a short interval follow-up MRI for diagnostic challenges in acute settings.

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# Trends in Hawai'i Ophthalmologists' Recommendations to Patients for Prevention of Age-Related Macular Degeneration

Kevin R. Card BS; Jamie Golez BS; Malcolm R. Ing MD

## Abstract

*The purpose of this study is to determine the current trends in recommendations made to patients by ophthalmologists in Hawai'i regarding the prevention of age-related macular degeneration (AMD) and to compare these recommendations to preventative therapies described in the literature. A review of the literature was done to determine the preventative interventions that can be made to significantly lower the risk of developing AMD. An anonymous survey was sent to 95 ophthalmologists in clinical practice in Hawai'i in 2020. The survey assessed recommendations for the prevention of age-related macular degeneration. The 4 interventions assessed were avoidance of smoking, utilization of antioxidant vitamins called AREDS2, adherence to a Mediterranean diet, and maintaining a normal body mass index (BMI). Responses were received from 41 ophthalmologists. Overall, 100% of participants responded "yes" to recommending smoking cessation to their patients, 76% of participants recommended AREDS 2, 42% recommended a Mediterranean diet, and 37% of participants recommended maintaining a normal BMI. Smoking cessation or avoidance was universally recommended by the respondents, and 22% recommended all the assessed interventions. The survey results suggest that some interventions, such as maintaining a normal BMI and adopting a Mediterranean diet are not as widely implemented into ophthalmologists' recommendations compared to others, such as AREDS2 formulation vitamins and smoking cessation.*

## Keywords

*Age-related macular degeneration; Patient education; Preventative medicine; Blindness prevention*

## Abbreviations

*AMD = age-related macular degeneration  
aMEDi = alternative Mediterranean Diet Score  
Anti-VEGF = anti-vascular endothelial growth factor  
AREDS 2 = Age-related Eye Disease Study  
BMI = body mass index  
CME = continuing medical education*

## Introduction

Age-related macular degeneration (AMD) is a leading cause of visual loss in those over 65 years of age in the industrialized world.<sup>1</sup> AMD is characterized by a slow, degenerative process involving the retina. More advanced stages typically progress to neovascular disease (neovascular AMD) or atrophy of retinal tissues and the choriocapillaris (geographic atrophy). Neovascular, or wet, AMD occurs as a result of inappropriate neovascular changes, or growth of abnormal blood vessels, in the choroid of the retina, which is the area between the retina and the sclera. When vasculature grows in a disorganized

fashion and penetrates the innermost membrane, called Bruch's membrane, it can lead to leaking, hemorrhage, and potential scarring.<sup>2</sup> Dry AMD, or geographic atrophy in its advanced form, occurs as a result of a thickening of the Bruch's membrane. This is usually due to oxidative changes and deposits of lipids or proteins called drusen. This eventually causes atrophic changes to the choriocapillaris, retinal pigmented epithelium, and the photoreceptors.<sup>2</sup> AMD overwhelmingly affects the aging population, with age being the most significant risk factor for its development. One pooled analysis showed that less than 1.3% of patients with AMD were under 65 years old.<sup>3</sup> Other risk factors include smoking, obesity, and race, with AMD most often occurring in White populations. It is expected that this disease will affect higher proportions of people in Hawai'i as the percentage of those over 65 continues to grow. Hawai'i adults over 65 increased by 37.6% between 2010 and 2019, with an annual average increase of 3.5%.<sup>4</sup>

A definitive drug treatment has not been developed for dry macular degeneration. Wet AMD is primarily treated with regular intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) to decrease the rate of neovascularization. This treatment, however, requires persistent and repeated doses and is not curative. One major emphasis in ophthalmologists' practice has been on methods to prevent or mitigate the development of AMD. Several preventative measures to mitigate risk factors have been shown to oppose the development of AMD, including smoking cessation, maintaining a normal body mass index (BMI), Age-related Eye Disease Study (AREDS) 2 vitamin supplementation, and consuming a Mediterranean diet.<sup>5-14</sup> The established significance of these interventions can be used to help prevent and slow the progression to advanced AMD for patients.

The link between smoking and AMD was established by the Rotterdam Study in 1996.<sup>5</sup> This cross-sectional study of 6174 patients aged 55 years or older found a significant increased risk of AMD in both current smokers and former smokers compared to non-smokers, particularly of the neovascular form. The relative risk was found to be highest in those with 10 or more pack-years (relative risk, 6.5; 95% confidence interval, 2.9-14.8). Correcting for atherosclerosis status did not impact the analyses, and a significant relative risk was not found when assessing patients 85 years of age or older.

Nutritional supplements (including vitamin C, vitamin E, zinc, copper, and beta carotene) were found to be helpful in prevent-

ing the progression of AMD from moderate to severe disease.<sup>6,7</sup> Progression prevention was shown in 25% of participants in the first AREDS study in 1993. In the second AREDS study, completed in 2007, the modification of the AREDS formula included the addition of lutein and zeaxanthin. Lutein and zeaxanthin are carotenoids, which have been shown to mitigate oxidative stress in the body and have also been shown to mitigate progression to advanced AMD.<sup>8,9</sup> Carotenoid antioxidant effects on the retinal pigment epithelium have been reported in studies such as Carotenoids in Age-Related Eye Disease (CAREDS) and the Pathologies Oculaires Liees - a l'Age (POLA) study.<sup>8,9</sup>

The association between BMI and AMD was established by Seddon et al in 2003 and further strengthened by Clemons et al in 2005.<sup>10-12</sup> Seddon et al performed a cohort study including 261 patients, which identified a statistically significant relationship between increased BMI and risk for progression to advanced AMD (relative risk, 2.35, 95% confidence interval [CI], 1.27-4.34) for BMI 30 or greater, and 2.32 (95% CI, 1.32-4.07) for BMI of 25-29).<sup>11</sup> The latter study, performed by Clemons et al, further identified from a cohort of 4757, a statistically significant increased risk for development of central geographic atrophy in obese patients compared to non-obese (odds ratio, 1.93, 95% CI 1.25-2.65).<sup>12</sup>

