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Arkansas Physicians' Interests and Learning Opportunities with Pharmacogenomics

Abstract

A clinical pharmacogenomics (PGx) program was established at Arkansas Children's Hospital (ACH) to deliver genomic-guided therapeutic care to children. ACH physicians order the PGx test via the electronic health record (EHR) and are supported by automated clinical decision support about each patient's genomic indicators. A survey was conducted before the program launched to understand clinician concerns, needs, knowledge, and familiarity with PGx. Results demonstrate that physicians are eager to learn about PGx and are most interested in the cost and efficacy of the PGx test.

Overview of Pharmacogenomics

Pharmacogenomics is a field of study incorporating pharmacology and genomics to determine how genetic composition impacts an individual's response to medications.[1,2] It is imperative for one's body to appropriately metabolize medications and have them delivered to the intended site of action within the body. This complex process takes place in multiple ways by impacting pharmacodynamics and pharmacokinetics of a drug, facilitated by drug metabolizing enzymes, drug receptors, and uptake transporters. In some cases, and in various ethnic groups, one's genetic composition predisposes the body to inappropriately interact with the drug, leading to an adverse drug reaction (ADR). In fact, ADRs cause over 131,000 deaths per year in the U.S., with an associated economic burden of $136 billion.[3] Currently, many medications are prescribed as "one size fits all;" however, they do not work the same way for every individual. The aim of PGx is to understand why individuals respond to medications differently. Presently, over 260 drugs need biomarker regulations to guide drug dosing.[4,5] PGx testing can improve health care by allowing physicians to know ahead of time how a patient will respond to a specific drug based on the patient's genetic predisposition.

ACH is among the largest pediatric hospitals in the U.S. and the only academic hospital system in the state solely dedicated to caring for children. ACH implemented a pediatric PGx panel test that covered the most commonly prescribed medications and was coupled with pediatric clinical guidelines to improve patient care. These commonly prescribed medications cover a number of medical specialties including anesthesia, cancer, cardiology, gastrointestinal, gauche disease, hematology, infectious diseases, neurology, pain, psychiatry and addiction, and transplantation. The test is performed in-house with approximately a five-to-seven-day turnaround time to facilitate timely decision making.

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PGx Workflow

A comprehensive PGx panel was deployed at ACH and consisted of 175 single nucleotide polymorphisms (SNPs) targeting 23 clinically actionable genes and genetic variants. The EHR orderable test provides clinical guidance on 57 prescription drugs commonly prescribed at ACH. DNA is obtained from blood or buccal swab material and analyzed in the ACH molecular genetic pathology laboratory by real-time polymerase chain reaction (PCR). The generated genotyping data is electronically sent to Translational Software Inc. (Bellevue, WA), who uses a proprietary software algorithm to determine the diplotype for each gene along with peer-reviewed, pediatric-specific, evidence-based gene-drug clinical guidance based upon Clinical Pharmacogenetics Implementation Consortium (CPIC) and Federal Drug Administration (FDA) guidelines.

Survey

Study data was collected and managed using Research Electronic Data Capture (REDCap) hosted by ACH and administered by the Arkansas Children's Research Institute (ACRI).[6,7] REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

The PGx survey was distributed to 1,122 clinicians and prescribing professionals practicing at ACH. The content of the survey was exported from the REDCap data.

The survey consisted of 17 questions, with many of these inquires derived from a nationwide survey done by Medco Health Solutions, Inc., in conjunction with the American Medical Association, dealing with a physician's knowledge of pharmacogenomics.[8]

Survey Demographics

Out of the 131 responses to the survey, 114 were MD, six DO, one PhD, two PA, and one APN. Of the 114 MD, 35 were residents. The other seven individuals preferred not to respond with contact information. Twelve departments were represented by the survey including hematology/oncology, nephrology, emergency medicine, cardiology, and hospital medicine (Figures 1 and 2).

