

# OFP

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# EDITOR'S MESSAGE

## The Road Not Taken

Paula Gregory, DO, MBA, FACOFP

*Two roads diverged in a yellow wood,  
And sorry I could not travel both  
And be one traveler, long I stood  
And looked down one as far as I could  
To where it bent in the undergrowth.  
Then took the other, as just as fair,  
And having perhaps the better claim,  
Because it was grassy and wanted wear;  
Though as for that the passing there  
Had worn them really about the same,  
And both that morning equally lay  
In leaves no step had trodden black.  
Oh, I kept the first for another day!  
Yet knowing how way leads on to way,  
I doubted if I should ever come back.  
I shall be telling this with a sigh  
Somewhere ages and ages hence:  
Two roads diverged in a wood, and I—  
I took the one less traveled by,  
And that has made all the difference.*  
—Robert Frost, 1874–1963

Dear readers,

The osteopathic path has been steep and rocky at times, yet we have not doubted our choice. Our healthcare friends and allopathic colleagues have supported us on this journey. Now the path is wider, with rocks that are half buried and well-worn over the years.

As we leave the gate open behind us for our residents and students, we continue to ensure that the path becomes less steep for those who follow.

Let us continue to leave a reputation of honesty, integrity and collegiality to all of our healthcare professionals so that our patients will be better for having had our care.

The only osteopathic family medicine journal continues to provide osteopathically focused articles from your peers and colleagues. It is designed to enhance your practice ability and provide current topics with you in mind. Your experiences in communities across America—serving rural and urban patients—are valuable.

Wherever your journey takes place, *OFM* will be there providing current topics. Our topics for the May/June issue are created with you in mind. We invite you to visit our online journal, patient education handouts and continue your journey with us as we explore timely healthcare information.

## FROM THE PRESIDENT'S DESK



### The Kind of Doctor I Wanted to Be

Bruce R. Williams, DO, FACOFP

It was so heartwarming to have the opportunity to share the fellowship of my osteopathic family in Dallas. This period of separation and isolation has taken its toll, and the doctor couldn't have written a better prescription than for us to be together. As I accepted the gavel from Dr. Bixler, I also accepted a great responsibility, but I have the experiences of Drs. Bixler, DeLuca, Koehler and others to draw upon, as well as the wisdom of an exceptional Board of Governors. And, with the support of our wonderful ACOFP staff, I am excited about the coming year.

Becoming a family physician was always my dream; my parents say it began when I was around four years old. It was then that I developed tonsillitis, and I watched and waited weekly for my physician to make his house call. While I did not like the shot of penicillin that accompanied his visits, I was impressed by the attention and care he gave. I could tell he enjoyed what he did and felt what he was doing was important, and I also liked the maroon Buick Riviera that he drove. My tonsils were eventually removed and, the following year, I got off the school bus with a high fever. I was apparently very sick because the bus driver delivered me to my house, and my mom immediately took me to my doctor, with whom I was developing a relationship. Because of this relationship, my mom would take me to W.T. Grant's department store and buy me the black doctor's kit with the candy pills, and I would pretend to be the neighborhood doctor.

When it came time to apply to medical school, I went back to my doctor (Dr. Simpson, an MD) and asked him where I should apply. After a discussion of Penn State University, Thomas Jefferson University, George Washington University and others, he asked me what kind of doctor I wanted to be. I quickly replied that I wanted to be a family doctor. The discussion then turned to osteopathic medicine, so I investigated further, eventually applying only to osteopathic medical schools. I was accepted to Kansas City University College of Osteopathic Medicine (then, the University of Health Sciences). Through my medical education, I never wavered from my desire to be an osteopathic family physician, and I have been very blessed to practice osteopathic family medicine for more than 31 years.

Throughout my years in practice, I learned a great deal from my patients—the people who entrusted me with their care, believed in my knowledge and ability as a physician and respected me as a person. The first lesson I learned is that I was their doctor, and they wanted me to take care of them. They didn't want to see every “-ologist;” they wanted me to address their problem. When I had a patient in the hospital, they would wait for me to explain the results and tell them what the consultant said, and they wanted to

discuss their treatment decision with me. I felt the responsibility to develop my skills so I could take care of as much as I could without sending them to a specialist,—unless, of course, that is what they wanted. I also felt disappointed that I didn't do more, like deliver babies or set bones, but I did as much as I could.

During my years in practice, I learned a great deal from my patients—the people who entrusted me with their care, believed in my knowledge and ability as a physician and respected me as a person.

The other lesson was what a gift osteopathic manipulative treatment (OMT) is. I built my practice doing OMT, and patients sought me out because of it. I realized that this was something I could provide my patients so that when they left my office, they felt better than when they walked in—and there was almost nothing else that would accomplish the same thing. I found that when I combined osteopathic manipulation with other standard treatment, my patients got better faster. They requested OMT, even if that wasn't why they were there, because it made them feel better. Moreso, this was a treatment that connected them with me. I had to earn their trust and help them to develop a sense of comfort with me for the treatment to be effective. That hands-on treatment was far more effective for the overall care of the patient than just the technique itself—it helped to establish and solidify the doctor-patient relationship that is so important.

We need to encourage our students and residents to develop their osteopathic manipulative skills and to use them. We need to educate them on documentation and billing, so they realize the benefit to their practice as much as they realize the benefit to their patients. Our osteopathic family medicine colleagues can seize this opportunity as well. With the 2022 Intensive Osteopathic Update coming up in August, there will be opportunities to refine your skills and learn new techniques that you can use in your practices every day, and with the ACOFP OMTtotal library, instructional videos are continuously at your disposal. We were given this gift, and we should be using it. Our patients deserve it.

So, as we emerge from isolation, it is time for our patients to get back to receiving the continuity of care they need—the screenings, the immunizations, the exams and the individual attention that has been missing. Our patients need their physician who will DO it all. It is time for osteopathic family medicine to rise to the top and get the recognition and respect we deserve.

This is a significant part of our ACOFP strategic plan. We will continue advocating for our patients and our practices and promoting osteopathic family medicine to achieve the quadruple aim of better care, lower costs, and improved patient and physician satisfaction. We will also continue the work we have started with incorporating diversity, equity and inclusion into our structure; developing our governance to align with the needs

and expectations of our members; updating our management platform and website to serve our members more efficiently; and advocating for our members and patients with a strong and deliberate voice.

It is my honor to serve as your ACOFP president this year, and I am eager to work with you for the benefit of our patients.

Osteopathically yours,

Bruce R. Williams, DO, FACOFP

2022-23 ACOFP President

## CALENDAR OF EVENTS

### JUNE 16-18, 2022

ACOFP Future Leaders Conference  
American College of Osteopathic Family Physicians  
San Diego, CA  
[acofp.org](http://acofp.org)

### JUNE 17-19, 2022

TOMA/TxACOFP 15th Annual Convention  
Texas State Chapter of the ACOFP  
Arlington, TX  
[txacofp.org](http://txacofp.org)

### JULY 15-17, 2022

Direct Primary Care Summit  
ACOFP  
Kansas City, MO  
[dpcsummit.org](http://dpcsummit.org)

### JULY 28-31, 2022

46th Annual CME Seminar & Convention  
American College of Osteopathic Family Physicians of California  
Anaheim, CA  
[acofpca.org](http://acofpca.org)

### JULY 28-31, 2022

FSACOFP Annual Convention  
Florida Society of the American College of Osteopathic Family Physicians  
Orlando, FL  
[fsacofp.org](http://fsacofp.org)

### AUGUST 5-7, 2022

ACOFP Intensive Osteopathic Update  
American College of Osteopathic Family Physicians  
Rosemont, IL  
[acofp.org](http://acofp.org)

### AUGUST 5-7, 2022

47th Annual CME Symposium  
Pennsylvania Osteopathic Family Physicians Society  
Hershey, PA  
[poma.org](http://poma.org)

### AUGUST 11-14, 2022

MAOFP 2022 Summer Family Medicine Update  
Michigan Association of Osteopathic Family Physicians  
Acme, MI  
[maofp.org](http://maofp.org)

### AUGUST 12-14, 2022

NCS-ACOFP Annual CME Conference  
North Carolina Society of the ACOFP  
Pinehurst, NC  
[nc-acofp.org](http://nc-acofp.org)

### OCTOBER 27-30, 2022

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### CME Resource: *Osteopathic Family Physician* Offers 2 Hours of 1-B CME

ACOFP members who read *Osteopathic Family Physician* can receive two hours of Category 1-B continuing medical education credit for completing quizzes in the journal. Visit the eLearning center at [www.acofp.org](http://www.acofp.org) to access the quizzes.

## RESEARCH ARTICLE

# OSTEOPATHIC STUDENT TRAINING ON PREVENTING DOMESTIC VIOLENCE

Carrie Downing-Larick, DO<sup>1,2</sup>; Madeline Moore, DO<sup>3</sup>; Mackenzie Dreher<sup>3</sup>; Alexis M. Stoner, PhD, MPH<sup>4</sup>; Natalie Fadel, PsyD<sup>5</sup>; Ning Cheng, PsyD<sup>6</sup>

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## KEYWORDS:

Domestic violence

Education

Intimate partner violence

Medical education

## Abstract

**Introduction:** Domestic violence is a serious and preventable public health issue. Student Training on Preventing Domestic Violence (STOP-DV) is an extracurricular program that educates medical students on domestic violence. This study sought to determine if STOP-DV is an effective method to increase the knowledge of domestic violence among medical students.

**Methods:** This study utilized a quasi-experimental research approach. Participants were recruited through a convenience sample of first- and second-year medical students from an osteopathic medical school with three campuses. The intervention group included the campus where STOP-DV was implemented and was then compared to the control group (the other two campuses) without the program. Intervention and control groups were given the same pre-survey and post-survey to assess for baseline knowledge, awareness, self-efficacy and health-seeking behaviors. Bivariate and multivariate statistical analysis of matched pre-surveys and post-surveys was completed during the 2018 and 2019 school year.

**Results:** Medical students in the intervention group (n=100) showed a statistically significant increase in self-efficacy and in the ability to recognize domestic violence in patients ( $p < 0.001$ ) and to discuss domestic violence with patients ( $p = 0.004$ ) compared to the control group (n=47). Based upon general linear regression analysis, survey stage significantly contributed to participants self-efficacy and domestic violence knowledge in both cohorts. Additionally, intervention group significantly contributed to participants' medical domestic violence knowledge.

**Conclusions:** This study was successful in implementing a domestic violence program and increasing awareness in medical students. The ultimate goal is to encourage schools to utilize a similar program to understand how domestic violence affects patients and their communities.

## INTRODUCTION

Domestic violence (DV) is abuse to any member of a household and can include intimate partner violence, child abuse and elder abuse.<sup>1</sup> It encompasses multiple capacities of abuse, including physical, emotional, sexual, digital and financial, along

with sexual/reproductive coercion.<sup>2</sup> In cases of physical abuse, only 34% of survivors injured by intimate partners receive medical care.<sup>3</sup> Survivors of DV may face several barriers when trying to access healthcare services, including personal factors, such as willingness to disclose the event; perception of safety; consequences of disclosure, such as increased abuse; and fear of losing children.<sup>4-7</sup> Survivors attribute difficulties at a healthcare level to inappropriate responses by healthcare professionals, perceived barriers to disclosing DV, absence of relationship with the healthcare provider and a lack of confidence in the outcomes of disclosure.<sup>4,5,8-13</sup> These barriers continue to persist despite improved policies and regulations within healthcare settings.<sup>6</sup>

## CORRESPONDENCE:

Alexis M. Stoner, PhD, MPH | [astoner@carolinas.vcom.edu](mailto:astoner@carolinas.vcom.edu)

Medical students, physicians and allied healthcare professionals need more training in DV and proper healthcare protocols to increase their knowledge to effectively help survivors of DV.<sup>13-16</sup> One study revealed the most important responsibility of healthcare professionals is identifying abuse, assessing safety and offering empathy, acknowledgement and support to survivors.<sup>17</sup> Several studies suggest that providing violence education to health professionals could increase the likelihood of reporting abuse.<sup>18-20</sup> This DV education includes screening tools, learning signs and symptoms suggestive of abuse, discussing interview strategies and providing resources with a safety plan for survivors.<sup>17</sup>

Students report barriers to identifying DV, such as a low index of suspicion, perceived need for certainty of the abuse, fear of incorrect diagnosis, the impact of report on physician-patient/parent relationship and perceived low incidence.<sup>21-23</sup> One study implemented a DV advocacy program at a women's shelter trained by undergraduate students.<sup>24</sup> DV survivors found community-based interventions effective in acquiring and utilizing local resources, such as housing, education, transportation, employment and healthcare information.<sup>24</sup> Furthermore, this study supported that comprehensive programs can change the behavior-seeking pattern of DV survivors to increase seeking resources on their behalf.<sup>24</sup>

This study aimed to create an open educational space for medical students to acquire knowledge and awareness of general and healthcare-related DV issues. It assessed whether exposure to DV education through a program called Student Training on Preventing Domestic Violence (STOP-DV) raised significant knowledge and awareness of DV among medical students.

## METHODS

### Study design

This study utilized a quasi-experimental study design conducted at the Edward Via College of Osteopathic Medicine (VCOM), across the Blacksburg, Virginia; Spartanburg, South Carolina; and Auburn, Alabama campuses. The study was approved as exempt by the Edward Via College of Osteopathic Medicine Institutional Review Board.

## PARTICIPANTS

All currently enrolled first- and second-year medical students at a VCOM campus during the 2018 and 2019 academic year were eligible to participate in the study. Students were non-randomly assigned to the intervention (Carolinas campus) and control (Auburn campus and Virginia campus) groups. The intervention group was subcategorized into two groups: "attendees" and "exposed." Attendees were defined as VCOM-Carolinas students who self-reported attending at least one STOP-DV event, while exposed were defined as VCOM-Carolinas students who did not participate in STOP-DV events but were on campus during its implementation.

## STOP-DV

STOP-DV was a voluntary extracurricular course provided to students after lecture hours from January to April within each academic year of 2018 and 2019. The course consisted of a speaker addressing attending students of the intervention group once a month on a topic about DV. Speakers varied from physicians, counselors, lawyers and program developers; event format differed by lecture and participation. STOP-DV events included hearing from a child abuse pediatrician; working with a local organization that assists with teen pregnancy and education; a program dedicated to ending human trafficking and sexual exploitation in upstate South Carolina; viewing a Med Talk with written reflection about adverse childhood experiences; participation in the Child Protection Training Center at The University of South Carolina Upstate; and a discussion with a sexual assault nurse examiner.

Before the start of STOP-DV, intervention and control groups were provided with a pre-survey consisting of 59 questions to record baseline demographics, self-efficacy, DV resources, knowledge and awareness. The survey had a variety of question formats, including true/false, multiple choice and categorical. It was adapted and modified from the Suicide Prevention Exposure, Awareness and Knowledge Survey (SPEAKS).<sup>25</sup> SPEAKS is used for assessing knowledge, awareness and perception of suicide on college campuses, specifically around prevention activities; perception of stigma surrounding mental health issues and seeking services for support; and myths and facts surrounding suicide, along with knowledge of resources for individuals in distress. SPEAKS was modified from suicide to DV with minor other additions, such as STOP-DV events, comments and DV counselor and contact information. To the best of our knowledge, this is the first application of SPEAKS to assess DV. However, due to the similar sensitive nature, stigma surrounding the topic, lack of public awareness and knowledge, and associated risk factors of DV and suicide, the SPEAKS survey was an appropriate tool.<sup>26-28</sup> Surveys were emailed on a secure server and responses were documented after obtaining free and informed consent. The appendix includes a full copy of the survey.

Over the course of 5 months, intervention participants had the opportunity to attend 1 of 5 STOP-DV events; the control group had no events. Upon completion of STOP-DV events, a post-survey, consisting of 72 questions was sent to both groups. The surveys would then be analyzed for significant outcomes. The increased question total of the post-survey accounted for questions evaluating event participation and event satisfaction.

## Analyses

Descriptive statistical analysis and general linear regression analysis were performed to assess for significant ( $p \leq 0.05$ ) differences between control versus intervention groups and attended versus exposed groups. Pre-surveys and post-surveys had to be at least 50% completed to be included in statistical analysis. Each participant's pre-survey was matched to the same participant's post-survey through a random 4-digit code assigned

during analysis. Variables of analysis included demographics, self-efficacy, knowledge and awareness of DV resources, general DV knowledge and medical DV knowledge.

## RESULTS

### Participants

Similar demographics were found between control and intervention groups and exposed and attendees. In 2018, 46 students completed both the pre- and post-surveys (22 of the intervention group with 4 as attendees and 24 of the control group); in 2019, 101 students completed the pre- and post-surveys (78 of the intervention group with 76 as attendees and 23 of the control group). Analysis of 147 matched surveys was completed over a span of 2 years (47 control and 100 intervention). The subdivisions were further divided into 80 participants who attended STOP-DV

and 18 participants who were exposed on campus. The average survey response rate was 25% for the pre-survey and 13% for the post-survey. From year 1 to 2, there was a 4- and 19-fold increase in matched surveys for intervention and attendees, respectively. The study population's majority included females (70%), expected graduates of 2022 (51%), age 20–25 years old (74%), and white (77%). Similar demographics were seen within the exposed and attended groups. A significant difference ( $p \leq 0.05$ ), regarding graduation year and survey year, existed between intervention and control groups as well as exposed and attended ( $p < 0.0001$ ).

An average of 77.5% of participants reported having prior healthcare work experience. An average of 43.5% reported witnessing a patient affected by DV, 44% knew of a DV protocol and 37% were provided with DV training. Only 38.5% of participants felt very confident or confident carrying out DV protocol in their settings.

TABLE 1:

Participant Demographics.