Merle et al established the association between a Mediterranean diet and reduced incidence of AMD in 2015.<sup>13</sup> The authors developed the alternative Mediterranean Diet Score (aMeDi), which is scored from 0-9 based on reported data from each patient on how often and in what quantities they consumed certain foods. This study included 2525 patients in the analysis. The assessment measured the intake of vegetables, fruit, legumes, whole grains, nuts, fish, red and processed meats, alcohol, and the ratio of monounsaturated to saturated fats. After adjusting for demographic, behavioral, ocular, and genetic covariates, a high aMeDi score (6-9) was significantly associated with a hazard ratio of 0.74 (95% CI, 0.61-0.91), suggesting that adherence to a Mediterranean diet lowers the risk of progression to advanced AMD.<sup>13</sup> Furthermore, Chapman et al performed a systematic literature review, which included 18 randomized control trials and observational studies.<sup>14</sup> The review showed a reduction in progression to advanced stages of AMD via adherence to a Mediterranean diet as a whole, as well as a slowed progression associated with increased intake of select micro and macronutrients. This study included quantitative analysis of nutrients that have been shown to decrease the risk of progression to advanced AMD: fatty acids, carotenoids, beta-carotene, lutein and zeaxanthin, zinc, vitamin D, and vitamin C. The study also reported that increased red meat consumption was associated with an increased risk of progression to advanced AMD. Overall, this review showed that both adherence to a Mediterranean diet as well as increasing intake of some of the individual components of the diet (such as fish oils, carotenoids) and limiting intake of red meat consumption and alcohol consumption can benefit AMD patients through a potential slowing of the progression of their disease.

Although significant associations between AMD and the aforementioned preventative measures have been reported and cited in the literature, it is not known if this information has extended into clinical practice. As of now, there is no protocol for integrating new preventative recommendations into clinical practice and communicating them to patients. There is also no standard of practice involving AMD prevention. This study aims to determine the extent to which of these recommendations is used in clinical practice, using a survey of practicing ophthalmologists in Hawai'i.

## Methods

A list of 95 ophthalmologists was provided by the Hawai'i Ophthalmological Society, from the state registration of all ophthalmologists in clinical practice in the state. All 95 ophthalmologists who are currently practicing in Hawai'i were sent an anonymous clinical question through [www.surveymonkey.com](http://www.surveymonkey.com) (SurveyMonkey®, San Mateo, California), a website-based survey tool. Two follow-up emails with links to the survey were sent over the following 6 weeks to those who did not initially respond. When the survey closed, 41 ophthalmologists completed the survey (43% response rate). This study was not advertised as eligible participants were identified prior to recruitment and emailed directly. No reward or incentive was offered for participating.

To assess the types of recommendations made to patients to prevent AMD, ophthalmologists were asked a single question: "When encountering a patient who is interested in preventing AMD or seeking to slow the progression of early AMD, do you...? (select all that apply)". The question answer choices included the 4 interventions shown to aid in preventing AMD: smoking cessation or avoidance, recommendation of taking AREDS 2, adherence to a Mediterranean diet, and maintaining a normal BMI. Delivery of this clinical question and collection of responses from enrolled participants took place over 6 weeks between October and November 2019.

The Mediterranean diet was defined as an increased consumption of vegetables, legumes, fruit, whole grains, and fish; decreased consumption of red meat; and drinking alcohol in moderation (wine limited to 1-2 glasses per day, consumed with meals). The definition of the Mediterranean diet was created based on the components in common between 3 studies which concluded that consuming a Mediterranean diet impacts the reduction in onset of AMD.<sup>13-15</sup> Although sunlight exposure has been linked to the development of early AMD, the literature suggests that the recommendation of wearing sunglasses has shown marginal preventative effect, so this was not included as an option in the clinical question.<sup>16</sup>

The number of responses per category and the different combinations of recommendations reported were collected and analyzed. The data analysis was tabulated using Microsoft® Excel® (Version 16.53, Microsoft Corporation, Redmond,



Washington). This study was reviewed and approved as exempt by the University of Hawai'i Human Studies Program Institutional Review Board (Honolulu, Hawai'i).

## Results

Of the 41 participants, 100% reported recommending smoking cessation to their patients. Three-quarters (76%) of participants reported recommending AREDS 2. However, only 42% (n=17) of participants reported recommending a Mediterranean diet, and 37% (n=15) reported recommending maintaining a normal BMI. Of the participants, 22% (n=9) answered recommending all 4 interventions (Table 1), while 24% (n=10) answered recommending 3 of the 4 recommendations, 39% (n=16) answered recommending 2 of the 4 interventions, and 15% (n=6) answered recommending only 1 of the 4 interventions. All participants reported recommending at least one of the 4 interventions.

## Discussion

Although significant associations have been made between multiple risk factors and the pathogenesis of AMD, the clinical impact of the data varies. These risk factors and interventions may be disproportionately communicated to patients by ophthalmologists when discussing prevention or mitigation of AMD. The differences in responses could be due to the length of time since the establishment of each risk factor publication. Smoking cessation and the utilization of AREDS 2 are relatively older recommendations, which may be more commonly known and discussed between patient and physician.<sup>5-9</sup> The risk factor of increased BMI and the incorporation of a Mediterranean diet to prevent AMD have been reported in more recent studies.<sup>10-15</sup> The lower percentage of ophthalmologists recommending these latter mitigation factors may suggest a delay between information available in the literature and the incorporation of this data into recommendations made to patients. This indicates that preventative action made by the ophthalmologists in Hawai'i has an opportunity for improvement and refinement in the face of an aging population. A standardized method of delivery of preventative information to patients with risk factors could be developed to mitigate the discrepancies in clinical recommendations. Additionally, establishing forms of continuing medical education (CME) for preventative information that enters into the literature could improve the impact on groups of clinicians and subsequently to their patients. Finally, this information may also serve to motivate clinicians and health care professionals outside the field of ophthalmology to arm themselves with potential preventative interventional advice. This would benefit patients with risk factors in cases where they may not have an ophthalmologist and would not otherwise receive this information. It is important to consider that differences in preventative recommendations by specialists, such as those elucidated in this study, may be present within other specialties as well, which may be explored in other studies.