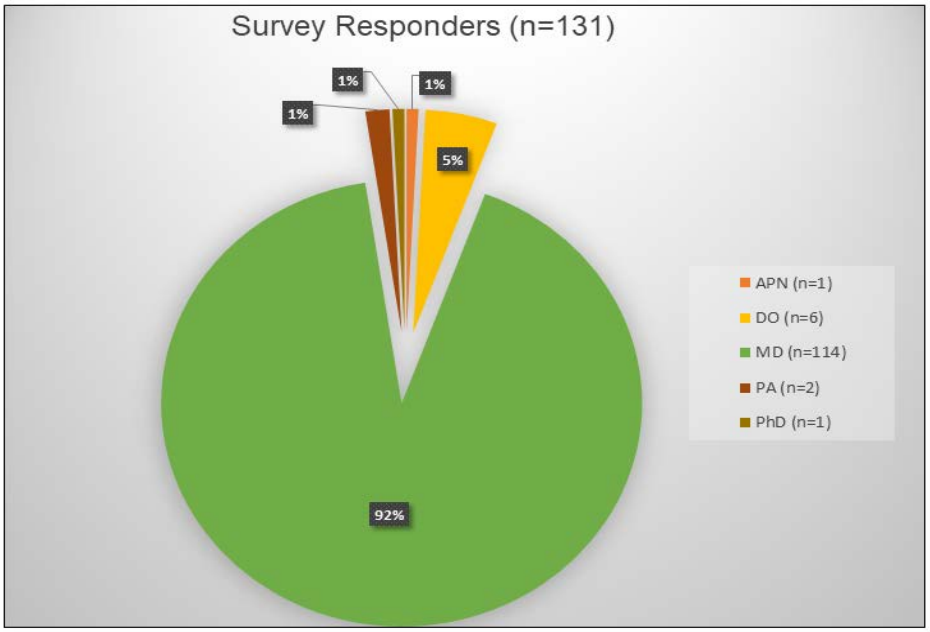

Figure 1: Survey Responders by Provider Type
Note: 114 of 131 survey providers were MD, 6 DO, 1 PhD, 2 PA, 1 APN, and 7 preferred not to share this information. 35 of total were residents; MD = Doctor of Medicine, DO = Doctor of Osteopathic Medicine, PhD = Doctor of Philosophy, PA= Physician Assistant, APN = Advanced Practice Nurse

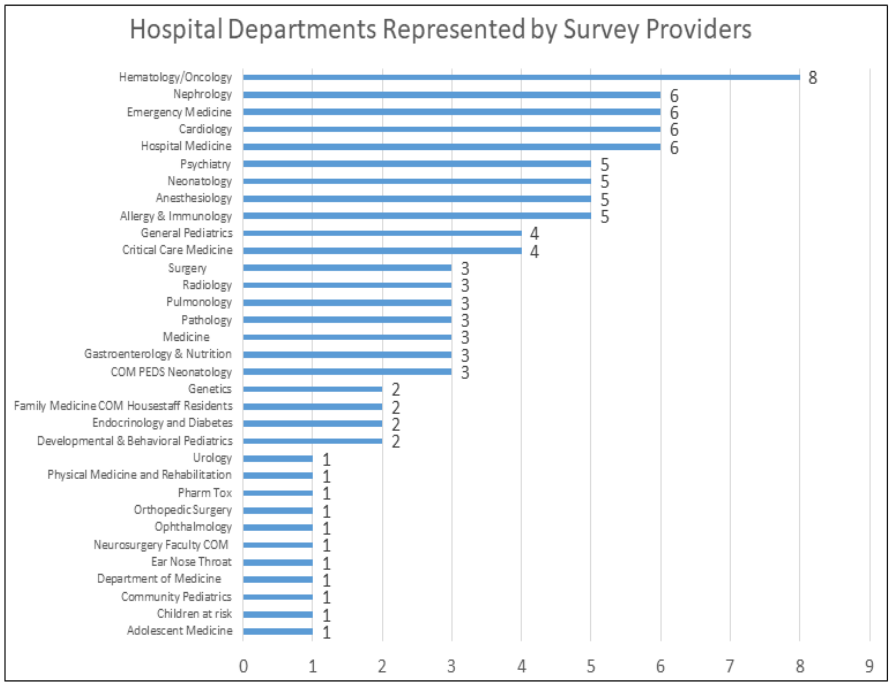

Figure 2: Survey Responders by Hospital Service or Department

Results

A group of specialty personnel was gathered at the introduction of Precision Medicine (PM) at ACH. These specialists included an MD with pharmacogenomics experience, an experienced PGx researcher, an MD informatics technology (IT) specialist, an MD director of molecular genetic pathology, an EPIC IT expert, and a project manager. With this PM group and four champion clinicians, the PM group was formed at ACH.