		CONTROL (N=47)	INTERVENTION (N=100)	TOTAL (N=147)	p-value	EXPOSED (N=18)	ATTENDEE (N=80)	TOTAL (N=98)	p-value
		Frequency (%)	Frequency (%)	Frequency (%)		Frequency (%)	Frequency (%)		
Graduation Year					0.0061*				0.0001*
	2020	4 (8)	11 (11)	15 (10)		8 (44)	2 (2)	10 (10)	
	2021	27 (57)	30 (30)	57 (39)		10 (56)	19 (24)	29 (30)	
	2022	16 (34)	59 (59)	75 (51)		0 (0)	59 (74)	59 (60)	
Gender					0.2361				0.4073
	Male	11 (23)	33 (33)	44 (30)			4 (22)	28 (35)	32 (33)
	Female	36 (77)	67 (67)	103 (70)		14 (78)	52 (65)	66 (67)	
Age					1				0.4117
	20–25	35 (74)	74 (74)	109 (74)		12 (67)	60 (75)	72 (73)	
	26–30	12 (26)	24 (24)	36 (24)		5 (28)	19 (24)	24 (24)	
	>30	0 (0)	2 (2)	2 (1)		1 (6)	1 (1)	2 (2)	
Race					0.598				1
	Asian	8 (17)	13 (13)	21 (14)		1 (6)	11 (14)	12 (12)	
	Black	1 (2)	4 (4)	5 (3)		0	4 (5)	4 (4)	
	White	35 (74)	78 (78)	113 (77)		17 (94)	60 (75)	77 (79)	
	Mixed	2 (4)	4 (4)	6 (4)		0	4 (5)	4 (4)	
	Other	0	1 (1)	1 (<1)		0	1 (1)	1 (1)	
Survey Year					0.0004*				0.0001*
	2018	24 (51)	22 (22)	46 (31)		16 (89)	4 (5)	20 (20) <sup>†</sup>	
	2019	23 (49)	78 (78)	101 (69)		2 (11)	76 (95)	78 (80)	

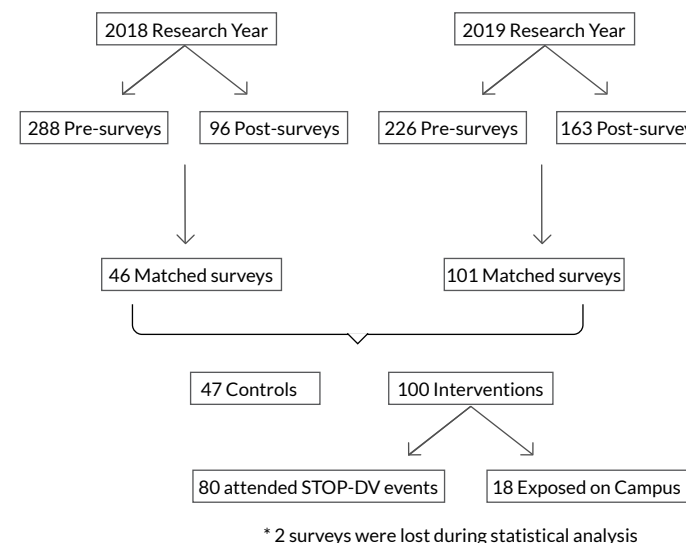
Chi-square and Fisher's Exact test analyzed the differences between intervention and control groups.

\*Statistically significant  $p$ -value ( $\leq 0.05$ )

<sup>†</sup>Two participants are missing from data collection

FIGURE 1:

Subjective reporting of overall improvement in sinus symptoms with OMT



### Self-efficacy

Self-efficacy was defined as a confidence level to which participants identified to a given question or scenario. There was no statistical difference ( $p > 0.05$ ) regarding self-efficacy questions in the pre-survey between the intervention and control groups. The post-survey results showed a statistically significant increase in the intervention compared to the control in the ability to recognize DV in patients ( $p < 0.001$ ) and to discuss DV with patients ( $p = 0.004$ ). No significant difference ( $p = 0.3$ ) was found between the control and intervention in the ability to refer DV patients to resources.

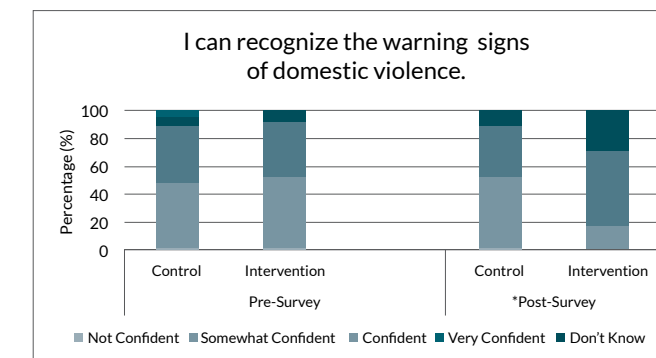
Further analysis of self-efficacy between exposed and attended showed no significance ( $p > 0.05$ ) in pre-surveys about recognition of DV warning signs and referral of patients at risk for DV. Statistical difference ( $p = 0.040$ ) of the pre-survey was of questions asking if someone was exhibiting DV warning signs and asking if they were in an abusive relationship. In the post-survey, the self-efficacy of the ability to recognize DV warning signs in patients increased with significance ( $p = 0.004$ ) in the attendees compared to the exposed. No significant difference was found between exposed and attended in the post-survey questions asking if someone was in an abusive relationship and if they would connect/refer to DV resources.

### Knowledge and awareness

The pre-survey had no significant difference in knowledge of local DV resources for the control or intervention group. The post-survey showed a significant difference ( $p = 0.012$ ) in knowledge of local DV resources. The intervention group increased by 7%, while control decreased by 7%. In the attended and exposed groups, there was no statistical significance ( $p > 0.05$ ) found during the pre-survey in the knowledge of local DV resources. However, those who attended STOP-DV events showed a significant difference ( $p = 0.029$ ) in the knowledge of local DV resources.

FIGURE 2:

Participants' confidence level for the survey question "I can recognize the warning signs of domestic violence."



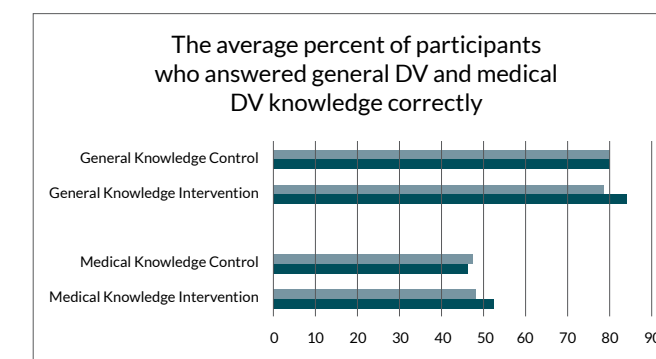
\*Post survey statistically significant,  $p < 0.0001$

Assessment of general DV knowledge contained 17 questions. The control group averaged 80% correct in the pre-survey and 80% correct in the post-survey. While the intervention group initially averaged 79% correct in the pre-survey, they improved to an average of 84% correct in the post-survey. While there was no significant difference in the overall score among both the intervention and control groups, two post-survey questions were significant ( $p < 0.05$ ): the false statements that DV causes minimal economic impact and police intervention is recommended in most DV situations. Exposed and attendees increased their averages from pre-survey to post-survey. The exposed increased by 3.7% and attendees increased by 6.7%. The exposed had higher averages in both pre-survey and post-survey compared to the attendees.

Sixteen questions were specific for medical DV knowledge. The control group averaged 48% correct in the pre-survey and 46% correct in the post-survey. While the intervention group initially averaged 48% correct in the pre-survey, they improved to an average of 52% correct in the post-survey. Four medical DV post-survey questions were significant. The exposed group increased their average by 0.48% correct from pre-survey to post-survey and had higher scores compared to attendees. The attendees showed a 6.8% average increase.

FIGURE 3:

The average percent of participants who answered a series of 16–17 questions related to general and medical DV knowledge correctly.



## Multiple regression results

General linear regression analysis for self-efficacy, general DV knowledge and medical DV knowledge used the following predictors: intervention groups (intervention vs. control or exposed vs. attendee), survey stage (pre-survey vs. post-survey) and the interaction term of the intervention group and survey stage.

Within the self-efficacy model—the intervention cohort including students only from the Carolinas campus—the survey stage significantly contributed to participants' self-efficacy ( $p=0.0104$ ). Within the exposed group, the effect of the intervention on participants' self-efficacy was 0.22. Within the attendee group, the effect of the intervention on participants' self-efficacy was 0.97. For the cohort including students from all 3 campuses, the intervention group and survey stage significantly contributed to participants' self-efficacy ( $p<0.05$ ). Within the control group, the effect of the intervention on participants' self-efficacy was 0.064. Within the intervention group, the effect of the intervention on participants' self-efficacy was 1.31.

Within the general DV knowledge model using the cohort with students only from Carolinas campus, the survey stage significantly contributed to participants' general DV knowledge ( $p=0.0046$ ). Within the exposed group, the effect of the intervention on participants' general DV knowledge was 1.05. Within attendees, the effect of the intervention on participants' general DV knowledge was 0.67. For the cohort including students from all three campuses, the survey stage significantly contributed to participants' general DV knowledge ( $p=0.0098$ ). Within the control group, the effect of the intervention on participants' general DV knowledge was 0.40. Within the intervention group, the effect of the intervention on participants' general DV knowledge was 1.17.

Within the medical DV knowledge model using the cohort with students only from Carolinas campus, the treatment group and survey stage both significantly contributed to participants' medical DV knowledge ( $p<0.0001$ ). Within the exposed group, the effect of the intervention on participants' medical DV knowledge was 2.72. Within attendees, the effect of the intervention on participants' medical DV knowledge was 5.79. For the cohort including students from all 3 campuses, the treatment group and survey stage both significantly contributed to participants' medical DV knowledge ( $p<0.0001$ ). Within the control group, the effect of the intervention on participants' medical DV knowledge was 1.53. Within the intervention group, the effect of the intervention on participants' medical DV knowledge was 3.52.

## DISCUSSION

The STOP-DV program is an innovative and educational program aimed to increase DV education in medical students. STOP-DV has continued to grow in interest and support from the medical student body. The results of this study indicate that STOP-DV was successful in its goals of increasing self-efficacy, knowledge and awareness of DV resources, general DV knowledge and medical topics in medical students. Similar studies showed the integration of a DV curriculum helped improve self-efficacy and knowledge.<sup>29</sup>

In addition, this curriculum, along with other DV curriculums within medical training, received positive feedback about its benefit to future care.<sup>30,31</sup>

The World Health Organization states that survivors of interpersonal violence and DV require services from many different sectors, including health care, to fulfill their needs and that the best way to improve service response to these survivors is to provide education/training and reform throughout all these institutions.<sup>1</sup> STOP-DV, on a smaller scale, provides building blocks to ensure survivors are getting the care they need and deserve from future healthcare providers.

One of the main barriers to physicians not discussing DV with patients is the physicians' lack of self-efficacy.<sup>32,16</sup> The intervention group showed a significant increase in self-efficacy at the end of the program compared to the control group. Within the intervention group, those who attended STOP-DV had a significantly higher increase in self-efficacy compared to those who were exposed. The data supports having the STOP-DV program on the campus. Regardless of whether students attended STOP-DV events, their DV self-efficacy increased. We suspect this relates to increased DV discussions, flyers and increased materials present on campus. If medical students become more confident and efficient in discussing DV with their peers, patients and attending physicians, both personal and perceived patient barriers may be reduced surrounding DV.<sup>16</sup>

Studies have shown survivors of DV support training of medical students in DV, with an emphasis on being trained to listen.<sup>33</sup> It has been suggested by other studies and academic leadership for schools to include DV training multiple times in standard curriculum through a student's academic career.<sup>29</sup> This study implemented the STOP-DV program was a step toward achieving that goal.

The philosophy of osteopathic medicine is built upon tenets. Two of these core tenets are that a person is a unit of body, mind and spirit and that the body is capable of self-healing. These 2 tenets are vital to osteopathic medicine and are also reflected in the aims of STOP-DV. This program provides the foundation to educate future physicians about domestic violence with the impactful aim to help those at risk. When healthcare providers integrate these practices, it reinforces the concepts osteopathic medicine were initially built upon. Survivors of domestic violence may initially present with physical symptoms; however, their mind and spirit are also equally affected. One key pillar of the STOP-DV curriculum was to go beyond just identifying domestic violence by providing patients with supportive resources.<sup>16</sup> Through the STOP-DV program, future physicians have increased awareness and confidence to approach a patient population present in every community.

## CONCLUSION

Overall, the STOP-DV program suggested an increase of DV self-efficacy, DV awareness of resources, and knowledge based on general and medical concepts within the intervention group. STOP-DV was well received by medical students, and we hope

future groups will continue to expand the program to positively impact more healthcare providers. Based on the data and overall success of this program, we would recommend implementing STOP-DV at medical schools. In addition, continued research is needed to develop a STOP-DV model other healthcare professional schools can utilize. If 1 DV survivor is discovered and receives the necessary resources and health care due to STOP-DV, this research team will consider this program a success.

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**APPENDIX :**

1. Have you been exposed to any materials on your campus related to domestic violence (eg, brochures, posters, videos, radio messages, orientation materials, etc.)?

1. Yes  
2. No  
3. Don't know

1A. If yes, what materials have you been exposed to?

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2. Have you directly participated in any domestic violence prevention activities sponsored by your campus (eg, seminar, workshop, orientation program, etc.)?

1. Yes  
2. No  
3. Don't know

2A. If yes, what activities have you participated in?

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**Please rate your *level of confidence* in your ability to interact with patients about the domestic violence behaviors described below from not confident to very confident. (check one). I feel confident that:**

3. I can recognize the warning signs of domestic violence in patients.

Not Confident  Somewhat Confident  Confident  
 Very Confident  Don't know

4. I would ask someone who was exhibiting the warning signs of domestic violence if they are in an abusive situation.

Not Confident  Somewhat Confident  Confident  
 Very Confident  Don't know

5. I would connect or refer a patient at risk for domestic violence to resources for help (e.g., hotline, social services, counseling, ER, etc.).Next, we would like to know a little bit about your campus, hospital, or healthcare clinic and resources available for students or patients at risk for domestic violence. Please respond to each of the items using the response options provided that best represents your answer.

Not Confident  Somewhat Confident  Confident  
 Very Confident  Don't know

6. There is a domestic violence protocol for students on my campus.

1. Yes  
2. No

7. I am aware of at least one local resource to which I could refer a patient who is at risk for or involved in domestic violence relationship.

1. Yes  
2. No

8. My campus values the mental health and wellbeing of its students.

Strongly Disagree  Disagree  Somewhat Disagree  No Opinion  
 Agree  Strongly Agree

9. If you knew a patient that was involved in a domestic violence situation, where would you refer him/her? (Free response)

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10. How confident are you with talking to a patient involved in a domestic violence relationship?

Not Confident  Somewhat Confident  Confident  
 Very Confident  Don't Know

11. How confident are you with talking to a professor/physician/ attending about a patient involved in domestic violence relationship?

Not Confident  Somewhat Confident  Confident  
 Very Confident  Don't Know

12. Have you ever identified a student, patient, family or friend who was at risk for domestic violence?

1. Yes  
2. No

12A. Have you ever referred a student, patient, family or friend to campus or community counseling services?

1. Yes  
2. No

12B. Have you ever provided someone the number to a hotline (eg, National Domestic Violence Hotline)?

1. Yes  
2. No

13. Have you worked/volunteered or are currently working/ volunteering in a healthcare setting? \*\*\*For post-test, changed to: "Have you started working/volunteer or continued working/volunteering at a healthcare setting since you took the STOP DV pretest?"

1. Yes  
2. No (If no, skip to question 14)

13A. At your healthcare setting, were or are you aware of domestic violence protocol for patients?

1. Yes  
2. No (If no, skip to question 14)

13B. At your healthcare setting, were you trained in patient domestic violence protocol?

1. Yes  
2. No (If no, skip to question 13d)

13C. At your healthcare setting, what did your training entail? (Free response)

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13D. At your healthcare setting, how confident were you in carrying out the patient domestic violence protocol?

Not Confident  Somewhat Confident  
 Confident  Very Confident  Don't Know

13E. At your healthcare setting, did you ever encounter or witness a patient(s) who was in a domestic violence situation?

1. Yes  
2. No (If no, skip to question 14)

13F. At your healthcare setting, what happened with the patient(s) above? (Free response)

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<b>We'd like to understand your perceptions of domestic violence help seeking. Please respond to each of the following using the scale provided. Select the number that best represents what you think. Personally:</b>	<b>Not Confident</b>	<b>Somewhat Confident</b>	<b>Confident</b>	<b>Very Confident</b>	<b>Don't know</b>
14. I think that it is a sign of personal weakness or inadequacy to receive help for relationship problems.					
15. I would see a person in a less favorable way if I came to know that he/she is seeing or has seen a mental health professional.					
16. I think that it is advisable for a student to hide from other students that he/she has been seen by a mental health professional.					
17. I think that it is advisable for a student to hide from faculty that he/she has been seen a mental health professional.					

<b>We'd like to understand the perceptions of help seeking on your campus. Please respond to each of the following using the scale provided. Select the number that best represents what you think most people on your campus think. On my campus:</b>	<b>Strongly Disagree</b>	<b>Disagree</b>	<b>No Opinion</b>	<b>Agree</b>	<b>Strongly Agree</b>
18. It is a sign of personal weakness or inadequacy to receive help for relationship problems.					
19. People would see a student in a less favorable way if they knew that he/she sought help from a domestic violence professional.					
20. It is advisable for a student to not tell other students that he/she is seeing or has seen a domestic violence professional.					
21. It is advisable for a student to not tell faculty that he/she is seeing or has seen a domestic violence professional.					

The following statements represent myths or facts about domestic violence. Some are true and some are false. Please indicate whether you believe the statement is true, false, or don't know (select one).	True	False	Don't Know
22. Domestic violence is rare.			
23. The presence of a gun in a domestic violence situation greatly increases the risk of homicide.			
24. The majority of individuals injured by intimate partners receive medical care.			
25. Few children are exposed to domestic violence.			
26. Physical abuse is the most common type of domestic violence.			
27. Healthcare workers are required to report adult domestic violence.			
28. All hospitals and other healthcare settings use effective evidence-based research in their domestic violence protocol for patients.			
29. Domestic violence has minimal economic impact.			
30. Healthcare workers are required to report child abuse.			
31. Women abused by their intimate partner are more likely to contract STIs.			
32. Men are not victims of domestic violence.			
33. Individuals living in low socioeconomic conditions are more likely to be in domestic violence situations.			
34. Children who are abused or witness abuse are more likely to become abusers as adults.			
35. Men are rarely affected by domestic violence.			
36. Less than half of teenage dating abuse survivors tell someone about their situation.			
37. 18–24-year-old women are the most frequently abused by an intimate partner. (*this is only on the 2018 survey)			
38. Campus sexual assault, date rape and rape are uncommon.			
39. Survivors of domestic violence who continually return to their abuser are weak.			
40. Most medical schools provide adequate information for students to deal with domestic violence in healthcare.			
41. Physicians frequently screen for domestic violence.			
42. Psychological abuse is the most common type of domestic violence.			
43. Hospitals are required to have at least one healthcare worker trained in domestic violence.			
44. All survivors of domestic violence want to leave their partner.			
45. Police intervention is recommended in most domestic violence situations.			
46. Healthcare facilities are required to have a domestic violence protocol.			
47. The emergency medicine physicians see the most patients affected by domestic violence compared to non-emergency medicine physicians.			
48. Couples involved in domestic violence relationships should undergo general couples counseling.			