Table 1. AMD Prevention Recommendation Survey Outcomes (N=41)

Recommendation	Participants reporting this recommendation n (%)
Smoking Cessation	41 (100)
Antioxidant AREDS 2	31 (76)
Mediterranean Diet	17 (41)
Maintaining a normal BMI	15 (37)
All of the above	9 (22)

Notably, another potential reason for the observed disproportion in physician-patient recommendations could be the case-by-case differences in relevance of risk factors, as not every patient will be equal regarding smoking status or BMI. Physician recommendations are tailored to each patient based on an array of clinical insights and experiences, and some will be more relevant than others in each case. Broadening the scope of preventative recommendations may prove beneficial as some of the preventative measures such as the Mediterranean diet and AREDS2 have similar preventative effects despite being recommended in unequal proportions (42% vs 76% respectively). Future iterations and follow up of this study could take into consideration the number of years that each clinician who participated in the survey has been in practice. This could highlight any potential differences in rates of recommending interventions that are more recently available in the literature in comparison to number of years in practice.

## Limitations

Potential limitations of this study include a limited sample size of practicing ophthalmologists in Hawai'i. Also, not every ophthalmologist who received the invitation for the survey responded, so the sample size was lower than the actual statewide population. The survey relied on self-reporting, therefore, recall bias is a potential variable in the results. Finally, the survey issued to participants did not include an option to list other recommendations than those already listed in the survey. This creates some bias towards the 4 interventions included in the survey and potentially underreports what physicians recommend to patients in practice.

## Conclusion

All 4 of the interventions included in this study have shown with statistical significance to aid in preventing or mitigating advancement of AMD. However, only 22% of the ophthalmologists surveyed reported to include all of these interventions when counseling their patients on prevention. Ophthalmologists may be able to help patients secure a better outcome by including all the information of the known risk factors in their recommendations to patients seeking to be proactive about their



ocular health. Therefore, it is important for ophthalmologists as well as other clinicians to practice all preventative measures that have shown to be effective. In doing so, patients would have the best chance at staying up-to-date and informed of the possible ways of improving their own health outcomes.

Moving forward, presentation of these preventative measures and the data that support them may be delivered at ophthalmologic meetings and conferences. This would improve immediate appreciation of new data by clinicians. Thereafter, a standardized protocol for delivering preventative interventional recommendations or establishing CME credits with emphasis on preventative measures in the literature could improve the impact into clinical practice in Hawai'i. Pursuing these avenues and continuing to develop ways to improve and broaden the preventative recommendations given to patients by ophthalmologists in Hawai'i would likely serve to decrease the long-term incidence of this common cause of vision loss in the elderly, especially crucial in the aging population.

### Conflict of Interest

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# Recurrent Tibial Periostitis Due to Blunt Trauma

Morgan Hasegawa MD; Dylan Singh BS; Nicholas Yim BA; F. Don Parsa MD

## Abstract

*Periostitis is characterized by periosteal inflammation surrounding tubular bones. The pathophysiology is now considered to be multifactorial and a spectrum of disorders, recently being redefined as medial tibial stress syndrome (MTSS). Current treatment modalities include preventative and conservative measures, such as activity modification and footwear alterations. There is a paucity of literature for more invasive treatments, such as steroid injections. In conflict with the currently available limited literature, this study reports a case of recurrent tibial periostitis due to blunt trauma treated with steroid injections resulting in symptom resolution and no adverse events. While this case may suggest a therapeutic role for steroids in the treatment of MTSS from blunt trauma, it also highlights the need for additional studies to elucidate the safety profile and therapeutic efficacy of steroid injections.*

## Keywords

*Periostitis, Medial Tibial Stress Syndrome, Trauma, Steroid Injections*

## Introduction

Periostitis, also known as periostalgia, is a condition characterized by inflammation of the periosteum around tubular bones, most commonly affecting the hands and feet.<sup>1</sup> In the tibia, it is colloquially known as shin splints or medial tibial stress syndrome (MTSS) and has traditionally been treated with anti-inflammatories and activity modification.<sup>2</sup> The pathophysiology is considered multifactorial. Recent studies have suggested a spectrum of injuries including muscle imbalance, abnormal tibial loading, and chronic repeated stress all contribute to a pathology now known as medial tibial stress syndrome.<sup>2</sup> A majority of the literature is solely based on expert opinion. The paucity of randomized controlled trials (RCTs) along with the lack of quality in existing RCTs suggest that high quality research is needed. Current treatment modalities are centered around preventative measures, such as footwear and activity modification. Even in refractory cases, treatment regimens remain limited and are primarily targeted towards symptom management.<sup>3</sup> Rest, ice, elevation, compression, non-steroidal anti-inflammatories, massage therapy, dry needling, and various other techniques have been described for acute treatment.<sup>4-9</sup> Beyond the acute phase, therapies include splinting, bracing, crutches, shockwave, and physiotherapy with proprioceptive training.<sup>6,7,10</sup> Surgery is reserved for recalcitrant cases and may include posterior fasciotomy, procedures to address the tibial bone surface, and tibial nailing for stress fractures.<sup>11</sup>

The role of steroids for treatment of MTSS has been described in the literature, though with a limited examination into effective-

ness, safety profile, and adverse effects. One study described the role of steroid treatment in a case series of 2 patients who were treated with steroids for recalcitrant MTSS. Neither patient had resolution of symptoms and both developed fat and muscle atrophy and hyperpigmentation. The authors recommended avoiding steroid use for MTSS, even in recalcitrant cases.<sup>12,13</sup>

This study presents a case of traumatic periostitis refractory to conservative treatment, with subsequent improvement of symptoms after a series of steroid injections. To the authors knowledge, no such case of traumatic periostitis refractory to conservative measures has been reported in the literature. The patient's periostitis seemed to respond differently than what is described in the existing, albeit limited, literature on steroid use in periostitis and MTSS.