The PGx survey returned 11.67% (131/1122) responders. Although very few physicians had previously ordered a pharmacogenomic test outside of ACH, a high percentage (91.6%), were eager to learn more about pharmacogenomics. E-learning and department-specific PowerPoint presentations were preferred education formats (61% of respondents). In addition, 70% of responders had reservations about using the PGx test, citing cost (24%) and efficacy (18%) concerns (Figure 3).

Very few providers had ordered a PGx test for their patients, themselves, a colleague, or a family member in the six months previous to the survey (7.6%, 2.3%, 1.5%, 0% respectively), and of those who had ordered a PGx test, they did so a small number of times over the previous six months (90.4% stated they had not ordered a test). While 60.8% of clinicians stated not anticipating ordering the PGx panel in the next six months and 63.8% noted that they had insufficient PGx knowledge, 39.3% exhibited an interest in ordering the PGx test in the future. The ACH PM group concluded that the percentage of providers ordering the PGx test would increase as the knowledge of PM increases; therefore, continuous education was paramount.

It was encouraging to find that almost all (99.2%) of our survey participants realized that a patient's genetic profile could influence his/her response to drug therapy. Only a very few (7.0%) providers had a patient bring in their own PGx or genetic test. As clinicians feel more comfortable about PGx, so will patients.

Patient Genetic Privacy

One of our concerns when issuing the survey to our prescribing clinicians and nurses was how much more concerned they would be about the loss of privacy of a patient's genetic information than from the results of other laboratory or diagnostic tests. With surprising pleasure, the survey showed that most physicians (18.0%) were not concerned since patient health information, including genetic testing and family history, is protected under the Health Insurance Portability and Accountability Act of 1996 (HIPAA); in fact, 82% were anxious to provide this test to their patients. Most clinicians stated that it was important (77.7%) or very important (90.8%) to have specialty-specific guidelines when ordering a pharmacogenomic test (Figure 4). These levels of evidence

included FDA recommendations, scientific journals, experience of respected colleagues, and physician-specialty guidelines.

Conclusions

A PGx survey was deployed to obtain a better understanding of the knowledge and educational needs of the ACH prescribers.

The PGx survey showed that prescribing clinicians are interested in the opportunity to provide PGx testing to their patients. Prescribers recognized the need for additional information about PGx and welcome eLearning and specialty-specific educational sessions as alternative means of education. In addition, clinicians are concerned about cost, turnaround time, and efficacy of the test. Of note, a representative sample of younger clinicians (resident house staff) responded to the survey, perhaps presenting as a marker for their openness to considering PGx as part of their decision-making process.

Pharmacogenomics is fast becoming a mainstay for the 21st century health care delivery. Clinicians are open to learning more about the promise of PGx and eager to utilize this process to improve the quality of clinical care that they deliver to their patients.