**Background Information**

49. Which best describes your graduation year?
- 2019
  - 2020
  - 2021
  - Other
50. What is your gender (select one)?
- Female
  - Male
  - Transgender
  - Other (specify): \_\_\_\_\_
51. What is your age? years \_\_\_\_\_

52. Are you Hispanic or Latino (select one)?
1. Yes
  2. No
53. What is your race (select one or more)?
- American Indian or Alaska Native
  - Asian
  - Black or African American
  - Native Hawaiian or Other Pacific Islander
  - White
  - Other (please describe: \_\_\_\_\_)

**2019 ADDITIONAL QUESTIONS 54–59 (NOT ON 2018)**

We'd like to understand your knowledge of domestic violence. Please respond to each of the following question with the best answer choice.

54. Women in what age group are most frequently abused by an intimate partner?
- A. 12–17 years old
  - B. 18–24 years old
  - C. 25–31 years old
  - D. 32–37 years old
  - E. 38–45 years old
- Answer: B
55. A 6-year-old male presents to the office with his mother for a well-child check. His mother says the child's behavior in school has been bad and he frequently gets sent to the principal's office where she must pick him up. Physical examination reveals a circular erythematous mark on his thigh and a couple residual scars on bilateral arms and buttocks. His mother explains the child likes to play with the car cigarette lighter when she is not looking. What is your next most appropriate step in treatment?
- A. Ask more questions to mother and child about the history of these marks.
  - B. Ask mother to leave the room and privately interview mother outside.
  - C. Ask mother for permission to interview child separately.
  - D. Continue with the examination and plan for further review on next visit.
  - E. Refer to a social worker without further questioning.
- Answer: C
56. A 10-year-old female presents to the office with her mother due to decline in academic achievement over the past 2 months. Her mother is worried about her daughter lacking the ability to pay attention and not doing well in school. She looked up information on the internet and is concerned her child has attention-deficit-hyperactivity disorder (ADHD). Her mother works as a nurse in the evenings, and the grandmother takes care of the girl while she works. She explains that the father is not involved, and they divorced about 2 years ago due to irreconcilable differences. What is the next best step in management of this patient?

- A. Tell mother she needs to take more nights off at work to spend time with her daughter.
  - B. Explain that this is a phase in every child's life, and she will grow out of it.
  - C. Prescribe the child ADHD medications and ask them to return in 2 months to evaluate if any progress has been made.
  - D. Refer both mother and daughter to therapy for further evaluation.
  - E. Explain to mother this is normal behavior for a child prior to puberty.
- Answer: D

57. A 9-year-old female presents with her mother to her pediatrician's office for a well-child checkup. Her mother expresses concern that she is acting different. After an in-depth interview and examination, there is suspicion she is a victim of sexual abuse. Which of the following findings is most suggestive of this diagnosis?
- A. She is fearful of her father and other male adults.
  - B. She has cut marks to both wrists.
  - C. She has interest in things of sexual nature.
  - D. She has no friends at school or in her neighborhood.
  - E. She has decreased interest in school activities.
- Answer: C
58. A 42-year-old female returns to her primary care physician's office for follow-up on her past diagnosis of tension headaches. She states the headaches have not improved with naproxen or meditation. She has been married to a policeman for the past 8 years and has 3 children (aged 4–10 years old). She begins to cry when asked if she has any increased stressors. On further questioning, she states her husband hits her when he is drunk. She says, "He is a good husband when he's sober. But when he drinks, oh, he's awful! Last night, he said he would kill me if I tried to leave him." Her husband is also a patient of the physician. Physical examination reveals ecchymosis on both arms, and her lip has a healed abrasion. Which of the following is the most appropriate intervention?
- A. Tell her to leave immediately without her children.
  - B. Recommend her husband attend an Alcoholics Anonymous meeting and get therapy.
  - C. Gather more information while remaining neutral, since both are clinic patients.
  - D. Refer her to a domestic violence program.
  - E. Seek a restraining order against her husband on her behalf.
- Answer: D
59. A 4-month-old male presents to the emergency department as he has been unconscious for the past 20 minutes. He is accompanied by his mother and father, who are 23 years old and 34 years old, respectively. The mother reports she was holding the baby having a conversation with the father while preparing dinner for the other 3 children in the home. The father cuts in and says, "She is so clumsy. She should not multitask. Right, don't you always drop things." Mother agrees to the father's statement and continues to say that

while conversing about financial problems the conversation became intense. The father cuts in again, “Don’t you love to shop online? Did you not just buy a new crib yesterday?” As the mother again agrees to the father’s response, she can barely continue when he again comments, “She just was not paying attention when I was trying to explain the importance of money, and she bumped our baby’s head against the wall, leaving him unconscious.” Vital signs reveal a respiratory rate of 22 breaths/min. All other vitals are normal. Physical examination reveals no response to stimulation and decreased respiratory effect. What is the method used by the father in this conversation?

- A. Gas lighting
  - B. Verbal abuse
  - C. Physical abuse
  - D. Hoovering
  - E. Financial abuse
- Answer: A

**FOR POST-SURVEY ONLY**

- 60.** Did you attend any STOP-DV events?  
 1. Yes  
 2. No
- 61.** If you attended any STOP-DV events, which ones did you attend? (Please select all the events you attended.)  
 (All events will be listed, and participant will check off)
- 62–66.** From the events you attended, please select how beneficial or not beneficial they were.  
 (Events they attended will be selected from the previous question: very beneficial, beneficial, neutral, not beneficial)

**67.** What events did you like the best. Why?  
 (Free response)

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**68.** What events did you like the least. Why?  
 (Free response)

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**69.** Did you attend any domestic violence related events that were not a part of STOP-DV? (No: Skip to end of survey)  
 1. Yes  
 2. No

**70.** What events that were not a part of STOP-DV did you attend?  
 (Free response)

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**71.** What did you like about these events?  
 (\*this is only on the 2018 survey) (Free response)

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**72.** What did you not like about these events?  
 (\*this is only on the 2018 survey) (Free response)

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**Survey Questions and Measures**

Question Numbers	Measures	Answers	Pretest	Posttest
1–2	Prior school related DV exposure	Yes/No & FR	X	X
3–5	Self-efficacy	Likert Scale	X	X
6–7	Health Seeking Behavior	Yes/No	X	X
8	Health Seeking Behavior	Likert Scale	X	X
9–12B	Knowledge and Awareness	Likert Scale, Yes/No & FR	X	X
13	Pretest: Ever worked/volunteered in a healthcare setting.  Posttest: Started working/continued working since pretest.	Yes/No	X	X
13A–C	Knowledge and awareness	Likert Scale, Yes/No & FR	*X	*X
13D–F	Self-efficacy	Likert Scale, Yes/No & FR	*X	*X
14–21	Health seeking behavior	Likert Scale		
22, 23, 25, 26, 29, 33, 34, 35, 36, 37, 38, 39, 42, 44, 45, 48, <b>54#</b>	General knowledge and awareness	True/False	X	X
24, 27, 28, 30, 31, 32, 40, 41, 43, 46, 47, <b>55-59#</b>	Medical knowledge and awareness	True/False	X	X
49–53	Participant demographics		X	X
60–72	STOP-DV perception “posttest only”	Yes/No & FR		X
<b>FR= Free Response, *X= dependent on previous answers. #Questions only on 2019 survey</b>				

## REVIEW ARTICLE

# CUTANEOUS HEMOSIDEROSIS IN CHRONIC VENOUS INSUFFICIENCY: A REVIEW

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## KEYWORDS:

Chronic venous insufficiency

Cutaneous hemosiderosis

Hyperpigmentation

Lipodermatosclerosis

Venous ulcer

## Abstract

Hemosiderosis is the deposition of hemosiderin, a storage form of iron derived from the breakdown of erythrocytes. This process commonly occurs in patients with chronic venous insufficiency (CVI) due to venous hypertension and vascular ectasia. Cutaneous accumulation of hemosiderin in CVI causes brown hyperpigmentation and contributes to lipodermatosclerosis and ulceration, further highlighting the pathogenic role of iron metabolism in these disorders. In this review, we examine the pathophysiology and clinical presentation of hemosiderosis in CVI, summarize its management and prevention strategies, and explore its impact on quality of life.

## INTRODUCTION

Chronic venous insufficiency (CVI) is a common disorder that affects millions of Americans.<sup>1</sup> Clinical manifestations can vary in severity from varicose veins, which may be viewed as a cosmetic concern, to venous ulcers, which can greatly impact quality of life. Skin changes that are common in CVI include edema, dermatosclerosis, eczema and pigmentation.<sup>2</sup> The Clinical-Etiology-Anatomy-Pathophysiology (CEAP) classification system is widely used to describe the clinical range of manifestations (C1–C6) with the following categories: C1) telangiectasias or reticular veins; C2) varicose veins; C3) edema; C4) changes in skin and subcutaneous tissue secondary to chronic venous disease, which is then subcategorized into C4a) pigmentation or eczema, C4b) lipodermatosclerosis and C4c) corona phlebectatica; C5) healed ulcer; and C6) active venous ulcer.<sup>3</sup>

Hemosiderin is a storage form of iron, which is derived from the breakdown of erythrocytes.<sup>4</sup> Both melanin and hemosiderin are seen in dermal histiocytes and contribute to the observed CVI-related pigmentation. However, hemosiderin is believed to play an important role in the evolution toward the more severe CVI-related skin changes, such as lipodermatosclerosis and ulceration.<sup>5,6</sup> Thus, diligent prevention and management of

hemosiderosis-related skin changes in CVI is critical to avoid the progression of disease and to improve patients' quality of life.

## Literature search and data sources

PubMed was searched on February 20, 2021, for each of the following terms separately: "cutaneous hemosiderosis," "hemosiderosis," "iron metabolism," "chronic venous insufficiency," "chronic venous insufficiency treatment," "chronic venous insufficiency quality of life," "venous leg ulcers," "lipodermatosclerosis," "stasis dermatitis" and "hyperpigmentation."

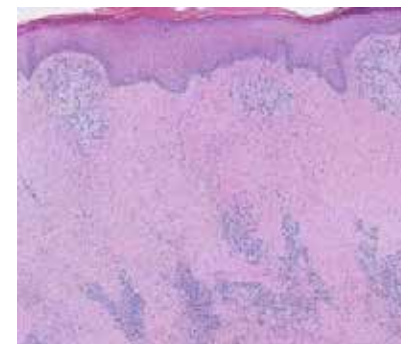
## PATHOPHYSIOLOGY

CVI is characterized by incompetent valves, which lead to reflux and venous hypertension. Chronic reflux increases pressure in the veins, which further worsens valve insufficiency and perpetuates a cycle of venous dilation.<sup>7</sup> Enlarged intercellular spaces from increased venous pressure allow extravasation of erythrocytes into the perivascular spaces, termed erythrodiapedesis.<sup>8</sup> Lysed dermal erythrocytes release hemoglobin, ferritin and hemosiderin.<sup>9</sup> Stromal hemosiderin deposition over time, as well as an increased production of melanin in the epidermis, is thought to cause hyperpigmentation in CVI.<sup>10</sup> One study found that all biopsies taken from pigmented discolored skin of limbs with varicose veins showed a higher content of melanin in the epidermis compared to controls, while stromal hemosiderin was found mostly in the severely pigmented skin areas of lipodermatosclerosis.<sup>5</sup>

Hemosiderin deposition into dermal stroma may also contribute to venous ulcer pathogenesis. Typically, the accumulation of hemosiderin deposits and iron-laden macrophages is visualized within the wound bed of chronic venous ulcers (Figures 1A–1C). In contrast, there is a decrease in hemosiderin and erythrocyte extravasation associated with venous ulcer healing.<sup>11,12</sup> Some authors suggest that hemosiderin deposits are involved in the pathogenesis of venous ulcers through the generation of reactive oxygen species (ROS).<sup>12–14</sup> ROS can lead to persistent inflammation, excessive production of matrix metalloproteinases (MMPs), increased connective tissue degradation, lipid peroxidation and ulcer formation.<sup>13</sup> This ongoing state of oxidative stress may also prevent ulcer healing.<sup>14</sup> Iron release may be directly involved with the hyperexpression of MMPs,<sup>11</sup> although it is normally controlled by the ferritin-ferroxidase system. This system is usually effective in preventing the activation of this cascade. Of significance, the HFE ("High Iron [Fe]") gene mutation that encodes for human homeostatic iron regulator protein is the most recognized genetic defect in iron metabolism. Therefore, it has been proposed that a HFE gene mutation could also be present in patients with CVI ulcers.<sup>9</sup> One study found that C282Y mutation of the HFE gene had significantly increased the risk of ulcer formation in primary chronic venous disease by more than sixfold.<sup>9</sup>

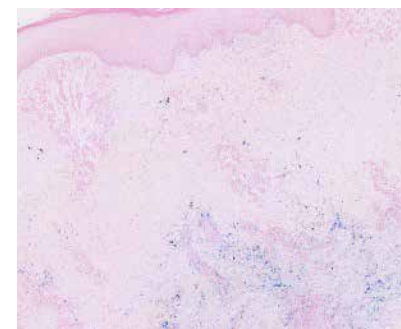
## FIGURE 1A:

Reactive proliferation of capillary lobules in upper dermis with underlying dermal fibrosis with perivascular chronic inflammation (H&E 5x)



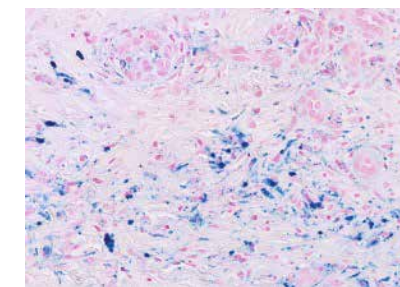
## FIGURE 1B:

Same field demonstrating stromal hemosiderin deposits highlighted with blue cellular uptake (Prussian blue 5x)



## FIGURE 1C:

Numerous hemosiderophages highlighted with iron stain by showing cytoplasmic blue staining uptake (30x of iron stain (Prussian Blue))



## CLINICAL MANIFESTATIONS

Pigmentation in CVI is typically located on the lower medial third of the lower leg but can involve the entire gaiter area. It can manifest in several ways, such as small patches of mild dyschromia or as extensive skin darkening.<sup>5</sup> A variety of skin changes associated with hyperpigmentation can occur in CVI, including stasis dermatitis, xerosis and lipodermatosclerosis (Figure 2). Stasis dermatitis is the cutaneous inflammation observed in CVI, which presents with erythematous, scaling, eczematous plaques that are most commonly located in the area of the ankle.<sup>15,16</sup> Acute forms may be associated with pruritus and can present with vesicles, weeping plaques, crusting and fissuring.

## FIGURE 2:

Lower extremities demonstrating atrophie blanche, hemosiderosis, stasis dermatitis, venous ulceration and severe lipodermatosclerosis



Stasis dermatitis can progress to lipodermatosclerosis, a chronic form of fibrosing panniculitis associated with CVI that is characterized by induration, cutaneous thickening, loss of tensile strength, and hyperpigmentation (Figure 3).<sup>17</sup> Lipodermatosclerosis is a sclerotic tightening of the soft tissues that can lead to a band/tourniquet-like constriction of the ankle region and has been classically described as an inverted "champagne bottle" appearance (Figure 4).<sup>17</sup> The "acute" form of lipodermatosclerosis refers to painful erythema, which can mimic cellulitis, although this visibly subsides with leg elevation (Figure 5).<sup>18</sup> A slower onset of lipodermatosclerosis manifests over weeks to months and is typically associated with a bilateral leg presentation and a lack of warmth and edema, leading to a favorable diagnosis of lipodermatosclerosis over cellulitis.<sup>18</sup>

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FIGURE 3:

Bilateral lower extremities with lipodermatosclerosis and hemosiderosis



FIGURE 4:

Left lower extremity demonstrating severe lipodermatosclerosis—the “inverted champagne bottle shape” with hemosiderosis



FIGURE 5:

Bilateral lower extremities with acute lipodermatosclerosis, mimicking cellulitis



## EFFECTS ON QUALITY OF LIFE

More severe manifestations of CVI include lower extremity edema, hemosiderosis and ulcerations. CVI may also cause significant pain, depression, sleep disturbance and discomfort. All of these factors can lead to a decreased quality of life (QoL).<sup>19</sup> A study of 1893 patients with CVI found that this disease had a significant negative impact on physical, psychological and the social functioning components on QoL.<sup>20</sup> A decrease in QoL was correlated with increasing severity of CVI based on CEAP classification.<sup>20</sup> CVI symptoms can also impact one's ability to perform activities of daily living (ADLs), such as standing for a long time, putting on shoes, climbing stairs, carrying heavy loads, and performing housework.<sup>21</sup> One study found that women were more likely than men to report their effect on ADLs due to CVI.<sup>21</sup>

Additionally, a large study of 16,251 patients including both sexes with venous disease found that the presence of leg symptoms, such as tiredness, heaviness and pain, positively correlated with the worsening of visible findings that included telangiectasia, varicose veins, edema, and ulcers.<sup>22</sup> The correlation between these leg symptoms and the visible signs of disease was more marked in women than men, suggesting that women may be more negatively impacted by CVI-related skin changes than men.<sup>22</sup> Despite the chronic nature of CVI, one study found that patients with a higher CEAP class were more likely to seek emergency care services for CVI-related symptoms, including heaviness in the legs, pain and swelling, suggesting that there is a greater physical, emotional, and financial burden on patients with more advanced skin disease.<sup>23</sup> The visual nature of hemosiderosis may also have a negative impact on self-confidence and self-esteem. Additionally, the use of continuous compression therapy can further contribute to unsightliness and discomfort, particularly in the summer months.