## Case Report

A 58-year-old healthy male sustained blunt trauma to the distal medial aspect of his left tibia after a heavy object, weighing about 45 kilograms, fell onto his leg from a height of approximately 0.6 meters. The patient had no history of previous blunt trauma and no physical activity including exertion, running, or hiking as the patient led a sedentary lifestyle. He had no systemic symptoms in his initial presentation, denying fever, chills, local site infection, or recent illness. His past medical history was only significant for a bilateral hernia repair in the past and he was on no medications. Initial physical exam showed erythema, edema, faint ecchymosis, and tenderness to the distal medial tibia above the malleolus in an area measuring 12 by 5 centimeters. The patient was diagnosed with periostitis due to blunt trauma. Treatment revolved around conservative management with ice, elevation, and compression. Pharmacotherapy included celecoxib 400 mg initially followed by daily 200 mg for 10 days. Pain, erythema, and local tenderness gradually subsided over a period of 4 weeks. The edema diminished gradually in about 5-6 weeks.

A second episode of pain, swelling, and erythema subsequently occurred approximately 1 year later. The patient presented with similar symptoms and findings at the same location with no further history of trauma or exertion to the affected area. On physical exam, there was noted pain, redness, edema, and tenderness over the distal medial tibia. The patient was treated similarly with ice, compression, leg elevation and the same regimen of celecoxib as previously prescribed. The pain, local tenderness, and redness subsided within 3 weeks. The edema lasted about 5 weeks.

A third episode occurred about 6 months later. He presented with similar symptoms and findings of erythema, pain and tenderness in the same location (Figure 1). As in his previous recurrence, there was no history of repeated trauma or exertion to the affected area. Due to recurrence and symptoms refractory to traditional treatment regimens including ice, anti-inflammatories and activity modification, a decision was made to expand treatment modalities, including the use of steroid based therapy. One mL of a triamcinolone 10 mg/mL suspension was diluted with 5 mL of a lidocaine 1% with 1:100,000 epinephrine solution and was injected immediately above the periosteum in the affected area at 5 different sites approximately 2 cm apart. A 30 gauge needle was used with direct bone contact during injection to minimize infiltration into subcutaneous fat and to avoid skin and subcutaneous soft tissue atrophy (Figure 2). The injected deposits were massaged over the entire area of affected periosteum. An elastic bandage was applied over the leg and the patient was encouraged to elevate the leg when not ambulating. No other activity or weight bearing restrictions were recommended at that time. Erythema, pain, and tenderness subsided

3 days after the triamcinolone injection but the edema did not subside until 10 days after injection (Figures 3 and 4). The patient reported that the pain, erythema, tenderness and edema of the recovery period was significantly reduced compared to previous conservative treatments.

There were 3 more recurrences, with identical signs and symptoms as the time of his initial injury, over the next 2 years. All of these recurrences were treated with the same steroid injections and the patient responded with symptom resolution after each treatment.

Since his last treatment approximately 6 years prior to the time of this writing, the patient has not had recurrence of symptoms and reports total resolution of edema, erythema, and pain to his medial distal tibia. At no time after steroid injections did the patient suffer adverse effects including skin or muscle atrophy, hypopigmentation, erythema, nerve injury, or injection site soreness.



Figure 1. Left medial distal leg at 24 hours after occurrence of pain, redness and tenderness.



Figure 2. Technique of injection with deposit of 1 mL of triamcinolone lidocaine combination directly on top of the periosteum with 30-gauge needle.





Figure 3. Three days after triamcinolone injection. Erythema has subsided. Edema is still present.



Figure 4. Seven days after triamcinolone injection: skin pinch shows absence of edema.

## Discussion

To the authors' knowledge and literature review on the topic, there have not been similarly reported cases of recurrent tibial periostitis due to blunt trauma successfully treated with steroid injections. In a case series by Loopik et al, 2 patients without acute history of trauma to their tibias developed MTSS. The first patient was an 18-year old female who developed MTSS over her tibia with a remote history of prior trauma. She received 3 local injections of in total 1ml Kenalog and 3ml lidocaine 2%, with limited relief of pain and subsequent development of hypopigmentation and fat atrophy surrounding the injection sites. The patient also experienced refractory pain requiring surgical treatment including fasciotomy and posterior tibialis release. The second case was a 22-year old female who also developed MTSS without acute trauma. She received 2 injections of in total 1ml Kenalog, 40 mg/ml and 3ml lidocaine 2%, with minimal pain relief and subsequent fat atrophy and skin hypopigmentation surrounding the injection sites. Their pain associated with MTSS improved after injections, but was never fully alleviated. Both patients underwent lipofilling in the sites of fat atrophy by a plastic surgeon.<sup>14</sup> Ultimately, the minimal pain relief, refractory pain requiring surgical intervention, and adverse effects of the injections led the authors recommending against steroid use in the treatment of MTSS. Likewise, Park et al reported a case in which a 46-year old female developed fat atrophy, hypopigmentation, muscle atrophy, and possibly nerve injury after receiving a single triamcinolone acetate 20 mg injection for wrist pain. All her symptoms resolved, and

she did not require further operative treatment.<sup>15</sup> The clinical improvement in this case report without adverse effects from the steroids is in contrast to the previous reports, and may suggest therapeutic benefits of steroid injections for periostitis or MTSS due to more acute blunt trauma, a mechanism which was not present in the previous reports.