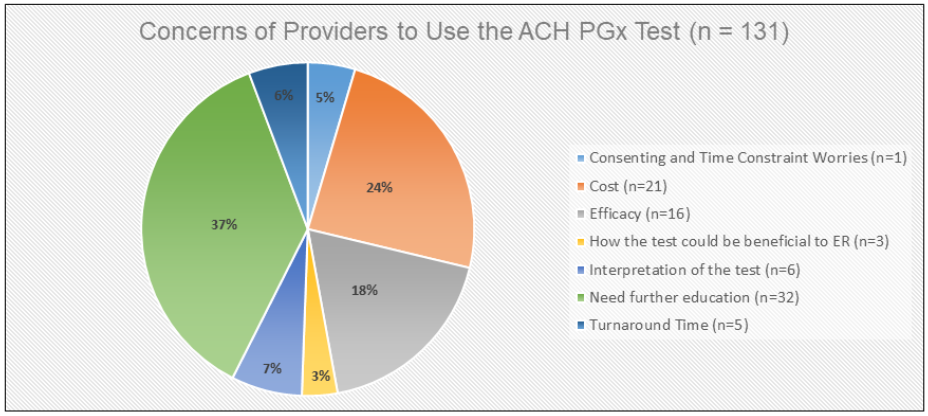

Figure 3: Concerns of Providers to Use the ACH Pharmacogenomic (PGx) Test.
Note: 37% of our professional prescribing staff at ACH that participated in the survey (131) stated that they needed further education and that they were concerned about the cost (24%) and efficacy (18%) of the test.

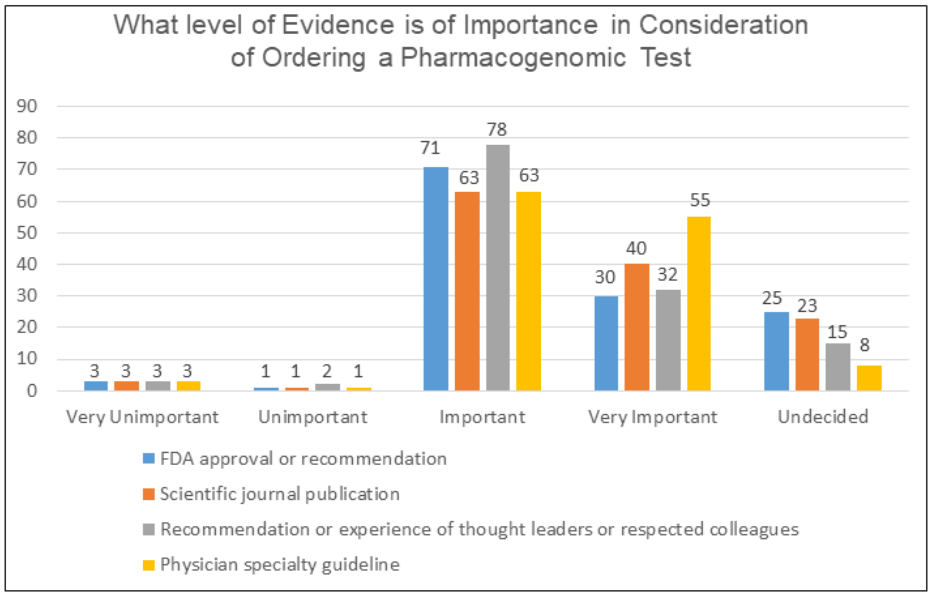

Figure 4: Concerns of Providers to Use the ACH Pharmacogenomic Test

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by JORDAN PILKINGTON

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This 60-year-old post-menopausal woman presents with mildly atrophic, mottled hyper- and hypopigmented patches with telangiectasias located symmetrically on the anterolateral neck. The immediate submental area is spared. The area is asymptomatic and has slowly developed over the past 2-3 years. The patient finds these changes cosmetically objectionable and is interested in treatment options.

What is an appropriate intervention for this patient?

A. Use of intense pulsed light or pulsed dye laser therapy in addition to daily sunscreen.

B. Punch biopsy of the affected area in order to narrow the differential diagnosis, as the cutaneous changes are not distinctive enough to allow definitive diagnosis based upon clinical features alone.

C. Extended use of oral niacinamide 500mg BID. Niacinamide is a mildly anti-inflammatory form of vitamin B3 that has also been shown to be somewhat UV protective.

D. Serial use of microdermabrasion over the affected area.

E. Narrowband UVB (311nm) light therapy twice weekly for approximately 3 months.

Answer: A

The clinical findings are highly characteristic of Poikiloderma of Civatte (PC). PC commonly occurs in middle-aged and older women, and develops symmetrically in areas of chronic sun exposure, particularly the anterolateral neck and "V" area of the upper chest. The submentum, shaded by the chin, is typically spared. PC is characterized by reticulated hyperpigmentation, hypopigmentation, and telangiectatic erythema, as well as mild epidermal and papillary dermal atrophy ("poikiloderma"). Chronic sun exposure along with lighter Fitzpatrick skin types, decreasing estrogen levels, and potentially photosensitizing toiletry products are precipitating factors, and there may be a genetic predisposition as well. PC is a clinical diagnosis, and skin biopsy is rarely necessary. PC differs from other chronic dyschromias in that it is often restricted to the anterolateral neck and upper chest.