## MANAGEMENT AND PREVENTION

No specific therapies have been established to target the problem of hemosiderosis in CVI. Treatment of skin hyperpigmentation often requires a multi-therapy approach that involves in-office procedures.<sup>24</sup> While bleaching agents, such as topical hydroquinone, are the mainstay therapy for hypermelanosis, hemosiderosis is thought to be unresponsive to bleaching agents.<sup>25</sup> However, intense pulsed light and lasers have been reported to successfully treat hyperpigmentation in CVI.<sup>26,27</sup> Effective management of hemosiderosis involves treating the underlying venous hypertension and chronic stasis induced dermatitis. Conservative measures such as compression therapy, skin care, leg elevation and exercise are first-line measures for the treatment of CVI.<sup>28</sup> Skin changes induced by chronic venous stasis, such as skin darkening and lichenification, may be significantly reversed with application of systematic compression, in addition to preventing chronic stasis effects. Patients with this condition require education on the importance of daily use of compression garments due to the fundamental effect of this measure in slowing the progression of disease and potentially reversing the cutaneous changes.

Patients who have persistent symptoms and documented superficial venous reflux may benefit from a referral to a vascular

specialist to consider more invasive vascular procedures, such as radiofrequency endovenous thermal ablation, vein stripping, phlebectomy, or sclerotherapy. Patients with acute stasis dermatitis usually benefit from a high- or mid-potency topical corticosteroids once or twice daily for 1–2 weeks over affected skin.<sup>16</sup> Simultaneous compression therapy is crucial in management. A short course of systemic corticosteroids may also be considered in patients who do not respond to topical steroids, or who have secondary allergic contact dermatitis.<sup>16</sup>

Although no substantial treatment evidence exists regarding cutaneous hemosiderosis, there is significant evidence that oral pentoxifylline facilitates healing time in stasis-induced leg ulcers.<sup>29</sup> The mechanism of action has been attributed to the reduction in blood viscosity and vascular permeability when administered orally at 400 mg three times daily for a range of 2–3 months, as either monotherapy or in combination with compression.<sup>29</sup> Research also indicates that oral pentoxifylline at higher dosage (800 mg three times daily) may be more beneficial in chronic leg ulcers.<sup>30</sup> However, gastrointestinal intolerance may preclude the treatment at a higher dose. As cutaneous hemosiderosis can be a sequela of increased vascular permeability, oral pentoxifylline may be an additional useful management option.

Given the progressive nature of hemosiderosis, its prevention is key to reducing the disease burden. Initiation of CVI treatment at its early stages (CEAP 1–3: telangiectasias, varicose veins, and/or edema) is paramount. Lifestyle changes to prevent venous ulcers should be implemented in patients with CVI, both with and without hyperpigmentation. Such interventions include minimizing prolonged standing, elevating legs, compression hosiery, weight loss, avoiding local trauma, and seeking medical care when the skin is damaged.<sup>31</sup> Proposed risk factors for the development of first-time venous leg ulcers may include: a family history of CVI of maternal origin, a history of deep vein thrombosis, multiple pregnancies, occupational exposures and history of strenuous exercise.<sup>31</sup>

## CONCLUSION

CVI is an extremely common disorder with a variety of dermatologic manifestations. Cutaneous hemosiderosis is a pathogenic mechanism seen in CVI, contributing to the development of hyperpigmentation, stasis dermatitis, lipodermatosclerosis, and potentially venous ulceration through the generation of ROS. Cutaneous hemosiderosis is disfiguring, can greatly affect quality of life, and may increase the use of emergency care services. The first-line treatment to avoid hemosiderosis and to reduce its progression is preventive measures, including compression therapy, lifestyle modifications and early medical interventions.

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## REVIEW ARTICLE

## KNEE DISLOCATIONS AND MULTI-LIGAMENT KNEE INJURIES: A REVIEW

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### KEYWORDS:

Knee dislocation

Multi-ligament knee injury

Knee reduction

Traumatic knee injury

### Abstract:

Acute knee dislocations are a relatively rare type of injury that can lead to serious neurovascular compromise and ligament instability. These injuries can be potentially limb threatening if not properly identified and managed. The following review discusses the relevant anatomy of the knee joint and different classification systems of dislocations in order to highlight the complications that could occur. Timely evaluation and management, including reduction, is paramount to ensure stability and determine the need for additional imaging or urgent consultation. Knee dislocations are also associated with the unique presentation of a multi-ligament injury. This text provides an overview of multi-ligament knee injuries and the various surgical modalities currently being used. Finally, considerations are given on the role of the osteopathic approach in restoring function of the knee in the context of a dislocation.

### TERMINOLOGY, EPIDEMIOLOGY AND ANATOMY OF THE TRAUMATIC KNEE DISLOCATION

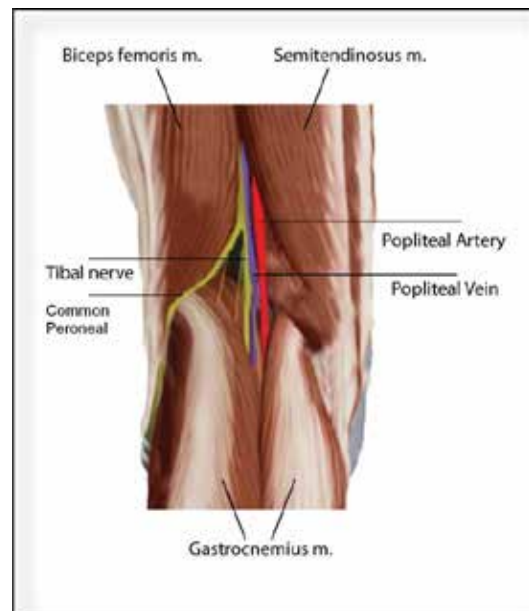
Acute knee dislocations—although rare compared to other orthopedic injuries<sup>1</sup>—are a serious type of injury that can result in severe neurovascular and soft tissue damage. This injury can be potentially limb threatening. By definition, a dislocation refers to a disruption of the tibiofemoral articulation. Dislocations occur via high velocity mechanisms (such as motor vehicle collisions), falls from heights, crush injuries or via low velocity mechanisms (such as missteps while walking or jogging). Obese patients in particular are at an increased risk for low velocity injuries. High velocity mechanisms are more likely to result in damage to multiple different soft tissue structures within and about the knee. Dislocations tend to occur more frequently in males than females (4:1) and tend to occur more frequently in the second to fourth decade of life.<sup>2</sup>

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The neurovascular structures that should be of most concern in the context of this type of injury are the popliteal artery and the peroneal nerve, due to the intimate relationship of these structures to the posterior aspect of the knee (Figure 1). The popliteal artery courses deep in the popliteal fossa before branching into anterior and posterior tibial arteries at the lower border of the popliteus muscle. During its course in the fossa, it runs close to the distal femur and is thus vulnerable to injury and can result in significant blood loss during a dislocation. The peroneal nerve courses along the medial border of the biceps femoris through the popliteal fossa and wraps around the neck of the fibula, and given its proximity to the neck of the fibula, it is also vulnerable to injury during a high velocity injury. It is specifically vulnerable during posterolateral corner injuries. This can include a posterolateral force directed at the anteromedial portion of the tibia or a force upon a flexed knee that causes varus angulation. In a varus stress, the nerve is exposed to damage through a stretching type of injury, due to location about the fibula. It has been reported that injury to the popliteal artery occurs in 16% of knee dislocations,<sup>3</sup> while injury to the peroneal nerve has been shown to occur in 25%–33%.<sup>4</sup> Prompt and accurate identification followed by appropriate treatment is critical in avoiding neurovascular compromise and improving better functional outcomes.

FIGURE 1:



As knee dislocations are often associated with multiple traumas, fracture incidence can be as high as 60%.<sup>5</sup> Tibial plateau fractures, and avulsed or sheared-off bone fragments from either the distal femur or proximal tibia, are the 2 fracture types with the highest incidence in medial or lateral dislocations. Unstable tibial plateau fractures are of further importance as they can be included in the classification of knee dislocation due to their association with capsular or ligament disruption. Moore separated these injuries from pure fractures, defining them as fracture-dislocations.<sup>6</sup> Fracture-dislocations require a combination of both bone stabilization and soft-tissue repair to achieve joint stability and therefore should be treated differently than pure dislocations.

Knee dislocations have been described into two distinct classification systems in the literature. Kennedy *et al* and others<sup>7,8</sup> use a classification system that divides dislocations into anterior, posterior, medial, lateral and rotary dislocation, which are named in terms of direction of tibial displacement with respect to the femur (Table 1). Alternatively, Schenk *et al*<sup>1,8</sup> classify dislocations by the number of structures involved (Table 2). These injuries can further be classified as closed or open, with the latter requiring urgent surgical intervention. These classification systems are useful in helping aid a clinical diagnosis and guide management and treatment decision-making. Regardless of the classification system utilized, it is imperative that the clinical provider properly identifies and reduces knee dislocations urgently.

TABLE 1:

KENNEDY <i>et al</i> CLASSIFICATION	MECHANISM	CHARACTERISTICS
Anterior	Hyperextension	Most common (40%) Sequential injury of the posterior capsule, PCL and ACL
Posterior	Posteriorly directed force across proximal tibia	Second most common (33%)
Medial	Valgus directed force across proximal tibia	Comprises 4% of dislocations
Lateral	Varum directed force across proximal tibia	Comprises 18% of dislocations
Rotary	Tibia rotates around femur	PCL remains intact

TABLE 2:

SCHENK <i>et al</i> CLASSIFICATION	ACL	PCL	COLLATERAL LIGAMENTS
KD I	Disrupted	Intact	Intact
KD II	Disrupted	Disrupted	Intact
KD III	Disrupted	Disrupted	Only one intact (either medial or lateral)
KD IV	Disrupted	Disrupted	Disrupted
KD V	KD with periarticular fracture		

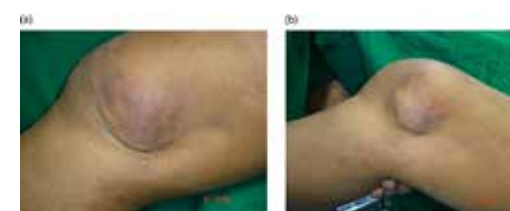
### INITIAL EVALUATION AND ASSESSMENT: KNEE DISLOCATIONS

Identification and diagnosis of knee dislocation is typically not difficult when present on the initial exam. Often these present with gross malalignment and swelling, as well as history of injury, similar to the methods noted above. Neurovascular status should be assessed as soon as knee dislocation is suspected. Closed reduction should be attempted immediately if vascular impairment is found. Pre-reduction radiographs should only be considered if the patient is neurovascularly intact.<sup>9</sup>

Once identified, an urgent attempt at a closed reduction should be made. A closed reduction can be done rapidly in the field or in an outpatient setting. This can be performed by stabilizing the distal femur and applying longitudinal traction to the tibia. Often, traction is sufficient to achieve reduction, though translatory forces to the proximal tibia in the direction that would restore normal anatomy (ie, anterior force for a posterior dislocation) is sometimes needed. Care should be taken not to apply undue pressure on the popliteal fossa to avoid additional injury to the neurovascular structures.<sup>10</sup> Once reduction has been achieved, the knee should be immobilized in 15°–20° of flexion. It is essential to attempt closed reduction prior to obtaining advanced imaging such as computed tomography (CT) or magnetic resonance imaging (MRI), as any further delay lowers the chances of restoring normal function and increases the risk of infection.

In rare cases, closed reduction should not be attempted. Clinicians should be aware of a “pucker sign” or “dimple sign,” as this indicates an irreducible knee (Figure 2). Jang *et al* described this as a puckering or entrapment of subcutaneous tissues, and possibly skin, between the femoral condyles and tibial plateau.<sup>11</sup> Most often, this is due to a posterolateral dislocation which includes an internal rotatory component. These incarcerated soft tissue structures prevent reduction, and these patients should be taken to the operating room for urgent open reduction.

FIGURE 2:



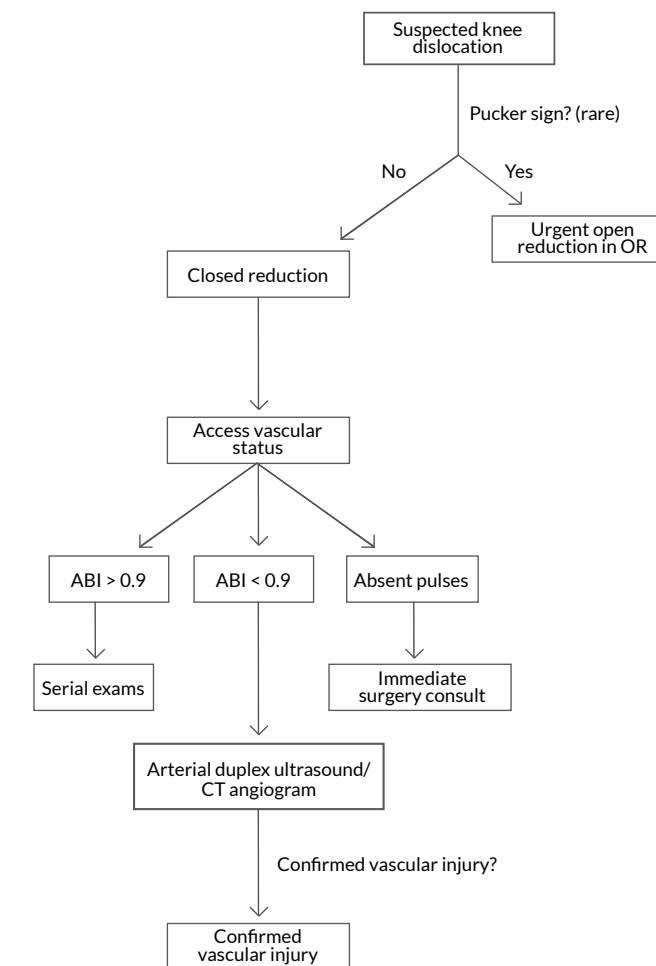
Most knee dislocations spontaneously reduce prior to presentation. Therefore, the clinician must rely heavily on the physical examination. A large effusion is not always present due to capsular disruption, and the exam may also be limited by patient discomfort and soft tissue injury. Multiplanar instability, or substantial laxity of 2 or more of the major ligaments in the knee, is sufficient for a presumptive diagnosis of knee dislocation.

Once successful reduction is achieved, neurovascular status should immediately be reassessed through exam. Previous studies have shown that recognition of occlusive injury beyond 8 hours is likely to result in irreversible limb ischemia and above the

knee amputation. Any patient with hard physical signs of vascular injury, including absent pulses, expanding hematoma, hemorrhage and bruit, should get urgent vascular surgery consultation for intraoperative angiogram. However, palpation of pulses is not adequate to rule out vascular injury. In the absence of hard physical signs, an ankle-brachial index (ABI) should be obtained and documented (Figure 3). Normal ABI values range from 1.0–1.4. If a patient is found to have an ABI above 0.9 and within the normal range, the clinician should monitor the joint with serial examinations over the next 24 hours. If a patient is found to have an ABI below 0.9, vascular compromise should be suspected, and a CT angiography or arterial duplex ultrasound should be obtained next. If vascular compromise is confirmed with imaging, vascular surgery should be consulted.

FIGURE 3:

Initial approach to a dislocated knee



Other emergent complications to be aware of with this type of injury include acute compartment syndrome (ACS) of the lower leg or foot. ACS occurs when an increased volume of fluid raises the pressure within a fascial compartment, causing cellular anoxia and ischemia. Significant pain upon passive movement and exquisite tenderness to light palpation to the compartment suggests the diagnosis, and an emergent orthopedic or general surgical consultation for fasciotomy is indicated.

After reduction of the acutely dislocated knee joint, initial immobilization via splinting or external fixation is recommended, followed by expedited treatment of vascular injuries. In the absence of an absolute acute surgical indication, such as irreducibility, open dislocation or ACS, further surgical treatment is typically delayed at least 10 days to 2 weeks. This delay is recommended to reduce swelling, increase preoperative range of motion and decrease the risk of postoperative arthrofibrosis. During this time, additional imaging can be obtained, including CT if osseous injury was detected on prior radiographs or MRI to determine the extent of soft tissue injury. After the delay, a spectrum of definitive surgical treatment options exist that can stabilize the dislocated knee from multidirectional instability, including external fixation, ligament reconstruction and ligament repair.

## MULTI-LIGAMENT KNEE INJURY IN THE CONTEXT OF A KNEE DISLOCATION

A multi-ligament knee injury (MLKI) in the context of a dislocated knee is defined as two or more ligaments with or without meniscus involvement, which can be confirmed with MRI. Within the literature, there is limited data describing the diagnosis and complex treatment of this subtype of dislocation.

The knee contains four main ligaments, each of which provide stability to the tibiofemoral articulation: the anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), medial cruciate ligament (MCL) and lateral cruciate ligament (LCL). Injury to 2 or more ligaments is a relatively rare form of dislocation as it requires greater forces applied to the knee. In fact, Shelbourne et al investigated a population of 5583 patients with knee ligament injuries and found that 495 (8.8%) were multi-ligamentous injuries.<sup>12</sup> Mook *et al* report an incidence of multi-ligament knee injuries to be .02% of all other orthopedic injuries.<sup>13</sup> Due to its rare nature, it is likely that orthopedic and sports medicine physicians might not encounter this injury type in their training or practice.

Although rare, clinicians should be prepared to address a multi-ligamentous injury, as it often poses additional challenges for the patient. Kosy *et al* found that 20% of multi-ligament knee injuries were associated with either a medial or lateral meniscal root tear,<sup>14</sup> compared to 10% of isolated ACL ruptures being associated with a lateral meniscus tear<sup>15</sup> and 3% of isolated ACL ruptures being associated with a medial meniscus tear.<sup>16</sup> Meniscus tears that occur with ligament ruptures can further increase knee instability and laxity given their role as secondary translatory stabilizers. Furthermore, Jabara *et al* found an incidence of tibiofibular joint disruption in 129 multi-ligamentous injuries to be 9%, which is a type of disruption that, if gone unrecognized, can lead to persistent instability and dysfunction of the knee.<sup>17</sup> Given the added complexity of having multiple structures damaged with a multi-ligamentous injury, it is essential for the treating provider to understand the treatment strategies to provide appropriate care.

## SURGICAL TREATMENT MODALITIES FOR THE MLKI

Multi-ligament injury in the context of a knee dislocation can be managed both nonoperatively or operatively, though nonoperative management is associated with significantly worse Lysholm scores and lower International Knee Documentation Committee (IKDC) percentages.<sup>18</sup> The Lysholm score and IKDC percentages are standardized subjective rating systems used for a variety of knee conditions that consider both symptoms and functionality and are thus useful outcome measures. Nonoperative management is typically reserved for older, sedentary patients or patients with polytrauma that require primary life or limb saving operations.