In this patient, no adverse effects were noted with the steroid use. Providers must carefully weigh the potential benefit of steroid use in refractory cases of periostitis against the risks. This case may suggest that steroids have a role in the treatment of refractory MTSS after an acute traumatic mechanism, though a full understanding of periostitis is still unknown. Periostitis is often used to describe multiple pathologies. Pathophysiologic differences in etiology of periostitis, for example from blunt trauma, repetitive microtrauma, or infection, could alter or dictate responses to treatment modalities. More research is needed to elucidate ideal imaging modalities, treatment options, and disease pathology to determine optimal treatment and patient care.

## Conclusion

Periostitis is a condition characterized by inflammation of the periosteum around tubular bones and in the tibia, known as shin splints or MTSS. There is a paucity of literature around traumatic periostitis and the role of steroids for its treatment. Limited case reports have previously advised against steroid use for MTSS. This case presents a possible role for therapeutic

steroids in the treatment of MTSS from acute blunt trauma. Further studies are needed to elucidate the safety profile and effectiveness of steroid injections in the treatment of periostitis.

### Conflict of Interest

None of the authors identify any conflict of interest.

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## **Cautious Optimism: Service Patterns in the Child and Adolescent Mental Health Division During the COVID-19 Pandemic**

Trina E. Orimoto PhD; Kalyn L. Holmes MA; David S. Jackson PhD; Max Sender BS;  
Scott K. Shimabukuro PhD; Charles W. Mueller PhD

*Insights in Public Health is a monthly solicited column from the public health community and is coordinated by HJH&SW Contributing Editor Tetine L. Sentell PhD from the Office of Public Health Studies at the University of Hawai'i at Mānoa and Contributing Editor Lola Irvin MEd from the Hawai'i Department of Health.*

### **Keywords**

*Child and Adolescent Mental Health, COVID-19, Mental Health Outcomes, Service Utilization, Functional Impairment, Problem Severity*

### **Introduction**

Since 2020, the coronavirus pandemic has led to considerable life disruption for young people, bringing with it concerns regarding mental health impacts, treatment utilization, treatment outcomes, and other public health challenges. School closures and limits on organized social activities have impacted the educational and psychosocial development of children worldwide.<sup>1</sup> National research warns us to anticipate widespread increases in suicidal ideation, self-harm, depression, and anxiety in youth and adolescents.<sup>2,3</sup> Research also suggests that we might see increases in stress,<sup>4</sup> depression, and substance use among caregivers,<sup>5</sup> as well as greater risks of family violence,<sup>6</sup> intimate partner violence,<sup>7</sup> and adverse childhood experiences.<sup>8</sup>

Children, youth, and families in Hawai'i seem to be experiencing many of the same challenges as those seen nationally. In May 2021, a community survey of 117 caregivers found that 46% of respondents indicated the pandemic has had a negative impact on the mental health of their children.<sup>9</sup> A little over half of these caregivers indicated their child(ren) were exhibiting feelings of depression (58%) and anxiety (57%).

Access to effective mental health services during and after periods of community stress is essential for youth and family well-being. Across the state of Hawai'i, the Department of Health's Child and Adolescent Mental Health Division (CAMHD) provides mental health services for thousands of eligible youth and their families with serious emotional and behavioral challenges. Services include assessment, case management, and an array of intensive therapeutic support provided in the home and community or in temporary out-of-home placements. Throughout the pandemic, the CAMHD and its contracted providers have relied heavily on telehealth technology to ensure that mental

health services could be provided to youth and families with limited disruption. The goals of this column are to report youth enrollment, functional impairment at intake, and treatment progress patterns in the CAMHD before and after the start of the COVID-19 pandemic and to recommend next steps in ensuring continuous access to effective mental health services for young people in Hawai'i.

### **The CAMHD Youth Enrollment**

Figure 1 displays the CAMHD open case counts (enrollment) for each month in the year before and after the start of the COVID-19 pandemic (set at March 1, 2020, since the first presumptive positive case in Hawai'i was identified in early March). The expected open case numbers based on the one-year pre-COVID-19 pattern are displayed. Although monthly enrollments vary historically, the onset of the pandemic saw a noticeable drop in the CAMHD cases (54% decrease in applications from March to April 2020), primarily due to fewer new referrals for treatment. Naturally as cases are closed, the total caseload continues to decline. Application numbers began to increase in the summer of 2020 but remained low compared to the corresponding month in the prior year. The recent increase in referrals might relate to the return of in-person schooling and the loosening of social gathering restrictions for many youth. That said, there is no indication of a greater number of new youth and family applications, which would be predicted by both the stressors and mental health challenges posed by the pandemic and the presumed pent-up demand given the nearly year-long service utilization reductions. Thus, the CAMHD has instituted a variety of outreach efforts to increase access and utilization, including expanded statewide campaigns such as Children's Mental Health Awareness Month (for more information visit <https://health.hawaii.gov/camhd/cmha21/>), community and media appearances by advocates within the CAMHD, partnerships with provider agencies in pro-active screening, and promotion of its public health information web pages and social media accounts (@CAMHDHAWAII).