PC is often considered unsightly by patients, but currently available treatment options are suboptimal. Photoprotective measures including daily sunscreen use may slow progression, and perfumed toiletries should be avoided in affected areas. Topical therapies include hydroquinone, retinoid, or alpha-hydroxy acid containing preparations. Pulsed dye laser, intense pulsed light therapy, and non-ablative fractional lasers remain the most potentially effective interventions.

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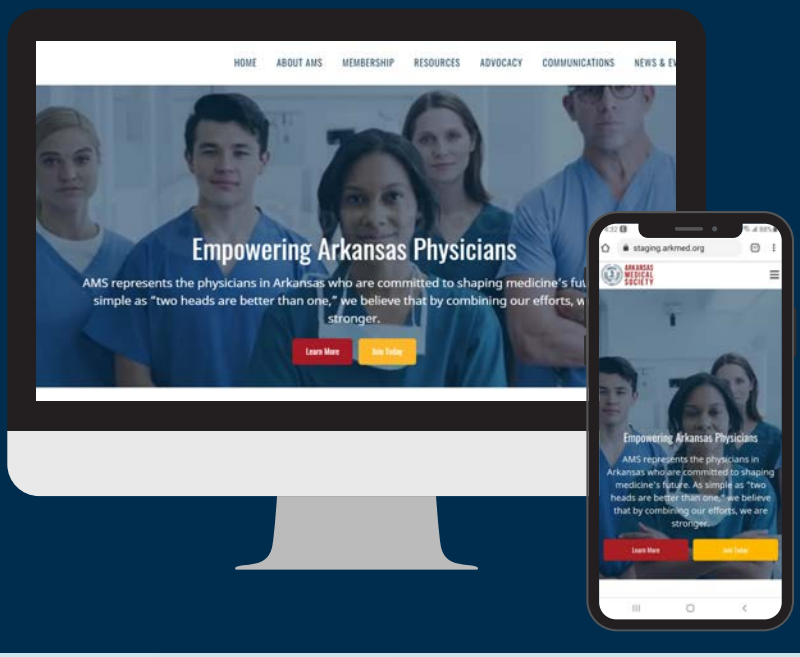

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Telemedicine Patient Satisfaction in Eye Care

Abstract

The use of telemedicine has rapidly increased since the onset of the COVID-19 pandemic. Many divisions of health care have looked to telemedicine for a solution to limit human interactions and the potential for exposure to the virus. This study employs a satisfaction questionnaire following the use of telemedicine in eye care to determine the patient's level of satisfaction and comfort with the encounter. The majority of patients reported that they were satisfied with the telemedicine visit; however, a smaller percentage of patients reported being willing to use telemedicine outside of COVID-19 circumstances.

Introduction

Patient satisfaction is one of the key aspects in measuring quality of care in the field of medicine. Through the spread of COVID-19, a number of health care systems had to alter the physician-patient interaction while maintaining a high quality of care. Telemedicine use has rapidly accelerated since the onset of COVID-19 [1] and offers a solution to limit in-office visits and face-to-face interactions. The adoption of telemedicine allows social distancing as well as conservation of personal protective equipment.

In telemedicine, usability allows the physician and patient to conduct successful interactions and plays a large role in patient satisfaction. Usability is defined as the extent to which a system or product is used to achieve specific goals efficiently and effectively.[2] The technology delivery system used for telemedicine must be usable for both the physician and the patient.

To evaluate the usability of a telemedicine system, a satisfaction questionnaire may be conducted. Measuring this data provides a way to evaluate and improve the effectiveness of both the system used and the services provided. The telemedicine questionnaire employed in this study not only evaluates the usability of the system, but also focuses on satisfaction, confidence, and the patient's level of comfort with the encounter.