### Ligament reconstruction

Reconstruction of the disrupted ligaments (most commonly the ACL or PCL) in a MLKI is a widely utilized surgical treatment modality. The Achilles, anterior tibialis, patellar, quadriceps, and hamstring tendons can all be used as allografts, whereas the patellar, quadriceps and hamstring tendons are typically harvested in an autograft.<sup>19</sup> Graft selection depends upon both the surgeon and patient's preferences; however, allografts are used more frequently in multi-ligament reconstructions due to limited stock of autograft tissue available for multiple ligament reconstructions and to decrease donor site mortality. Allografts also have the potential benefit of shorter operating room (OR) times due to eliminating the harvesting procedure in autografting.

Despite the consensus that ligament reconstruction provides better outcomes compared to the other surgical modalities, there is conflicting data on the exact timing of when the reconstruction should be performed. A reconstruction performed within 3 weeks of injury is classified as acute. Cases in which extra-articular ligaments (medial and lateral collateral ligaments) are reconstructed acutely while intra-articular ligaments (anterior and posterior cruciate ligaments) are reconstructed at a later date are classified as staged reconstructions. Those performed after 3 weeks of the injury are classified as delayed or chronic.<sup>20</sup> A meta-analysis of 8 studies (260 patients) by Hohman *et al* found that acute intervention resulted in higher IKDC scores compared to chronic intervention. However, another systematic review by Jiang *et al* found that the staged reconstruction, in which intra-articular ligaments were constructed at a later time, resulted in better overall outcomes in 153 knees at the KD-III classification according to the Schenk *et al* classification.<sup>21</sup> Mook *et al* reviewed 396 knees and report more flexion deficits in patients managed acutely compared to patients managed chronically, yet found a significantly increased need for additional treatment secondary to joint stiffness and arthrofibrosis in the acute and staged reconstruction compared to chronic management. Despite this, staged treatments yielded the best subjective outcomes in this systematic review. Given these varied findings, a thorough discussion of the risks and benefits of each reconstruction pattern should be had during the treatment decision making process.

Reconstructing more than one ligament in a MLKI is also a widely utilized methodology. National trends from 2007–2016 revealed that 588 patients underwent a multi-ligament reconstruction and

that 30.4% of patients with a knee dislocation underwent a multi-ligament reconstruction.<sup>22</sup> This same study found that in patients undergoing multi-ligament reconstruction, 90-day complications occurred in 5.8% of patients and readmissions occurred in 8.3%. Some of the factors associated with an increased likelihood of needing additional ligament surgery after a multi-ligament reconstruction included concomitant neuroplasty, knee dislocation and prior placement of an external fixator. With this in mind, patients who have a MLKI in the setting of knee dislocation should be counselled on the increased likelihood for reoperation and/or post-operative complications. Furthermore, posterolateral corner (PLC) structures (such as the LCL, popliteus tendon, popliteofibular ligament and iliotibial band) are often injured in multi-ligament injuries and so reconstructing PLC structures using a single-graft technique in addition to the ACL and PCL yielded satisfactory outcomes.<sup>23</sup>

### Articulated external fixation

Complementing multi-ligament reconstruction with an articulated external fixation, as opposed to rigid immobilization, has been shown to improve outcomes. A study of 33 knees demonstrated that the addition of an articulating external fixator onto subacute or chronic multi-ligament reconstructions allowed for earlier range of motion, particularly flexion, along with improved Lysholm scores after at least 14 months postoperatively.<sup>24</sup> The control group in this study were knees with subacute or chronic reconstructions followed by rigid cast immobilization in full extension. Another study by Stannard et al found that a group of 157 knees undergoing acute ligament reconstruction followed by articulated external fixators resulted in only 11 failed ligaments (7%), compared to 22 failed ligaments (21%) out of 105 knees undergoing acute ligament reconstruction followed by rigid bracing.<sup>25</sup>

Mook *et al* described aggressive rehabilitation after acute ligament reconstruction in the form of earlier and more extensive post-operative mobility exercises resulting in less severe final range-of-motion deficits. Articulated external fixators seem to be an optimal mechanism by which knee range of motion can be started while providing stability and protection of the recently reconstructed ligaments.

### Ligament repair

Ligament repairs have been gaining traction more recently among surgeons with trends of improved outcomes over the past decade. Ligament repair attempts to reattach the remaining ligament to its anatomic origin, often using additional experimental techniques to augment the remaining tissue.

There are a few key advantages of a repair compared with a reconstruction. By avoiding graft harvesting and allografts, repairs seek to preserve native ligaments with its blood supply and to potentially preserve some proprioceptive function. Repairs also avoid bony tunnel drilling, and thus do not contain a risk of tunnel convergence - an unfavorable complication in multi-ligament reconstructions.<sup>26</sup> Many authors have reported good outcomes with repairs. Hua *et al.* performed repairs on all ligaments in 18 multi-ligament knee dislocations and reported

Lysholm scores of 87.5, with no knee laxity at 4.8 years follow up.<sup>27</sup> Similarly, Owens et al. performed repairs on all ligaments in 28 multi-ligament knee dislocations and reported high Lysholm scores of 89.28 Others have developed supplemental techniques such as suture augmentation and bridging scaffolds to further reduce residual knee laxity in ligament repair.

Several disadvantages exist for the ligament repair that should be considered. For example, careful consideration must be given to the eligibility of a patient for a primary repair. Repairs are often limited to patients with either a proximal or distal avulsion type tears. Repairs may also only be possible when there is sufficient integrity of the ligament fragment, as well as a sufficient length of fragment to work with. Goiney *et al* found that the ability to perform a proximal femoral PCL repair, as opposed to PCL reconstruction, required a threshold distal tibial PCL length of 41 mm or greater.<sup>29</sup> Moreover, a systematic review by Levy *et al* found that patients undergoing primary repairs experienced decreased stability and range of motion, with none of their patients returning to preinjury levels in terms of those outcomes. This was compared to 33% of patients undergoing reconstruction who achieved the same preinjury stability and range of motion.<sup>30</sup> Levy *et al* also report higher failure rates with repair of PLC structures (37%) compared to reconstruction (9%), suggesting that reconstruction is the best modality for addressing the PLC specifically.

## OSTEOPATHIC CONSIDERATIONS

The osteopathic approach to a patient with knee pain, as with patients with any other complaint, is centered upon restoring the overall well-being of the patient through hands-on manipulation and a focus on facilitating the healing process inherent to the body. For patients with non-traumatic knee pain, osteopathic manipulative treatment (OMT) is often incorporated into a comprehensive treatment plan that includes medication, physical rehabilitation and exercises, activity modification, nutrition and lifestyle counseling. For example, the use of various OMT techniques, such as manual lymphatic drainage, in addition to exercise has been shown to improve function and reduce pain from underlying osteoarthritis of the knee compared to exercise alone.<sup>31</sup>

Little is known, however, about whether OMT has been shown to improve outcomes in the acutely traumatic knee injury. Although the evidence is lacking, it is likely that lymphatic drainage and myofascial techniques applied to the lower extremity proximal and distal to the knee joint can help reduce excess inflammation and fluid that accumulates in the joint space post-trauma. In the case of lymphatics, specific “pumping” techniques have been shown in multiple studies to increase the rate at which lymph moves through the lymphatic system, thus reducing excess fluid in the interstitial space and reducing edema.<sup>32</sup> If tolerated by the patient and if the knee has been adequately managed as described above, then lymphatics techniques directed proximal or distal to the knee preoperatively may improve recovery and functionality for the patient.



It also should be noted that a traumatic knee injury imparts a significant psychological toll on patients. Patients face a long and challenging rehabilitation process, and full recovery with restoration of prior function and capability may not be possible. Studies suggest that patients who sustain an ACL injury report higher rates of depression symptoms than national averages, which can lead to worse outcomes.<sup>33</sup> This effect could be exacerbated in athletes as those who suffer a knee dislocation have a lower return to play rate, and struggle to make it back to their preinjury performance statistics.<sup>34</sup> Therefore, the provider should also address psychosocial challenges that arise from injury and changes to the patient's lifestyle and habits.

## SUMMARY AND RECOMMENDATIONS

Based on our review of the literature, we recommend that, when presented with an acute knee dislocation, clinicians should urgently reduce via closed or open techniques. After the knee has been reduced, the neurovascular status of the knee must be assessed and ABI should be documented. If the knee dislocation involves injury to more than 2 ligaments, it is deemed a MLKI, and surgical intervention should be strongly considered. The decision to surgically stabilize the knee with either an acute, staged or chronic ligament reconstruction cannot be made definitively based on the current evidence. However, augmentation with an external fixator to allow for more aggressive rehabilitation programs is agreed upon as an effective strategy. Ligament repair should be reserved for select patient populations and injury patterns, though if a patient is deemed eligible and the surgeon has adequate resources and comfort with the technique, it is a viable alternative to ligament reconstruction with similar functional outcomes. It is therefore essential for both the surgeon and patient to come to a joint decision regarding the best treatment plan based on surgical technical abilities, patient preference, and desired outcomes for this rare but complex injury pattern.

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## REVIEW ARTICLE

# ASSESSMENT AND MANAGEMENT OF ADULT PATIENTS WITH AN ACUTE ASTHMA EXACERBATION DURING THE COVID-19 PANDEMIC

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## KEYWORDS:

Acute asthma exacerbation

COVID-19

SARS-CoV-2

Telemedicine

According to the most recent national data from the U.S. Centers for Disease Control and Prevention (CDC), asthma is a chronic respiratory disease that affects approximately 8%–9% of the U.S. population and roughly 300 million worldwide. CDC data from 2019 shows 3524 deaths from asthma as the underlying cause. During the COVID-19 pandemic, it has been challenging for healthcare providers to treat asthma exacerbations due to similarities in symptom presentation. Due to the high transmission rate of COVID-19, and variation in symptoms, many primary care providers have integrated telemedicine to deliver care. Utilizing telemedicine in the clinical setting integrates social distancing, reducing the exposure and transmission rate of COVID-19 while offering patients the ability to be examined. Although telemedicine can provide care for patients in remote areas, decrease travel time and deliver care for patients with COVID-19 symptoms, many healthcare providers and patients have not had much experience with this type of technology. The purpose of this article is to provide a framework that primary care providers can use to effectively screen, evaluate and treat patients with acute asthma exacerbations during the COVID-19 pandemic.

## INTRODUCTION

Asthma is a chronic respiratory disease that is estimated to affect 300 million individuals worldwide.<sup>1,2</sup> Within the United States, acute asthma exacerbations in adults account for 1.8 million hospitalizations and has a mortality rate of approximately 13.3 deaths per million.<sup>3</sup> Asthma management focuses on adequate symptom control assessment of future risk.<sup>2</sup> Recently, the SARS-CoV-2 virus, commonly known as COVID-19, can resemble symptoms of asthma exacerbations.<sup>4,5</sup> The World Health Organization (WHO) declared COVID-19 a global pandemic in early March 2020.<sup>4,6,7</sup> As of August 27, 2021, there have been 214,468,601 confirmed cases worldwide and 4,470,969 documented deaths.<sup>8</sup>

The virus responsible for COVID-19 is highly communicable, and its presentation varies from person to person.<sup>9</sup> While most patients exhibit mild-to-moderate symptoms, others require intubation and often die from complications.<sup>10</sup> COVID-19 infections can be difficult to recognize at times. Asymptomatic carriers can transmit to other people causing unknown harm.<sup>9,11</sup> In many cases, COVID-19 infections and acute asthma exacerbations were indistinguishable due to similar presentation of symptoms.<sup>11</sup>

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Both conditions may present with shortness of breath, dry cough and chest tightness, which has made it challenging for providers to treat patients with acute asthma exacerbations during the COVID-19 pandemic.<sup>12</sup>

About 80% of asthma exacerbations are related to viral infections. Recent studies show that asthma is not a risk factor for acquiring COVID-19 infection.<sup>4,7,13–17</sup> However, a few studies suggest asthma patients have an increased risk of COVID-19 co-infection.<sup>1,4,7,17</sup> It is questionable whether there is an overrepresentation of patients with asthma symptoms, as COVID-19 may trigger asthma exacerbations. The concern for patients with asthma is reasonable, as COVID-19 can infect upper and lower airways.<sup>13</sup>

Due to the high transmissibility and heterogeneous variance in symptoms, many providers have started using telemedicine to deliver healthcare services to patients with COVID-19-like symptoms.<sup>18–20</sup> Technological advancements have allowed clinicians to use audio or audiovisual communication methods to provide healthcare services remotely to minimize the possibility of exposure.<sup>18–21</sup> This has the potential of lowering infection rates by decreasing risk of disease propagation.<sup>18</sup>

The focus of this review article is to provide a framework for providers to use to effectively screen and triage individuals, examine, diagnose, and treat patients with acute asthma exacerbations. We also seek to provide insight into strategies for follow-up visits.

## SCREEN AND TRIAGE

### COVID-19 transmission

According to the WHO, as of August 27, 2021, there have been 214,468,601 confirmed cases documented worldwide.<sup>8</sup> When compared with other known coronaviruses, the COVID-19 virus has a higher transmission rate.<sup>22</sup> The COVID-19 virus enters and infects host cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor in the lung cells of its host.<sup>4,22</sup> Recent research suggests there may be reduced symptom severity in patients infected with COVID-19 who also have asthma.<sup>4</sup> It is hypothesized that reduced ACE2 expression in lung cells of asthma patients reduces viral entry which accounts for the decrease in symptom severity.<sup>4</sup> Cellular entry and viral replication of COVID-19 is theorized based on SARS-CoV and MERS-CoV-2 coronaviruses, which share genetic sequence similarities.<sup>5</sup> COVID-19 shows a higher transmission competence in comparison with the two previous coronaviruses mentioned.<sup>22</sup> In a research study conducted by the Severe Asthma Research Program-3, inhaled corticosteroid therapy was associated with decreased ACE2 expression in sputum samples.<sup>4</sup> This can potentially account for the decrease transmissibility of viral particles into host cells with asthma and emphasizes the importance of asthma treatment, which usually involves using inhaled corticosteroids.

### Screening for COVID-19 symptoms and triaging patients

Due to the high transmission rate of COVID-19, the WHO now recommends prescreening all individuals entering a healthcare facility to limit exposure and transmission. In addition, patients should be prescreened to limit the contact of medical staff and patients to anyone who is at high risk of being infected. Healthcare workers performing the screening questionnaires are recommended to wear a mask and be at a distance greater than 1 meter (slightly greater than 3 feet) from individuals being screened.

The U.S. Centers for Disease Control and Prevention (CDC) has developed a questionnaire that can be used to screen anyone entering a healthcare facility.<sup>23</sup> The questions assess whether individuals have experienced concerning symptoms such as fevers, chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, loss of taste or smell, sore throat, congestion or runny nose, nausea, vomiting, or diarrhea within the last 48 hours.<sup>23</sup> It also evaluates whether individuals have been in close contact—within 6 feet and for 15 or more minutes—of someone with known COVID-19 infection or have symptoms suggestive of infection in the last 2 weeks. The questions also ascertain whether the individual entering the facility has been quarantining because they believe they may be sick. Lastly, the questionnaire inquires whether the individual was recently tested for COVID-19 and if they are awaiting results. If the individuals answer yes to any of these questions, it is recommended they are not approved to enter the healthcare facility to minimize exposure to any staff or patients, which may result in them becoming potential COVID-19 carriers.<sup>23</sup>

The American Medical Association (AMA) has also created a prescreening template that shares many of the same questions

as the CDC, in addition to questions that evaluate whether the individual was recently hospitalized or if they have visited a nursing home, long-term care facility or healthcare facility in the last 30 days. It also asks if the individual or anyone in their household has traveled outside of the country and if the individual is a healthcare provider or an emergency responder.<sup>24</sup> Per AMA recommendations, if a person answers yes to any of these questions, a medical professional should review their case and use clinical judgment to determine whether the patient may keep their appointment and enter the facility.

After employing remote triage or in-person prescreening questions, providers should risk stratify patients and determine whether it is appropriate to have a face-to-face interview or telemedicine encounter based on screening questions discussed. For example, patients with acute asthma exacerbations will unlikely meet the criteria for an in-person visit, as they will likely exhibit shortness of breath, chest tightness or cough.

If at any point during the screening process the patient begins to exhibit trouble breathing, persistent chest pain or pressure, new confusion, inability to stay awake or cyanosis over the lips or face, they should receive emergency medical care immediately, as these can be signs of a life-threatening condition.<sup>11</sup>

Although many healthcare practices have instituted prescreening procedures with COVID-19 testing, there are no current global testing guidelines or recommendations in place. Accuracy of testing and COVID-19 infection stage impacts results. COVID-19 testing can be performed with reverse transcriptase-polymerase chain reaction (RT-PCR) or rapid antigen testing. RT-PCR has a sensitivity between 71%–98% and has a false negative rate between 2%–29%.<sup>25</sup> The accuracy of testing samples also is impacted by the quality and location of the sample obtained. Lastly, the stage of the COVID-19 infection also affects the reading. False-negative testing results could cause false reassurance; therefore, it is best to use clinical judgment.<sup>25</sup>

## TELEMEDICINE, EXAMINATION, TREATMENT AND FOLLOW-UP

### Telemedicine encounters

Telemedicine, or telehealth, is a form of delivering health care remotely through audio or audio-video interactions between providers and patients.<sup>19–21,26,27</sup> Telemedicine provides a cost-effective and convenient method of delivering healthcare services while reducing the exposure of potential infections to staff and other patients.<sup>20</sup> These virtual consultations have played a vital role during the COVID-19 pandemic to ensure continuity of care while reducing the risk of infection within the community. Conducting telemedicine encounters for patients with asthma has been particularly beneficial. In a meta-analysis conducted by McLean *et al*<sup>10</sup> randomized control trials demonstrated that telemedicine improved the quality of life for asthmatic patients.<sup>8</sup>

This form of healthcare service has increased since the onset of the COVID-19 pandemic. Before this pandemic, reports indicated that only 11.8% of family physicians and pediatricians practicing in the United States used telemedicine services as a part of their

practice.<sup>26</sup> Two months after the onset of the COVID-19 pandemic, this increased considerably, as only 9% of primary care physicians did not offer telemedicine visits to their patients.<sup>26</sup>

Physicians and other healthcare providers differ in their level of training with telemedicine. It can be challenging to implement telemedicine visits if either healthcare personnel or patients have not adequately trained to use software or telemedicine equipment.<sup>20,27</sup> With the rapid progression of the COVID-19 pandemic, telemedicine visits are often a new learning experience for many providers and patients as well. Although the telemedicine encounter may be as thorough as an in-person visit when obtaining a history of present illness, it still has limitations. By forgoing a face-to-face physical exam, a provider may miss minor cues from the patient and would be unable to perform in-office testing, such as peak expiratory flow, or imaging, such as a chest X-ray.<sup>12</sup> Relying on a digital method of communication impacts the provider-patient relationship, where the clinician or patient may appear to be dispassionate or distracted on the screen during the encounter. This perception can result in a loss of confidence by either party.<sup>3</sup>

It is important to note local, state and federal guidelines regarding telemedicine visits as they vary geographically. Laws should be followed according to jurisdiction.