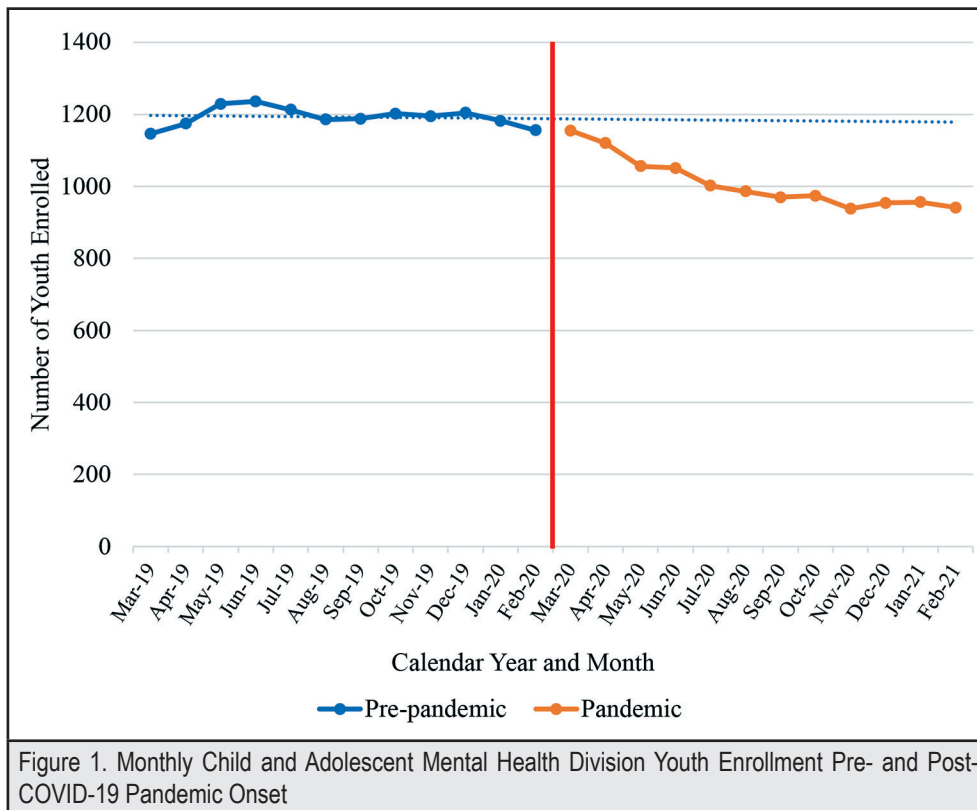


Figure 1. Monthly Child and Adolescent Mental Health Division Youth Enrollment Pre- and Post-COVID-19 Pandemic Onset

Note. COVID-19 onset date set at March 1, 2020. Dotted blue line reflects anticipated linear trend based on 12-month pre-COVID patterns. Enrollment refers to number of open cases within the CAMHD in the given month.

### Youth Clinical Status at the CAMHD Entry

Given reported increases in mental health challenges for young people, both locally and nationally, it is natural to expect similar increases in the initial severity of clinical problems for clients entering mental health services. The CAMHD routinely collects and monitors standardized measures of youth status, at intake and periodically throughout treatment. The Child and Adolescent Functional Assessment Scale (CAFAS) is completed by the assigned care coordinator and assesses functional impairment over the preceding 90 days across multiple domains (School, Home, Community, Behavior Toward Others, Moods/emotions, Self-Harm, Substance Use, and Thinking).<sup>10,11</sup> The Ohio Scales Problem Severity scale, Parent Form assesses emotional and behavioral problems and is completed monthly by caregivers.<sup>12</sup> Lower scores indicate fewer challenges and problems (CAFAS range 0-240 and Ohio Scales Problem Severity Scale range 0-100). Both measures have demonstrated reliability and validity in numerous large, community studies including as used in the CAMHD.<sup>13-17</sup>

Figure 2 displays initial total (1) functional impairment (CAFAS) and (2) parent-reported problem severity (Ohio Scales) scores for children and youth admitted during each of the 12

months preceding and following the beginning of the COVID-19 outbreak. While the CAMHD anticipated serving more highly impaired youth with more severe emotional and behavioral problems during the pandemic (ie, higher initial scores), that has not manifested in the data. Instead, the average functional impairment scores (CAFAS) are about the same compared to the prior 12 months and are lower than expected given the upward linear trend projected from the prior 12-month pattern. Similarly, initial levels of emotional and behavioral problems (Ohio Scale) have not considerably changed after COVID-19 onset. These trends might be related to (among other things) limited opportunity for youth to engage in problematic behavior or fewer occasions for adults or caregivers to observe such behavior. Thus, these patterns need to be interpreted with caution. That said, the clinical meaning is mixed. On one hand, new youth in the CAMHD are not reporting unusually high levels of symptoms or functional impairment as initially predicted. On the other hand, given lower enrollment in the CAMHD and the likely higher levels of societal stress, these same data (the absence of a bump up in scores) suggest that there are a good number of youth and families in need who are not entering services with the CAMHD. With the lessening of COVID-19 restrictions, behavioral health services might anticipate increases in demand and should likely prepare for such an increase.