This study aims to address whether the patient feels they benefited from the telemedicine encounter, if the patient trusts the services provided during the telemedicine encounter, and if the patient would opt for telemedicine when given the option between an in-office visit versus telemedicine. Furthermore, patient demographics will be evaluated to better categorize the population receiving care through the telemedicine system.

Methods

In this study, 50 patients, ages 1 year and older, were provided eye care through telemedicine between March 1 and June 1, 2020. The telemedicine encounters were conducted using the Google Duo platform. Patient phone calls were triaged during this time and, if determined appropriate, the patient was offered a telemedicine visit versus an in-office visit. Patients who opted for a telemedicine visit were asked to complete a five-question satisfaction questionnaire following the encounter. The questionnaires were conducted via phone call, email, or the MyChart messaging system. Forty-seven patients successfully completed the satisfaction questionnaire with "yes" or "no" answers to evaluate their telemedicine visit during the COVID-19 pandemic. The questionnaire may be found below:

1. Was the telemedicine system simple and easy to use?
2. Were all your questions and concerns resolved during the telemedicine visit?
3. Were you comfortable communicating with the physician using the telemedicine system?
4. Are you confident that the proper management was delivered using the telemedicine system?
5. Are you willing to use the telemedicine system outside of COVID-19 circumstances?

Patient-demographic data including age in years, distance from clinic in miles, visit frequency prior to telemedicine, and most recent best-corrected visual acuity was also analyzed to better characterize the participants completing the questionnaire. Per UAMS policy, the project did not require IRB approval.

Results

Questionnaire results may be found in Table 1. Patient demographic data may be found in Table 2.

Discussion

The questionnaire in this study was administered to patients to ensure quality of care and satisfaction with the telemedicine process in eye care. Upon analyzation of the questionnaire responses, data shows 74% of patients who received a telemedicine visit during the COVID-19 pandemic reported the system was simple and easy to use. Greater than 90% of patients reported having all of their questions and concerns resolved during the telemedicine visit. Greater than 90% of patients also reported being comfortable communicating with the physician through the telemedicine platform. One hundred percent of patients were confident that they received the proper management.

Overall, these statistics show that patients were satisfied with the usability of the telemedicine system and the services

Table 1: Satisfaction Questionnaire Results

Number & Percentage of YES & NO Answers to COVID-19 Telemedicine Questionnaire					
	# YES Responses	# NO Responses	TOTAL Responses	% YES	% NO
Question 1	35	12	47	74%	26%
Question 2	46	1	47	98%	2%
Question 3	43	4	47	91%	9%
Question 4	47	0	47	100%	0%
Question 5	25	22	47	53%	47%
TOTAL	**196**	**39**	**235**	**83%**	**17%**

Table 2: Patient Demographics

Age (years)		
	n	%
<40yrs	14	29.8%
40-59yrs	14	29.8%
60-79yrs	18	38.3%
80+ yrs	1	2.1%
Distance from Clinic (miles)		
<20mi	27	57.4%
20-39mi	5	10.6%
40-59mi	5	10.6%
60+ mi	6	12.8%
No street address on file	4	8.5%
Visit Frequency Prior to Telemedicine (months)		
New patient	5	10.6%
<4mos	26	55.3%
4-7mos	11	23.4%
8-11mos	0	0%
>11mos or PRN	5	10.6%
Most Recent Visual Acuity in Better Eye		
No Snellen acuity documented	4	8.5%
Better than 20/40	35	74.4%
20/40 to 20/60	4	8.5%
20/70 to 20/100	2	4.3%
Worse than 20/100	2	4.3%

provided by the physician. In comparison, only 53% of patients reported that they are willing to use the telemedicine system outside of COVID-19 circumstances. This data point represents the value a patient holds regarding a face-to-face encounter with a physician.

Patient demographic analysis allows better characterization of the population completing the telemedicine satisfaction questionnaire. The largest age population receiving a telemedicine encounter in this study was the age group of "60-79 years" totaling 38.3% of encounters. Patients in this specific age group are more likely to have motility issues, a need for transportation or a visitor to accompany them for an in-office visit. In regards to COVID-19, this age group may also have taken greater precautions to avoid unnecessary human interactions and the potential for exposure to the virus.