### Patient history and symptom severity

Using open-ended questions, ask the patient to describe their symptoms and discuss what brings them in for evaluation.<sup>12</sup> While many of these symptoms may have been asked during the initial prescreening period, it is imperative to get a thorough history from the patient, as questions may have been missed or misunderstood.

As the patient responds to the questions, closely observe how they sound when they speak and note the tone of their voice. It is essential to pay close attention to whether they sound breathless or are struggling to complete sentences. This determines if they are in respiratory distress and whether immediate action is needed.<sup>12</sup> If the patient cannot complete sentences, or if the respiratory rate is greater than or equal to 25 breaths per minute, treat their condition as severe or life-threatening and seek immediate medical intervention. For patients with pre-existing asthma, ask if their symptoms feel like an asthma attack.<sup>12</sup> Figure out whether they have had any previous hospitalizations for asthma and whether their asthma symptoms are generally under control (eg, baseline asthma symptoms).<sup>2</sup> Inquire about their current medication usage. Review current medications they may be taking, including any inhaled or oral corticosteroids, long-acting beta-agonists, or combination inhalers. Next, determine whether they have been using their medications as prescribed or recommended. Use their history in conjunction with their symptoms to further risk stratify and assess the severity of the disease.<sup>2</sup> It is also imperative to ask the patient about any recent or new hospitalizations and to determine if they have an action plan already in place, while assessing the patient's understanding to implement said plan.<sup>2</sup>

COVID-19 symptoms are wide-ranging and include fever, dry cough, gastrointestinal symptoms (eg, nausea, vomiting, diarrhea), fatigue, myalgias, chest tightness, dyspnea, tachycardia, and headache.<sup>7,11,12,14,15,28</sup> Additionally, patients suffering from COVID-19 may also exhibit sore throat, loss of taste, ageusia and headaches.<sup>9,29</sup> According to the CDC, after exposure to the COVID-19 virus, symptoms may appear anytime between 2–14 days.<sup>11</sup> It is essential to recognize, however, that a single sign cannot diagnose or rule out COVID-19.<sup>29</sup>

In many cases, taking a thorough history can help distinguish asthma from COVID-19.<sup>12</sup> In comparison with COVID-19, asthma does not typically present with fevers, loss of taste or smell, or gastrointestinal symptoms.<sup>12</sup> Although no one symptom can be used for differentiation, the presentation should be considered, along with the screening questions to determine whether they exhibit COVID-like symptoms, have had exposure to someone with COVID-19 or have a considerable risk of having contracted the virus.

Once it has been determined the patient is experiencing an asthma exacerbation, there are several standardized tools for risk stratification and assessing symptom control. The Global Initiative for Asthma (GINA) published the *Global strategy for asthma management and prevention*, which clinicians can use to direct management and to assess symptom control and risk factors for poor asthma outcomes.<sup>2</sup> Other standardized questionnaires include the asthma control test and the Asthma Control Questionnaire developed by the American Thoracic Society.

Emergency medical care should be initiated during any part of the encounter if a patient has trouble breathing, chest pain, chest pressure, new confusion, inability to stay awake, or cyanosis. Patients should be transferred to a facility to receive immediate care<sup>11</sup>.

### Risk factors and comorbidities

While most research does not support asthma as a risk factor for a severe disease of COVID-19, many chronic conditions have been associated with worsening outcomes.<sup>7,13</sup> Comorbidities including hypertension, chronic obstructive pulmonary disease, type 1 diabetes, cardiovascular disease (heart failure, coronary artery disease, or cardiomyopathies), obesity, pregnancy, sickle cell disease, smoking, age greater than 65, immunocompromised status, cancer, chronic kidney disease, are risk factors for severe COVID-19 infection.<sup>1</sup> Some studies include the male sex as being at notable risk of developing severe complications.<sup>14,15</sup> Due to limited data, it is unknown whether other underlying medical conditions also increase the risk of severe illness from COVID-19. Adults of any age might also be at an increased risk for severe illness if they have moderate-to-severe asthma, cerebrovascular disease, cystic fibrosis, hypertension, an immunocompromised state, neurologic conditions such as dementia, body mass index greater than 25 but less than 30 kg/m<sup>2</sup>, pulmonary fibrosis, thalassemia or type 1 diabetes. The CDC does not list hypertension as an increased risk factor for severe disease as opposed to other studies.<sup>1</sup> Table 1 summarizes risk factors and symptoms associated with COVID-19.

The WHO lists age greater than 60 years old, diabetes, hypertension, cardiac disease, chronic lung disease, chronic kidney disease, immunosuppression, cancer and smoking as having higher mortality in COVID-19.<sup>30</sup>

Obesity, chronic rhinosinusitis, gastrointestinal reflux disease, exposure to confirmed food allergies, anxiety and depression, are risk factors for poor asthma outcomes.<sup>2</sup> Additional risk factors include smoke exposure, allergen exposure if sensitized and air pollution, which may worsen asthma symptoms. These risk factors and medical adherence should be addressed to decrease

the likelihood of poor asthma outcomes and aid in secondary prevention. Several other factors can also be considered, including major socioeconomic problems, low FEV1 < 60%, sputum or blood eosinophilia, elevated exhaled nitric oxide test (FeNO) in allergic adults and individuals taking inhaled corticosteroids should be assessed, as those are also significant risk factors. Lastly, patients who have ever been intubated or have been in an intensive care unit for asthma, having at least one severe exacerbation in the last 12 months are at higher risk of poor outcomes.<sup>2</sup>

TABLE 1:

Comparing symptoms of COVID-19, asthma, influenzas A and B, and the common cold

CONDITION	SYMPTOMS	SPECIAL NOTES
<b>COVID-19</b>	Fevers/chills Cough Fatigue Anorexia Shortness of breath/difficulty breathing Myalgias Sore throat Nasal congestion Headache Diarrhea Nausea Vomiting Loss of taste (ageusia) Loss of smell (anosmia) Persistent	Loss of taste and loss of smell usually occur before respiratory symptoms.  Typically, a person develops symptoms 5 days after being infected; however, symptoms can occur as early as 2 days after infection or as late as 14 days after infection
<b>Asthma</b>	Cough Wheezing Shortness of breath Dry/pruritic skin rash Headache Fatigue	Fever is not typically a symptom of asthma
<b>Influenzas A and B</b>	Fever Cough Sore throat Runny or stuffy nose Muscle or body aches Headaches Fatigue Vomiting Diarrhea	Symptoms usually develop 1–4 days after infection.  Vomiting and diarrhea are more common in children than adults.
<b>Common Cold</b>	Nasal congestion Mucous production Fevers not typical Sneezing Sore throat Runny or stuffy nose Mild to moderate chest discomfort Cough Fatigue	Symptoms have a lot of overlap with influenza symptoms; however, symptom onset is gradual as compared to flu, which is abrupt.  Cold symptoms are generally milder than flu symptoms.

TABLE 2:

Underlying medical conditions at increased risk for severe illness from COVID-19

<b>Risk factors associated with COVID-19</b>	Age > 60 years Type 2 diabetes Hypertension Cardiac disease* Chronic lung disease** Cerebrovascular disease Chronic kidney disease
<b>Conditions that may increase the risk of severe illness from COVID-19 infection</b>	Moderate-to-severe asthma Cerebrovascular disease Cystic fibrosis Hypertension Immunocompromised state Neurological conditions*** Liver disease BMI > 35 kg/m <sup>2</sup> & <30 kg/m <sup>2</sup> Pulmonary fibrosis Thalassemia Type 1 diabetes
<b>Risk factors for poor asthma outcomes</b>	Rhinitis Chronic rhinosinusitis Gastroesophageal reflux disease Obesity Obstructive sleep apnea Depression Anxiety Confirmed food allergies Smoke/ allergen exposure

\*Cardiac diseases include heart conditions (eg, coronary artery disease, cardiomyopathies and heart failure)  
\*\*Chronic lung conditions include pulmonary conditions (eg, chronic obstructive pulmonary disease)  
\*\*\*Neurological conditions include conditions such as dementia

including assessing if they seem breathless or fatigued. Also, pay attention to whether patients are holding onto their chest or using accessory muscles while breathing, as this raises immediate concerns for respiratory distress. Listen to their vocal tone and whether they appear anxious. If a patient has a portable pulse oximetry device, ask the patient to show their readings.<sup>12</sup> Portable spirometry devices are also commercially available and able to be connected to the mobile phone using Bluetooth technology.<sup>32</sup>

**In-person assessment**

When performing in-person encounters, it is important to use personal protective equipment, including wearing a gown, gloves, eye protection, face mask, and possibly a respirator when interacting with patients.<sup>15,33</sup> The CDC recommends implementing universal source control measures, as well as executing source control, which includes wearing face masks, cloth masks, or respirators to decrease the spread of respiratory particles.<sup>34</sup> Additional recommendations include encouraging physical distancing of at least 6 feet by arranging seats accordingly and limiting the number of people in the facility. In confined areas, coughing, sneezing or any procedure that increases the presence of transmission (eg, intubations, extubations, bronchoscopy, nebulizer therapy, spirometry, sputum induction and rhinoscopy) significantly increase the risk of transmission. These procedures increase the number of aerosolized particles and are considered high-risk exposures, which should be avoided if possible.<sup>15</sup>

**Imaging and laboratory testing**

The CDC recommends testing for COVID-19 for the following people: those who have symptoms of COVID-19, have been in close contact with someone confirmed to have COVID-19 (ie, within 6 feet for a total of 15 minutes or more) or have taken part in high-risk activities, such as traveling or attended a large gathering. If tested, it is recommended to self-quarantine or isolate at home pending test results. For negative tests, it is vital to note that false negatives are possible. The negative laboratory result means patients were unlikely to have been infected when the sample was collected. However, there is always a chance a patient has been exposed since taking the test.<sup>35</sup>

Although no specific tests are recommended for asthma patients who exhibit COVID-19 symptoms, asthma patients had lower levels of ferritin, c-reactive protein and lactate dehydrogenase, which suggests a decreased inflammatory burden in asthmatic patients who are co-infected with COVID-19.<sup>1</sup>

Chest computerized tomography (CT) findings show that patients with COVID-19 infections had bilateral and peripheral ground-glass and consolidative pulmonary opacities.<sup>25,36</sup> The CDC and the American College of Radiology do not recommend using a CT as a screening tool or a first-line test to diagnose COVID-19. CT of the chest should be used sparingly and for symptomatic patients.<sup>37</sup>

**Treatment of acute asthma exacerbation**

After observation and evaluation, medical management of an asthma exacerbation should be initiated immediately. Beta-agonists and steroids remain the cornerstone of medical therapy for an acute asthma flare. Patients should be started on a short-

acting beta-agonist (SABA) promptly after initial assessment and corticosteroids should be administered concurrently. SABA medications are preferentially delivered by pressurized meter dose inhalers (pMDI) with a spacer. The pMDIs can be used for up to 10 puffs every 20 minutes. If possible, measure lung function after 1 hour of treatment. Steroids can be administered either orally or intravenously, mainly depending on the severity of the illness. Current dosing guidelines recommend 40–50 mg of prednisolone in an adult patient. Supplemental oxygen is also often used in initial management to maintain a 93%–95% targeted oxygen saturation in adults. If patients are still symptomatic after SABA treatment, inhaled ipratropium bromide can be added to the treatment regimen. For severe exacerbations, arrange transfer to an acute care facility, add ipratropium bromide or consider administering a SABA by nebulizer.<sup>2</sup> It is not recommended to routinely perform chest radiographs, obtain blood gases or prescribe antibiotics for acute asthma exacerbations.<sup>2</sup>

Box 11 of the Pocket Guide for Asthma Management and Prevention provided by GINA summarizes the approach to assessment and management of asthma exacerbations for patients presenting in the primary care setting.<sup>2</sup>

FIGURE 1:

Assessment of symptom control and future risk obtained from the Global Initiative for Asthma *Pocket Guide for Asthma Management and Prevention*

**Box 4. Assessment of symptom control and future risk**

In the past 4 weeks, has the patient had:	Level of asthma symptom control		
	Well controlled	Partly controlled	Uncontrolled
Daytime symptoms more than twice/week?	Yes <input type="checkbox"/> No <input type="checkbox"/>	None of these	1–2 of these
Any night waking due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>		
SABA reliever needed more than twice/week?	Yes <input type="checkbox"/> No <input type="checkbox"/>		
Any activity limitation due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>		

**B. Risk factors for poor asthma outcomes**

Assess risk factors at diagnosis and periodically, at least every 1–2 years, particularly for patients experiencing exacerbations. Measure FEV<sub>1</sub> at start of treatment, after 3–6 months for personal best lung function, then periodically for ongoing risk assessment.

Having uncontrolled asthma symptoms is an important risk factor for exacerbations. Additional potentially modifiable risk factors for exacerbations, even in patients with few asthma symptoms, include:

- Medications: ICS not prescribed; poor adherence; incorrect inhaler technique; high SABA use (with increased mortality if >1x200-dose canister/month)
- Comorbidities: obesity; chronic rhinosinusitis; GERD; confirmed food allergy; anxiety; depression; pregnancy
- Exposures: smoking; allergen exposure if sensitized; air pollution
- Setting: major socioeconomic problems
- Lung function: low FEV<sub>1</sub>, especially if <60% predicted; higher reversibility
- Other tests: sputum/blood eosinophilia; elevated FeNO in allergic adults on ICS

Other major independent risk factors for flare-ups (exacerbations) include:

- Ever being intubated or in intensive care for asthma; having ≥1 severe exacerbations in the last 12 months.

GERD: gastroesophageal reflux disease; FeNO: exhaled nitric oxide; ICS: inhaled corticosteroid; SABA: short-acting β<sub>2</sub>-agonist. See next page for rest of table.

**Box 4. Assessment of symptom control and future risk (continued)**

**B. Risk factors for poor asthma outcomes (continued)**

Risk factors for developing fixed airflow limitation include:

- Preterm birth, low birth weight, greater infant weight gain
- Lack of ICS treatment
- Exposures: tobacco smoke, noxious chemicals, occupational exposures
- Low FEV<sub>1</sub>
- Chronic mucus hypersecretion
- Sputum or blood eosinophilia

Risk factors for medication side-effects include:

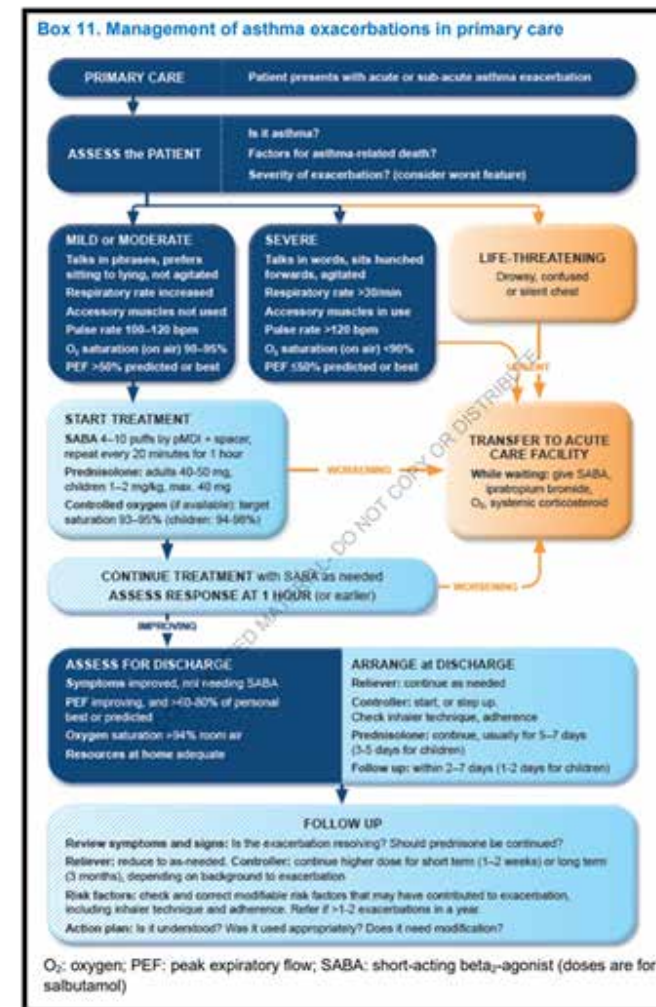
- Systemic: frequent OCS; long-term, high-dose and/or potent ICS; also taking P450 inhibitors
- Local: high-dose or potent ICS; poor inhaler technique

ICS: inhaled corticosteroid; OCS: oral corticosteroid

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FIGURE 2:

Management of asthma exacerbation in primary care



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**Osteopathic manipulative treatment**

Osteopathic manipulative treatment, or OMT, has historically been helpful as an adjunctive method to improve symptoms. There are several mechanisms by which OMT is theorized to benefit asthma management including biomechanical, respiratory/circulatory, neurologic and behavioral mechanisms.<sup>38</sup> Specifically, the biomechanical and respiratory mechanisms of OMT have been shown to enhance mechanical functioning of thoracic cage, balance the autonomic nervous system and improve overall chest wall function.<sup>38</sup> One study performed by Guiney *et al.* showed improved peak expiratory flow rates improved by 22%.<sup>38</sup> However, the authors could not find any specific literature to support using OMT treatment for asthma. Statistical data OMT usage was likely to have decreased during the COVID-19 pandemic.

No specific guidelines have been released regarding treatment recommendations for using OMT in the management of asthma exacerbations. Healthcare providers must carefully judge

whether their symptoms are suggestive of a COVID-19 infection. The American Osteopathic Association and American Academy of Osteopathy have developed an online learning activity that provides clinicians a structure for clinicians to use to improve pulmonary function COVID-19 for patients suspected of having a COVID-19 infection. These techniques are designed to be used to treat COVID-19; however, they could potentially also be used to improve lung function in asthma patients.