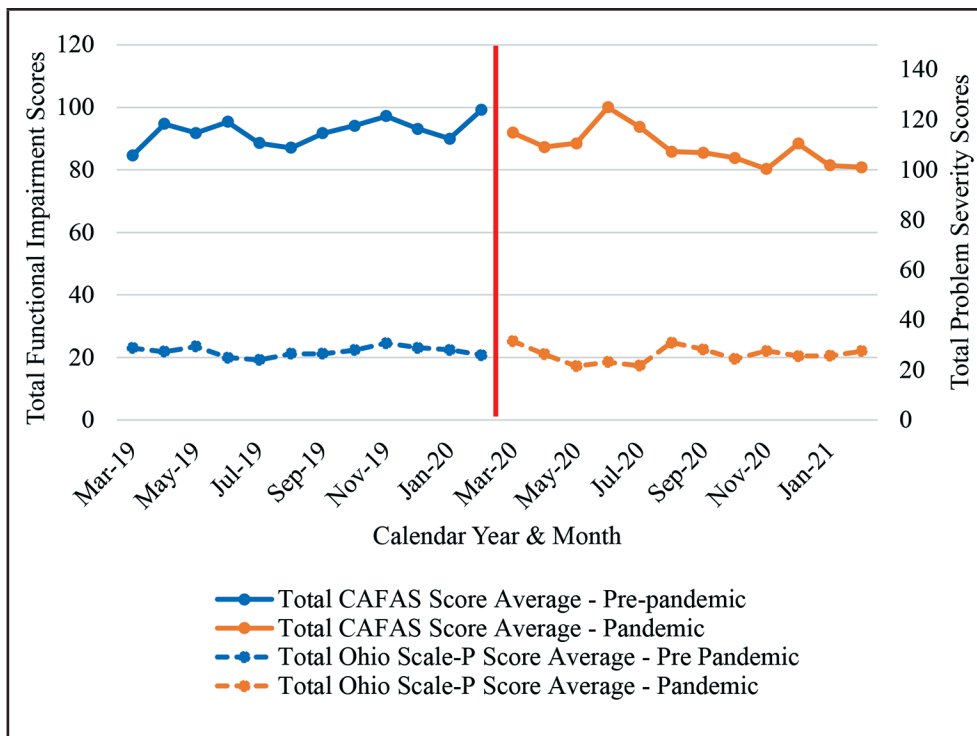


Figure 2. Monthly Average Impairment (Child and Adolescent Functional Assessment Scale; CAFAS) and Problem Severity (Ohio Scales) Scores for Newly Enrolled Clients Pre- and Post-COVID-19 Pandemic Onset

Note. COVID-19 onset date set at March 1, 2020. Impairment scores derived from CAFAS total scores (range 0 -240) and severity scores derived from Ohio Problem Severity Scale – Parent Form (range 0 – 100). Number of CAFAS responses each month ranged from 30 to 73 and number of Ohio Problem Severity Scale – Parent Form responses each month ranged from 19 to 67.

### Treatment Progress for the CAMHD Youth

Figure 3 utilizes data from routine system outcome reporting to examine treatment progress for clients in the CAMHD, comparing the periods before and after the start of the COVID-19 pandemic. The pre-and post-COVID onset scores are similar in pattern. During each time period, clients’ initial assessment score, final assessment score, and the amount of improvement over time are relatively comparable. This can tentatively be interpreted as a considerable success for clients, the CAMHD, and its provider partners, particularly considering the added COVID-19 related stressors and additional barriers to treatment. Whether or not treatment progress patterns will be sustained through the evolving stages of the pandemic are unknown and should be tracked.

### Conclusions and Recommendations

While the CAMHD enrollment rates following the initial COVID-19 outbreak have been lower than expected, there is some evidence that they are slowly returning to baseline. However, given known community stress and impairment levels and a period of lower utilization, the need for the CAMHD services is likely to be higher than it was pre-COVID. Level of youth

impairment at entry to the CAMHD has not changed and positive treatment progress remains comparable.

Overall, these findings can be interpreted with both caution and optimism. While the reported data is solely from the CAMHD, it provides insight on mental health services among youth affected by the pandemic. Lower service utilization during presumed increased community need suggests that some youth and families who could benefit from these services are not getting them or being served by other means (eg, outpatient therapy, school counseling, primary care, self-help). These lowered utilization rates also suggest that there might be a built-up need (and eventual demand) for services both due to COVID-19 related stressors and the under-identification of youth and families due to reduced opportunities for adults to observe problem behaviors. On the positive side, youth who are treated by the CAMHD and its provider agencies during the pandemic present with similar levels of functional impairment and show comparable progress over the course of treatment. Ongoing monitoring of such patterns of enrollment and outcomes by the CAMHD and other child-serving entities will be vital in the next stages of the pandemic so that policymakers and administrators can rapidly adjust interventions as needed.