Looking at the patient's distance from clinic (in miles), 57.4% of patients lived within 20 miles from the clinic. This statistic may have no correlation with the telemedicine encounter, but likely represents the clinical population as a whole living within close proximity to their eye care provider.

The frequency of in-office visits prior to telemedicine was less than four months for the largest population group. This visit frequency category consisted of 55.3% of all patients receiving a telemedicine visit. Patients seen more frequently by an eye care provider are more likely to have a complex ocular history with close follow-up visits. They may also have a greater likelihood for recurrence of ocular problems. A telemedicine encounter helped reduce the number of trips these patients had to make to the clinic and decreased their potential exposure to COVID-19.

The majority of patients receiving a telemedicine visit in this study had a visual acuity measurement "better than 20/40." This population consisted of 74.4% of all telemedicine encounters. Patients with better visual acuity may be less concerned about their eyes compared to those with decreased vision, and may therefore be more comfortable completing an ocular evaluation through a telemedicine platform.

In conclusion, telemedicine offers a solution to limit in-office visits during the COVID-19 pandemic. From the satisfaction questionnaire completed in this study, it may be concluded that patients were satisfied with the telemedicine system and the encounter with the physician. It may also be concluded that patients value the face-to-face encounter with the physician, since only about half of all patients surveyed would choose telemedicine over an in-office visit outside of COVID-19 circumstances. Further research could be conducted to identify specific patient encounters most appropriate for a telemedicine platform.

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by CLAIRE GIST

MD Candidate, Class of 2025, University of Arkansas for Medical Sciences, Little Rock, Ark.

A 65-year-old female presents with a three-week history of tender erythematous 5-10mm papules of the lateral aspects of the right index finger and the left fifth finger. Similar painful papules have occurred previously on the digits of the feet and hands in the colder months of previous years, particularly after spending time outdoors. She has experienced no concomitant systemic symptoms, including fever, shortness of breath, or cough. In previous episodes the papules have resolved spontaneously within a few weeks. Topical application of a triple antibiotic/lidocaine preparation has provided some symptomatic relief but has not expedited resolution of the eruption.

Based on the patient history and clinical images, what is the most likely diagnosis and appropriate intervention for this patient?

A. Chilblains (pernio); insulated gloves and footwear, avoidance of dampness, topical corticosteroids or vasodilators may be employed.

B. Raynaud phenomenon; screen for underlying autoimmune disease and begin a systemic calcium channel blocker.

C. Covid-19; obtain SARS Cov-2 PCR assay; self-quarantine and appropriate level of intervention depending upon presence and magnitude of symptoms.

D. Erythromelalgia; screen for underlying myeloproliferative disorder and begin aspirin therapy.

E. Sweet's syndrome; obtain absolute neutrophil count and serum protein electrophoresis and begin systemic corticosteroids.

Answer: A

Chilblains, also known as pernio, manifests as tender, burning, or pruritic erythrocyanotic papules with a strong predilection for the digits that appear after exposure to cold, damp climates. Persons of any age may be affected, but the condition is most frequently seen in young to middle-aged women. Symptoms characteristically begin in early winter and resolve in the spring. Low body mass index may be a predisposing factor. The exact etiopathogenesis is unclear, but it is presumed that cold-induced vasoconstriction and hyperviscosity result in localized hypoxia which in turn results in an inflammatory response.

Chilblains has been reported in association with autoimmune disorders (particularly lupus erythematosus), viral hepatitis and paraproteinemias. More recently, chilblain-like lesions have been described in patients of all ages with Covid-19 (colloquially termed "Covid toes") even in the absence of cold exposure. With respect to the clinical vignette presented above, the recurrent nature of the eruption in previous years (prior to the appearance of this coronavirus variant) makes Covid-19 less likely, although screening would be reasonable.

Management includes minimization of unprotected cold exposure as well as gloves and appropriate footwear. Attempting to keep the skin dry is also helpful. Smoking should be discouraged. Pharmacologic interventions include topical therapy (corticosteroids, minoxidil, nitroglycerin) and systemic agents (e.g., nifedipine).

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