### Review response and follow-up

Before discharge, it is imperative to arrange ongoing treatment and follow-up care. For most patients, providers will prescribe regular controller therapy or increase the patient's current dose, to reduce the risk of further exacerbations. Be sure to check the patient's inhaler technique and adherence. It is always helpful to provide an interim written asthma action plan for reference.

Exacerbations often represent failures in chronic asthma care, and they provide opportunities to review the patient's asthma management. A healthcare provider must follow up with all patients regularly until symptoms and lung function return to normal or their previous baseline. Consider referral for specialist advice after hospitalization or patients who repeatedly visit the emergency department for asthma exacerbations.<sup>2</sup>

Follow-up appointments should be arranged within 2–7 days after any exacerbation. At follow-up visits, the physician should review modifiable risk factors, assess the patient's understanding of their medication usage and inhaler technique skills, and revise their written asthma plan, if necessary. Regular review of these measures is both cost-effective and associated with improvement in asthma control and outcomes.<sup>2</sup>

### CONCLUSION

Asthma is a chronic medical condition, which affects a significant portion of the U.S. and world population.<sup>2</sup> An acute asthma exacerbation can be challenging to differentiate from COVID-19 symptoms.<sup>4,5</sup> This has made it difficult for outpatient providers to treat patients, and as a result, there has been a surge in the use of telemedicine.<sup>5,18,26</sup> Due the COVID-19 virus's high transmissibility, it is recommended to screen patients to determine if it is appropriate to be evaluated in person or via telemedicine.<sup>18–20,30</sup> Next, it is essential to assess symptoms, assess risk factors, obtain a history and perform a physical exam. Depending on your clinical suspicion, if an acute asthma exacerbation is suspected, immediately begin treatment. It is important to recognize life-threatening symptoms and transport them to an emergency care facility immediately if they should occur. Asthma treatment requires a multifaceted approach aimed toward symptom control, risk factor modification, development of action plan and treatment. Follow-up with patients and revisit asthma management even if symptoms are well controlled for long-term effectiveness.<sup>2</sup> While treating patients' acute symptoms, it is vital to recognize triggers and modifiable risk factors such as smoking. Although there are osteopathic manipulative techniques for asthma, there are no specific guidelines released regarding treatment recommendations.

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## BRIEF REPORT

# THE EFFECTS OF OMT ON PROGRESSIVE MASSIVE FIBROSIS: A BRIEF REPORT OF AN ADJUNCTIVE THERAPY TO IMPROVE RESPIRATORY FUNCTION IN APPALACHIAN COAL MINERS

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## KEYWORDS:

Appalachia

Black lung

Osteopathic manipulative treatment

Progressive massive fibrosis

Recently in central Appalachia, there has been a resurgence of the more complicated form of black lung disease known as progressive massive fibrosis (PMF). This brief report was aimed at determining the effects osteopathic manipulative treatment (OMT) could have to improve the lives of these individuals. This brief report involved a former Appalachian coal miner diagnosed with PMF. Over the course of a year, the patient was seen and treated with OMT. Though the patient reported improvement in his activities of daily living compared to previous, there was no significant data according to spirometry or quality of life metrics. This study illustrates that OMT has the potential to provide adjunctive treatment for patients with PMF. Limitations due to sample size and socioeconomic deficits of former Appalachian coal miners warrant further study.

## INTRODUCTION

Coal mining has played a significant role in the economy and stability of individuals who call the Appalachian Mountains their home.<sup>1</sup> Unfortunately, there are several work hazards associated with mining, specifically the inflammatory effects that inhaling coal dust causes to the alveoli—ultimately scarring lung tissue.<sup>2</sup> Over time, this damage leads to 1–2 mm inflammatory nodule cells, collagen fibers, and black dust—all of which indicate coal worker's pneumoconiosis (CWP).<sup>2</sup> In some instances, CWP can progress to a more complicated case of black lung known as progressive massive fibrosis (PMF), which is defined as parenchymal lesions  $\geq 2$  cm, which are most often found in the upper lung fields.<sup>3</sup>

Brandon Crum, DO, a radiologist in Eastern Kentucky, identified 60 cases of PMF in active and former coal workers diagnosed at his practice from January 2015 through August 2016.<sup>4</sup> This sample highlights an unexpected rise in coal workers suffering from PMF as the disease was thought to be essentially eradicated, falling to a prevalence of 0.08%, according to the Coal Worker's Health Surveillance Program (CWHSP) in 1998. Since that time, however, the prevalence of PMF cases has been on a logarithmic rise reaching 3.23% in 2012 and passing 5% in 2015.<sup>5</sup>

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Osteopathic manipulative treatment (OMT) provides a hands-on treatment that has been found to improve the respiratory function in several pulmonary etiologies.<sup>6</sup> In patients who have been hospitalized with pneumonia, various OMT techniques have been found to reduce a patient's length of hospital stay, duration of intravenous antibiotics and incidences of respiratory failure and death when compared to those who received conventional care alone.<sup>7</sup>

This report illustrates the effects of OMT as a possible adjunctive therapy to improve pulmonary function and quality of life in a former Appalachian coal miner diagnosed with PMF.

## PATIENT INFORMATION

### Presentation

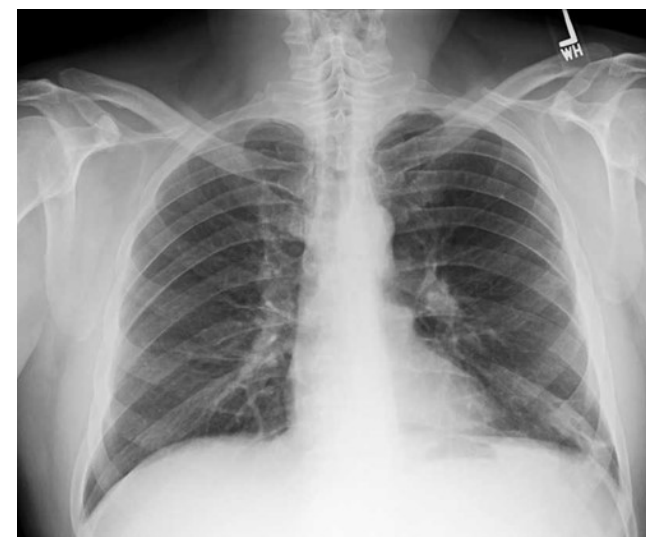
This is a 56-year-old male who worked underground in the Appalachian coal mines for 32.5 years. Despite the fact he has no history of tobacco use and was otherwise a healthy individual, the patient developed significant shortness of breath. He was diagnosed with chronic obstructive pulmonary disease (COPD) at that time and was found to have coal worker's pneumoconiosis. Due to his crippling shortness of breath, the patient was placed on disability on July 30, 2015.

Over the past several years, his symptoms have been chronic, worsened with exertion, and managed with budesonide/formoterol (Symbicort®) twice daily. Prior to the onset of this

study, the patient's most recent chest X-ray classified his black lung disease as category A progressive massive fibrosis, defined as one or more large opacities each  $>10$  mm in diameter with combined dimensions  $<50$  mm<sup>2</sup>, as seen in Figure 1.<sup>8</sup> Upon initial presentation at the onset of the study, the patient reported severe shortness of breath at rest that, in combination with a non-productive cough and exertion, had caused several syncopal events due to inadequate oxygenation.

### FIGURE 1:

This chest X-ray shows the patient's first imaging obtained on August 26, 2016, at the time of PMF diagnosis. Looking at the peripheral lung fields, there are small circular opacities throughout that are consistent with coal worker's pneumoconiosis, while the middle- to upper-lung fields show large circular areas of enhancement consistent with PMF.



## Patient history

Past medical history was notable for diminished sensation of the right lower extremity compared to the left from a mining accident that involved a ruptured calf muscle and right fibular fracture. He has chronic cervical paraspinal tenderness due to a disk herniation at C3/C4; a torn rotator cuff repaired in January 2009, causing chronic right shoulder pain; as well as chronic low back pain, all managed with diclofenac twice daily. He has no allergies, does not drink, use tobacco products or use illicit drugs, and his family history is non-contributory.

## Examination

Exam findings were consistent with a breathing pattern of mixed obstructive/restrictive lung disease showing bilateral inspiratory and expiratory wheezing, commonly seen in PMF cases.<sup>9</sup> The patient was tachypneic, but vitals were otherwise normal. Osteopathic structural examination revealed significant somatic dysfunction, most notably regarding specific suture restriction, upper extremities, ribs, thoracic and cervical regions as seen in Tables 1A and 1B.

### TABLE 1:

These tables denote the structural findings found during each patient visit throughout the study where structural regions pertain to the area of assessment with corresponding diagnosis. Common nomenclature for diagnosing the cervical-lumbar spine denotes a diagnosis in the degree of flexion/extension, side bending/rotation or neutral position based on Fryette's Laws of spinal motion such that a diagnosis of C-6 ERSL indicates that on structural examination, the sixth cervical vertebrae appeared extended, rotated and side bent to the left.<sup>11</sup> Table 1A corresponds to the patient's first 5 treatments with OMT, while Table 1B corresponds to the last 5 treatments with OMT.

\*See following page for Tables 1A and 1B.

TABLE 1A:

Treatment sessions 1-5

STRUCTURAL REGION	TREATMENT SESSION #1 DIAGNOSIS	TREATMENT SESSION #2 DIAGNOSIS	TREATMENT SESSION #3 DIAGNOSIS	TREATMENT SESSION #4 DIAGNOSIS	TREATMENT SESSION #5 DIAGNOSIS
<b>Cranial</b>	-	Suture restriction at the left and right occipitomastoid Right occipital petrous Right sphenoid squamous	Suture restriction at the left and right occipitomastoid Right occipital petrous Right sphenoid squamous	-	-
<b>Cervical</b>	C-6 ERS <sub>L</sub>	OA ES <sub>R</sub> R <sub>L</sub>	OA ES <sub>L</sub> R <sub>R</sub> C-3 ERS <sub>L</sub> C-4 ERS <sub>L</sub>	-	OA FS <sub>L</sub> R <sub>R</sub> C-3 FSR <sub>L</sub> C-5 ERS <sub>L</sub>
<b>Thoracic</b>	T-1 ERS <sub>L</sub> T-2 ERS <sub>L</sub> T-8 ERS <sub>L</sub> T-9 NS <sub>L</sub> R <sub>R</sub>	T-1 FRS <sub>L</sub>	T-2 NS <sub>L</sub> R <sub>R</sub> T-4 NS <sub>L</sub> R <sub>R</sub> T-6 NS <sub>R</sub> R <sub>L</sub>	T-2 NS <sub>L</sub> R <sub>R</sub> T-4 NS <sub>L</sub> R <sub>R</sub>	T-2 NS <sub>L</sub> R <sub>R</sub> T-4 NS <sub>L</sub> R <sub>R</sub> T-10 ERS <sub>L</sub>
<b>Lumbar</b>	L-5 ERS <sub>L</sub>	-	-	-	-
<b>Upper Extremity</b>	Bilateral ulnar deviated laterally Radial head posterior Bilateral distal and proximal carpal tunnel restriction Bilateral interosseous myofascial restriction Left AC joint inferior Right SC joint superior	Right SC superior Right bicep tendon Tightness Restriction at right upper and lateral scapula	-	Right AC joint inferior and right SC superior/ anterior	Right SC superior and right AC inferior Left SC joint inferior Right radial head posterior
<b>Lower Extremity</b>	-	-	-	Right distal fibula posterior	-
<b>Ribs</b>	Superior sternal restriction Ribs left 6-10, 3-5 and 1 exhaled	Ribs left 1-2 and 6-10 exhaled Ribs right 6-10 exhaled	-	Distal and proximal sternal restriction Ribs left 6-10 exhaled	Bilateral rib 1 exhaled
<b>Innominate/Pelvic/Sacrum</b>	-	-	-	Bilateral psoas tightness	-
<b>Diaphragm</b>	-	-	-	Right restriction	-
<b>Other</b>	-	-	-	-	Bilateral latissimus dorsi muscle tension

TABLE 1B:

Treatment sessions 6-10

STRUCTURAL REGION	TREATMENT SESSION #6 DIAGNOSIS	TREATMENT SESSION #7 DIAGNOSIS	TREATMENT SESSION #8 DIAGNOSIS	TREATMENT SESSION #9 DIAGNOSIS	TREATMENT SESSION #10 DIAGNOSIS
<b>Cranial</b>	-	Suture restriction at right and left occipital mastoid Right occipital petrous Right Sphenoid squamous Right frontal and right temporal suture	-	Suture restriction at right occipital-mastoid Right sphenoid squamous Left occipital petrous, Right greater wing/zygoma	Suture restriction showed ligamentous nuchae tightness
<b>Cervical</b>	OA FRS <sub>L</sub> C-2 ERS <sub>L</sub> C-4 ESR	OA ES <sub>L</sub> R <sub>R</sub>	C-5 ERS <sub>R</sub>	OA ES <sub>R</sub> R <sub>L</sub>	-
<b>Thoracic</b>	T-2 NSRR <sub>L</sub>	T-3 NS <sub>R</sub> R <sub>L</sub> T-4 NS <sub>R</sub> R <sub>L</sub> T-8 ERS <sub>R</sub>	T-2 ERS <sub>L</sub> T-3 NS <sub>R</sub> R <sub>L</sub> T-5 ERS <sub>L</sub>	T-1 ERS <sub>L</sub> T-12 NSLR	T-1 ERS <sub>L</sub> T-12 NSLR
<b>Lumbar</b>	-	-	-	L-5 ERS <sub>L</sub>	L-4 FRS <sub>L</sub>
<b>Upper Extremity</b>	Left radial head posterior, proximal carpal articular restrictions Left interosseous membrane tightness Left SC joint inferior Left AC joint inferior Right AC joint superior Right SC joint superior Right Triceps tightness	Left radial head anterior Right radial head posterior Right AC joint inferior Right SC joint superior Right glenohumeral joint	Right SC superior	Left SC anterior Right AC inferior	Right subscapularis tightness and scapular dyskinesia Right glenohumeral myofascial restrictions Pectoral muscle tightness bilaterally
<b>Lower Extremity</b>	-	-	-	-	-
<b>Ribs</b>	Ribs left 1-3 and 6-9 exhaled Right 6-9 ribs exhaled Sternal restriction to forward and superior glide	-	Ribs left 2-7 exhaled Sternal restriction	Ribs left 1-4 exhaled Sternal restriction	Ribs right 1-6 exhaled Sternal restriction
<b>Innominate/Pelvic/Sacrum</b>	-	-	-	Sacrum showed right on right torsion Innominate showed right anterior rotation	-
<b>Diaphragm</b>	Diaphragm bilateral restriction	-	-	-	-
<b>Other</b>	-	-	-	Abdomen showed line alba restriction Bilateral latissimus dorsi and trapezius tightness	-

### Diagnosis and treatment

The patient was treated using a multitude of techniques throughout this study. The most common techniques that provided resolution of somatic dysfunction included muscle energy, balanced ligamentous technique and functional. Other techniques that were implemented included both indirect and direct myofascial release, as well as craniosacral treatment of his suture restrictions. Most notably, ribs 6–10 were commonly found to be in exhaled dysfunction and the patient often had improved respiratory mechanics after treating this dysfunction using the muscle energy treatment as seen in Figure 2.

FIGURE 2:

This image denotes the proper position and steps used in treating exhaled ribs that are restricted in inhalation in the bucket handle family of ribs. Bucket handle ribs denote ribs that predominantly move about an anterior-posterior axis.<sup>11</sup> This technique was performed by the teaching faculty at the University of Pikeville – Kentucky College of Osteopathic Medicine.<sup>15</sup>



### RESULTS

The patient was treated at a total of 10 visits over the course of 1 year; however, we only compared data from the last 5 visits where the patient was treated on the most consistent schedule, receiving OMT approximately every 2 weeks in accordance with the original research protocol. As seen in Table 2, looking at pulmonary function testing, there was no statistically significant data from treatment number 6 compared to the conclusion of the study, treatment number 10. The 36-Item Short Form Health Survey (SF-36)<sup>10</sup> was graphed over time, as seen in Figure 3. Physical functioning and general health both showed gradual improvements in score over time while most categories stayed relatively constant throughout the study. The patient's most recent chest X-ray as seen in Figure 4 shows no significant reduction in opacity size, and in fact may indicate worsening of his fibrosis when compared to Figure 1.

TABLE 2:

The data represents spirometry findings during which the patient was treated on the most consistent basis, 5 treatment sessions between 6/14/2018–9/20/2018 (sessions 6–10) where a p-value <0.05 represented statistically significant data. Total duration of treatment occurred from 8/29/2017–9/20/2018.

FEV/ PREDICTED (%)	PRE-TREATMENT	POST-TREATMENT	T-TEST
Treatment #6	67	67	Not able to be determined
Treatment #10	66	66	
FVC (L)	PRE-TREATMENT	POST-TREATMENT	
Treatment #6	3.88	3.82	0.301
Treatment #10	3.63	3.86	
FEV1 (L)	PRE-TREATMENT	POST-TREATMENT	
Treatment #6	2.54	2.62	0.371
Treatment #10	2.56	2.57	
FEV1/FVC	PRE-TREATMENT	POST-TREATMENT	
Treatment #6	0.679	0.686	0.445
Treatment #10	0.706	0.667	

FIGURE 3:

This data represents the 36-Item Short Form Health Survey, developed by Rand Health. It is a set of questions pertaining to genetic, coherent and easy-to-administer quality of life measures.<sup>10</sup> It has been shown as a successful quality of life instrument correlating OMT with patients with deep infiltrating endometriosis with colorectal involvement and was adopted for this study.<sup>16</sup> Scores varied from 0–100 with a higher score indicating more improvement in that category while months correlated to the time during which treatments 6–10 were conducted.

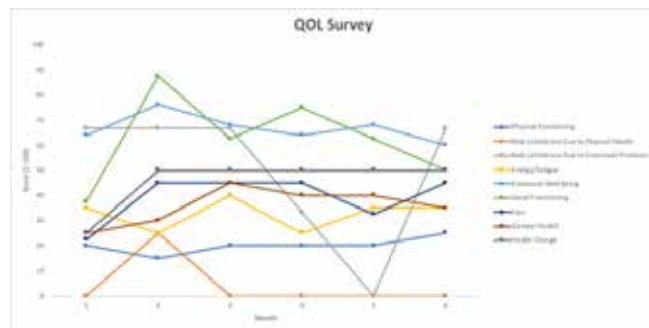


FIGURE 4:

This imaging denotes the patient's most recent X-ray obtained in 2019. Compared to his X-ray from his initial diagnosis of PMF, there appears to be increased evidence of interstitial markings, perihilar adenopathy and enlargement of previous opacities.