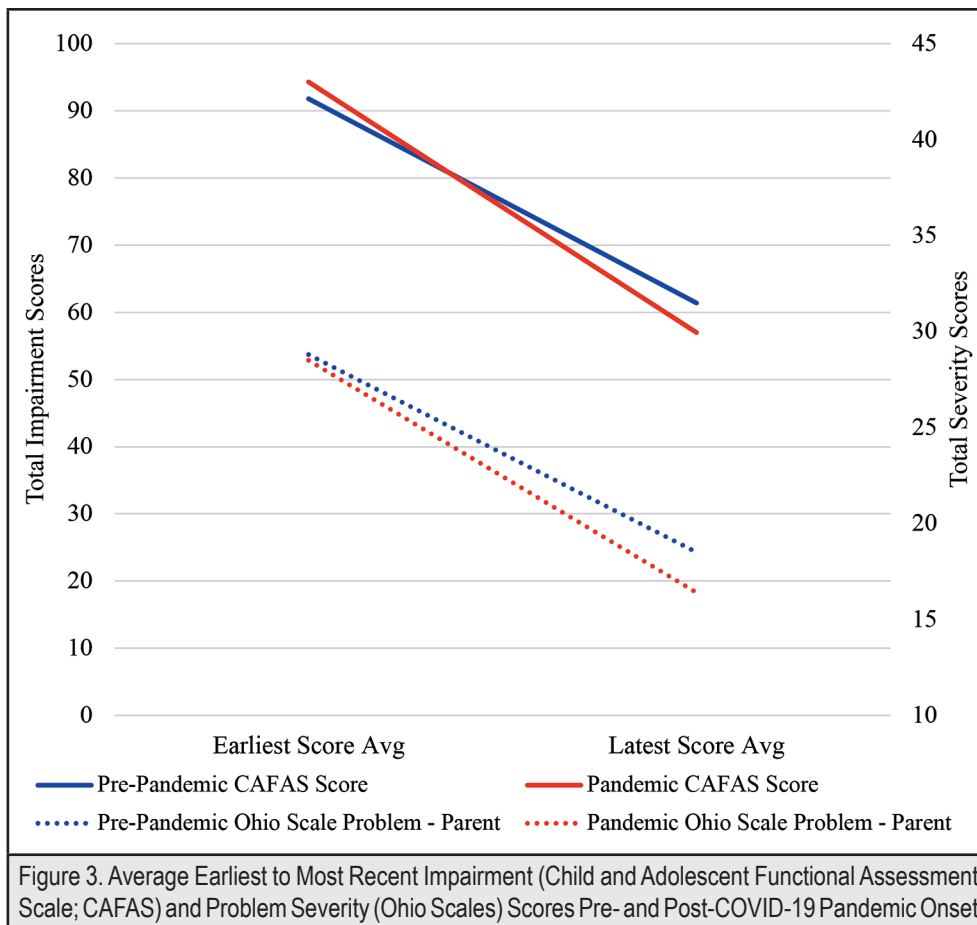


Figure 3. Average Earliest to Most Recent Impairment (Child and Adolescent Functional Assessment Scale; CAFAS) and Problem Severity (Ohio Scales) Scores Pre- and Post-COVID-19 Pandemic Onset

Note. COVID-19 onset date set at March 1, 2020. Impairment scores derived from CAFAS total scores (range 0 -240) and severity scores derived from Ohio Scales Problem Severity Scale – Parent Form (range 0 – 100). CAFAS Pre-Pandemic N = 402; Post-Pandemic N = 592. Ohio Scales Problem Severity Scale - Parent Form Pre-Pandemic N = 493, Post-Pandemic N = 364

At a broader level, and despite the numerous challenges posed by COVID-19, the pandemic has served as a stimulus for moving mental health systems of care forward by expanding the provision of, and demand for, telehealth services. Since the start of the pandemic, telehealth services have been offered to virtually all clients in the CAMHD, when clinically indicated. The CAMHD’s early adoption of telehealth services has been a crucial mechanism for maintaining effective treatment services. Not only did this decrease treatment barriers for clients, but it also allowed therapists on different islands to serve youth and families more readily in geographical locations with therapist shortages. Importantly, a large body of research suggests that clinical outcomes within telehealth are equivalent to standard care.<sup>18</sup> While telehealth has helped to facilitate access to services, it continues to be a challenge for many families with limited internet access or hardware, difficulty in navigating the technology, challenges with developing rapport with treatment teams in a virtual context or struggles in helping children sustain attention for sessions. There is still a need for the child- and youth-serving systems to determine how best to maximize telehealth by understanding and identifying the optimal conditions

for each client. For example, this might include considering blended therapy formats (ie, part telehealth, part in-person), decreasing session lengths while increasing session frequency, creatively engaging clients via online platforms, and incorporating different technology tools (eg, texting, therapy applications).

The pandemic has also led to the heightened importance of easily accessible, virtual, mental health informational resources for children, youth, families, and their providers. The locally-developed Help Your Keiki website (helpyourkeiki.com) had already been serving as a hub for evidence-based self-care resources, information on common problems, treatments that have proven to work, and ways to seek help when needed. At the onset of the pandemic, the CAMHD’s Evidence-Based Services Committee recognized the need for a central location of resource links on youth and family mental health during COVID-19 and began updating the Help Your Keiki page and social media accounts with relevant local and national information ([@helpyourkeiki](https://www.helpyourkeiki.com/covid19) on Instagram). While these recent page updates were built for the initial stress of the pandemic, such resources might benefit



from long-term strategic communication planning to ensure that families in need can both quickly find and easily access mental health information and services.

Children, youth, and families have arguably been the most impacted by the pandemic and there is a clear opportunity to strengthen the mental health system of care during the current crisis. Certainly, every effort must be made to monitor ongoing service patterns and continue to break down barriers to mental health access.

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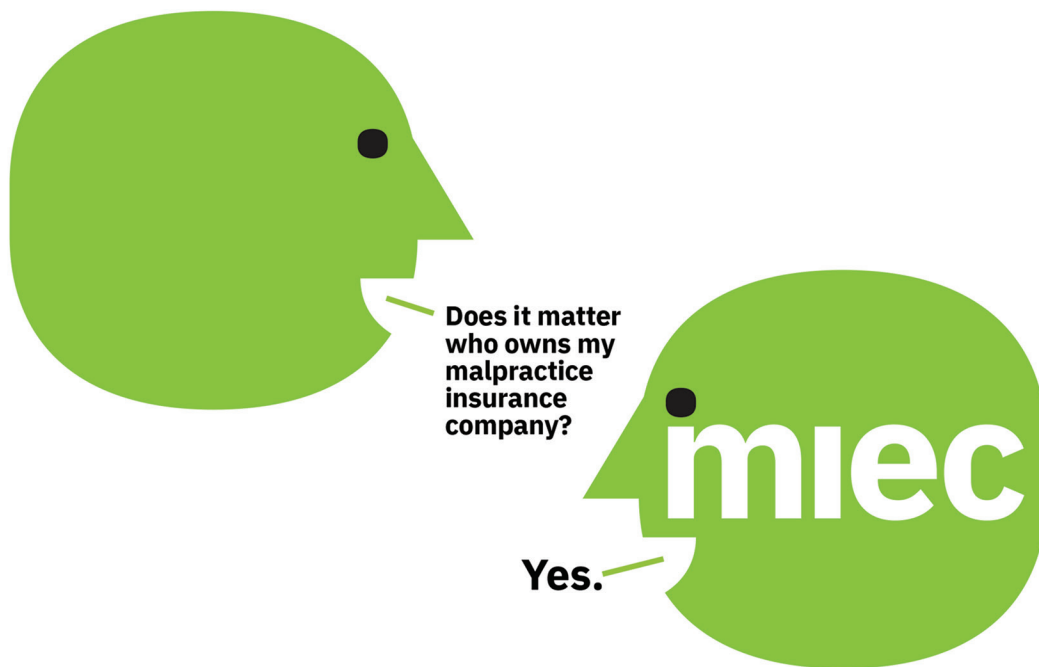
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