### DISCUSSION

Although we were unable to obtain statistically significant data, we were able to observe the subjective effects of OMT on the patient's quality of life. The patient reported throughout the study that he was able to participate in more activities, such as refereeing his grandchildren's soccer games and doing more chores at home. He reported feeling overall less fatigued and tachypneic from the first treatment session to the last treatment session. Incidentally, he was able to decrease the number of anti-hypertensives he was taking from 3 to 2 and, according to his continuous positive airway pressure settings, decrease his average apnea-hypopnea index from 3.3 to 2.9 over the course of 6 months.

The patient's SF-36 survey scores showed variability between visits but showed an overall increase in general health and physical functioning from start to conclusion of the study.<sup>10</sup> These metrics are consistent with the patient's reported increase in activities of daily living as above. His spirometry values also showed variability throughout the study, but always seemed to be acutely improved at each visit when comparing the pre-treatment and post-treatment data. This provides the possibility that OMT can have an adjunctive role in treating patients with PMF, as well as other chronic lung diseases. The patient's chest X-rays obtained from the United Medical Group in Pikeville, Kentucky, show the continued progression of black lung disease, despite osteopathic intervention. OMT has been shown to improve pulmonary function in cases of pneumonia by improving the elasticity of the ribcage and easing muscle tension related to respiratory fatigue.<sup>7,11</sup> However, there is no evidence to suggest OMT can reverse the fibrotic lung scarring associated with PMF, which is further evident when noting the increased interstitial markings between Figure 1 and Figure 4.

The patient was commonly found to have upper extremity, thoracic and rib pathology during almost every structural screening. The thoracic dysfunction likely represents a viscerosomatic reflex, an afferent input from a visceral organ that has an efferent output on a somatic structure in the body such as muscle attachments to bone.<sup>11</sup> The viscerosomatic reflex for the lungs is commonly identified as T2–T7, and this patient was commonly found to have segmental dysfunction within this region.<sup>11</sup> The rib dysfunction likely represents the impairment in the respiratory system and movement of air seen in mixed obstructive-restrictive lung disease. The upper extremity dysfunction may deal with how certain secondary muscles of respiration and bony attachments have origins and insertions involving the distal extremities.<sup>11</sup> One common finding was clavicular dysfunction—both at the acromioclavicular and sternoclavicular joints on the right. The clavicle serves as the major connection between upper appendicular skeleton and axial skeleton by acting as a strut between the scapula and the sternum.<sup>11</sup> While this patient has a history of chronic right shoulder pain, his PMF likely caused restricted movement at the clavicle that propagated to affect the movement of his shoulder concomitantly.

Several limitations effected this study, most notably was the limited sample size. According to the Center for Public Integrity, for more than 40 years, John Hopkins University has had the most sought-after readers of chest X-rays on behalf of coal companies seeking to defeat miners' claims.<sup>12</sup> One of the most sought out readers is Paul Wheeler, MD, who—in more than 1500 cases since 2000, in which he read at least one X-ray—had never found a diagnosis of PMF. However, other readers reviewing the same X-rays found PMF in more than 390 of these cases.<sup>12</sup> While judges have been aware of the inconsistencies from Dr. Wheeler and his colleagues, they are required in these hearings to identify a logical flaw or some other reason not to give his explanation greater weight than other doctors, a difficult task based on Dr. Wheeler's established credibility and the alternative explanations he finds.<sup>12</sup> As a result, about 85% of miners' claims against their former employers have been denied at the initial level.<sup>12</sup>

It is no surprise, then, that miners would be reluctant to participate in a research study that may affect their current litigations with coal companies as they already face an uphill battle to have their claims approved. The fact that so few of these claims are accepted, in an aging health burden demographic further leads to impoverishment in the Appalachian region. In central Appalachia, every county reported poverty rates greater than 20% for the period of 2007–11 compared to a national average of 14.3%.<sup>13</sup> Additionally, in 2011, the Appalachian Region Commission reported that central Appalachia received 31% less in federal expenditures per capita, compared to the national average.<sup>14</sup> With so many obstacles to overcome and an already low socioeconomic status, it is no surprise that miners would not partake in a research study as they are forced to focus on the day-to-day needs of their family.

Osteopathic manipulative treatment may provide a cost-effective adjunctive treatment to improve the lives of Appalachian



coal miners. However, until the socioeconomic deficits of the Appalachian region begin to improve, recruitment into studies such as this will continue to remain difficult. Innovative approaches to provide socioeconomic stability to the central Appalachian region warrants further study and would likely improve patient willingness to partake in clinical research.

## CONCLUSION

Progressive massive fibrosis may continue to increase in prevalence in coal miners in the Appalachian region. This report demonstrates that osteopathic manipulative treatment may provide a non-invasive, cost-effective treatment, that although cannot reverse the chronic changes of black lung disease, may improve quality of life. However, the current legal battles and economic burden that coal miners face may hinder their ability to receive additional treatment.

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## CLINICAL IMAGE

# A CASE OF CUTANEOUS BLASTOMYCOSIS

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A 70-year-old Caucasian male presented complaining of growths on his left toes for 5 months. He reported that they were enlarging, tender, irritated and occasionally bled when they rubbed against his clothing. He denied any previous trauma to the foot.

## FIGURE 1:

Verrucous plaques on dorsal aspect of the left toes with concomitant dermatophytosis of toenails



The patient previously had a renal transplant and has been taking antirejection medications, including tacrolimus, mycophenolate mofetil and prednisone. He also has a history of medication-controlled gastroesophageal reflux disease (GERD) and diabetes. His physical exam revealed raised lesions on the dorsal aspect of his second and third toes.

Initial biopsy of the lesion was conducted 3 months prior; the microscopic exam reading and diagnosis at that time was a pyogenic granuloma. The diagnosis was reconsidered when the patient failed to improve. Repeat punch biopsy of the left second toe demonstrated histological findings of epidermal acanthosis, hyperkeratosis and a mixed acute and chronic dermal inflammatory infiltrate. Grocott methenamine silver (GMS) stain revealed scattered yeast forms and possible hyphae in the dermis, consistent with deep fungal infection.

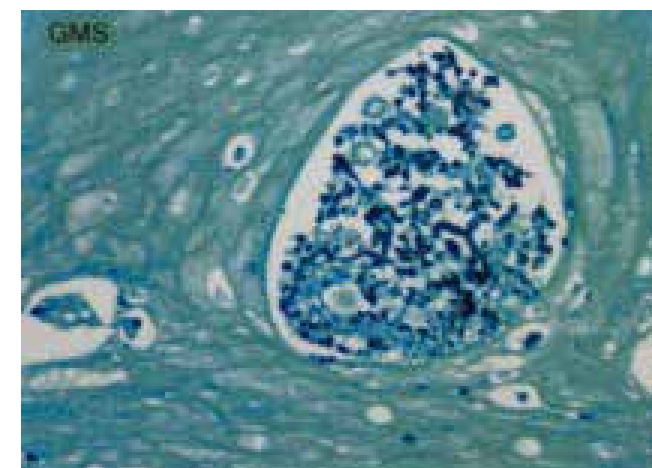
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Pathological examination of the specimen revealed round yeast-like cells up to 20 micrometers (0.000787402 inches) in diameter with thick non-pigmented walls, single broad-based buds and multiple nuclei. The patient was referred to an infectious disease specialist and started on treatment.

## FIGURE 2:

GMS stain showing presence of fungal organisms



## FIGURE 3:

Photograph of patient's foot 5 weeks after initiation of treatment



**QUESTIONS:****1. This histological finding of broad-based budding yeast is consistent with which infection?**

- a. Histoplasmosis
- b. North American blastomycosis
- c. Coccidiosis
- d. Cryptococcosis
- e. South American blastomycosis

**2. This fungus is endemic to which area?**

- a. Eastern and central United States
- b. Southwestern United States and California
- c. Central and South America

**ANSWERS:****1. This histological finding showing broad-based budding yeast is consistent with which infection?**

Correct answer:

*B. North American blastomycosis*

When visualized, *Blastomyces dermatitis* is differentiated from other yeast cells because of its size (8–15 µm in diameter), refractile cell wall and single, broad-based buds.<sup>1</sup> *Paracoccidioides brasiliensis*, which causes South American blastomycosis, is distinguished from North American blastomycosis by the presence of multiple, narrow-based buds arranged around the periphery of the mother cell.<sup>1</sup> *Coccidioides* pathologically is a spherule filled with endospores that resemble single yeast cells. However, they can be distinguished from blastomycosis in that they do not have broad based buds<sup>1</sup> Pathologically, cryptococcus is 5–10 µm with narrow budding, heavily encapsulated yeast and not dimorphic. The possibility of cryptococcus was considered by the pathologists examining the specimen; however, the multiple nuclei goes against that diagnosis. Cryptococcus is an opportunistic fungal infection found primarily in immunocompromised. Histoplasma capsulatum hides within macrophages.

**1. This fungus is endemic to which area?**

Correct answer:

*A. Eastern and central United States*

Blastomycosis is endemic in southeastern and southcentral states bordering the Mississippi and Ohio River basins, the midwestern states and Canadian provinces bordering the Great Lakes, and a small area in New York and Canada along the St. Lawrence River and the Nelson River. *Coccidioidomycosis* is endemic to the southwestern United States and California. *Paracoccidioides* has a geographic distribution limited to Central and South America.

**DISCUSSION:**

Differential diagnosis for verrucous plaques includes warts, benign tumors, cancer and infections. When blastomycosis disseminates to the skin it can cause verrucous skin lesions that mimic squamous cell carcinoma. Although blastomycosis has been reported to involve almost every organ, the lungs are the most common site of infection, followed by the skin, bones, and genitourinary system. The characteristic cutaneous finding is a verrucous lesion, with irregular borders.<sup>1</sup> This tissue is often friable and bleeds easily.

Blastomycosis is typically acquired via inhalation of airborne conidia. Primary cutaneous blastomycosis is uncommon but can result from traumatic inoculation.<sup>2</sup> It is unknown whether this patient's infection was from direct cutaneous inoculation or hematogenous spread from a pulmonary blastomycosis, as he denied both pulmonary symptoms and foot trauma.

Infection may be acquired through the environment, and blastomycosis infection is often associated with occupational exposure or with outdoor recreational activities. This patient reported that he frequently performed yard work at his home in South Carolina. He was at risk because he was immunocompromised from immunosuppressive therapy for his renal transplant. Endogenous and exogenous immunosuppression are well-documented risk factors for disseminated blastomycosis.<sup>3</sup> *Blastomyces* can behave as an opportunistic pathogen, especially in patients with advanced acquired immunodeficiency syndrome, transplant recipients, those who are prescribed TNF-alpha inhibitors and other immunocompromised patients.<sup>1</sup> Infection with blastomycosis in renal transplant patients receiving antirejection medications has been documented in several previous case reports.<sup>4,5</sup>

**TREATMENT:**

Patients with extrapulmonary blastomycosis require therapy. Treatment options for patients include amphotericin B or an azole drug. Itraconazole is preferred for patients with mild-to-moderate disease not involving the central nervous system. Absorption of the capsule formulation is highly variable, requires gastric acidity and is enhanced when the agent is taken with food. Thus, in patients who receive concomitant medications that decrease gastric acidity, blood levels are reduced.<sup>6</sup> This patient takes pantoprazole 40 mg daily to control his GERD, which would have decreased the efficacy of itraconazole.

All immunocompromised patients with blastomycosis should be treated due to the potential for dissemination.<sup>6</sup> Amphotericin B is usually the treatment option for blastomycosis in immunocompromised patients, but it has adverse effects on the kidney and was deemed unsafe in this patient who was a kidney transplant recipient. Of note, case studies of kidney transplant patients infected with blastomycosis have reported treatment with either amphotericin B or itraconazole.<sup>4,5</sup> It is not known exactly how long immunosuppressed patients should receive treatment. Serody *et al* described a heart transplant patient with recurrence of fungal infection after ketoconazole and amphotericin B therapy and suggested lifelong antifungal treatment in that case.<sup>4,5,7</sup>

Our patient was referred to an infectious disease specialist and was prescribed terbinafine HCl 250 mg twice a day. Terbinafine is also used as a first-line oral agent for mild-to-moderate dermatophyte onychomycosis. It is used to treat onychomycosis in immunocompromised individuals and has fewer drug-drug interactions than itraconazole. However, patients taking terbinafine should be monitored for liver enzyme elevations. This medication is contraindicated in chronic or active hepatic disease.<sup>8</sup> A thorough literature review did not reveal any prior case reports documenting terbinafine as the treatment of blastomycosis in a kidney transplant recipient; however, as evidenced by the pre-treatment and mid-treatment pictures, it appears that terbinafine was efficacious in treating our patient's cutaneous blastomycosis.

**CONCLUSION:**

In immunocompromised patients with verrucous skin lesions, the clinician must consider the possibility of fungal infections, including blastomycosis. Several cases of blastomycosis in patients receiving antirejection medications for organ transplants have been previously documented.<sup>5</sup> Given the patient's immunocompromised state, a further delay in diagnosis and treatment could have led to a poor outcome, like the fatal case of disseminated blastomycosis in a young man with rapid progression to multiorgan failure after exposure to corticosteroids described by Lu J *et al*.<sup>3</sup> Blastomycosis may be initially misdiagnosed. This patient was initially diagnosed with pyogenic granuloma and the referring surgeon had considered amputation. Various case reports have cited incidents of cutaneous blastomycosis being initially misdiagnosed as pyoderma gangrenosum.<sup>9</sup> Thus, a high index of suspicion for deep fungal infection and collection of multiple samples for microbiology and histological evaluation should be performed when the diagnosis is uncertain and patients live in or have traveled to areas endemic for blastomycosis.<sup>1</sup>

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# PATIENT EDUCATION HANDOUT



## Iron Deficiency Anemia

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### WHAT IS ANEMIA?

Anemia is a condition where your body does not have enough red blood cells to circulate oxygen in the body. There are many different types of anemia, but the most common type is iron deficiency anemia. Iron is an essential component for red blood cells and is needed to make blood. It is usually found in the foods that we eat, but some people need supplementation.

### WHO IS AT RISK?

The following groups could be at increased risk of developing iron deficiency anemia:

- Young children who drink mostly cow's milk
- Menstruating women, especially with heavy periods
- Pregnant women, due to an increased need to support the growth of a developing baby
- Vegetarians/vegans, as their specific diet may be lacking in iron-rich foods, such as meat and fish
- Frequent blood donors who donate blood as often as every 8 weeks
- People with recent surgery
- People with gastrointestinal disorders that result in malabsorption
- People with acute or chronic gastrointestinal bleeding
- People with certain cancers that increase blood loss

### Common symptoms include:

Chronic fatigue or lack of energy  
Dizziness or light-headedness  
Craving to eat non-food items, like ice or dirt  
Shortness of breath

### Common signs include:

Pale or yellow-tinged skin  
Brittle nails or hair loss  
Swollen or sore tongue  
Restless legs

### WHAT SHOULD I DO?

First, talk to your doctor if you think you are experiencing these signs and symptoms. The diagnosis of iron deficiency is determined by a simple blood test. If you are determined to have iron deficiency, you may need additional testing to determine if you are having bleeding within the stomach, small intestine or large intestine.

### Treatment Options:

**Diet:** One solution is to increase your iron intake through the food you eat. Foods that have high iron content are lean meats including beef, pork or lamb, as well as seafood, such as oysters, shellfish and sardines. Leafy green vegetables, such as broccoli and kale, and legumes, such as peas and pinto beans, are also good sources of iron.

**Supplementation:** Oral iron supplementation may be recommended. Your doctor will determine how much and how often you will be taking iron. Iron tablets may cause an upset stomach including nausea, vomiting or constipation.

**Infusions:** Iron can be given as an infusion when oral supplementation is not effective. If the anemia is significant, blood transfusions may also be indicated.

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# PATIENT EDUCATION HANDOUT



## Lung Cancer Screening

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### DO YOU SMOKE, OR HAVE YOU SMOKED IN THE PAST?

**Lung cancer is the number one cause of cancer-related deaths.** Tobacco smoking is the cause of 90% of lung cancers. The amount of cigarettes and number of years smoking contribute to the risk of cancer development. Even smoking on occasion increases the risk of lung cancer. Tobacco smoking is carcinogenic because of the inflammation and DNA damage caused by the chemicals like polycyclic aromatic hydrocarbons and N-nitrosamines. Other risk factors include secondhand smoke ingestion, radon exposure, prior chest radiation and exposure to environmental chemicals, like arsenic. Most of the time, lung cancer is asymptomatic, but other symptoms can go unnoticed for years, such as chronic cough, bloody phlegm, recurrent respiratory infections, fatigue or weight changes.

Early detection of lung cancer is crucial because early treatment leads to improved survival.

Lung cancer screening has been vastly effective and has led to a 20% reduction in lung cancer deaths. Screening for lung cancer involves a yearly low dose computed tomography (CT) scan of the chest. The images are evaluated by a radiologist to check for any lung nodules in individuals who are at risk. This is anyone who has had at least a 20 pack-year smoking history. Pack years are calculated by the number of packs of cigarettes smoked per day, multiplied by the years one smoked.

U.S. Preventive Services Task Force 2021 guidelines call for annual low-dose CT scans for adults aged 50–80 years old with a 20-pack year smoking history who either currently smoke or have quit within the last 15 years.

### WHEN CAN YOU STOP SCREENING?

Once it has been 15 years since someone has smoked, or once the person has been diagnosed with a health problem that limits life expectancy or precludes their ability to have treatment.

### WHAT CAN YOU EXPECT?

You lie on a table while a machine takes several images in order to reconstruct an accurate 3D image of your chest and lungs. A low-dose CT scan uses 5 times less radiation than a standard CT scan. These tests are covered by most insurance plans and Medicare.

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### HARMS OF SCREENING AND TREATMENT

The biggest harm includes false-positive results. This means that the CT could find something suspicious but is not actually cancer. This can lead to unnecessary tests and invasive procedures. Additionally, CT scans do have a theoretical risk of radiation-induced cancer, and CT imaging and cancer screening can also cause distress or anxiety.

### MEDICAL CARE AND TREATMENT OPTIONS

Do not hesitate to speak to your physician if you have questions about lung cancer screening, whether it is the right choice for you or if you have any questions or concerns about lung cancer.

If you are smoking today, consider talking to your physician about options for smoking cessation. sions may also be indicated.

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