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a record of
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Fold twice in each direction before tearing.

Table of Contents

See page 64 for an update from the Lancaster Medical Heritage Museum.

FROM THE EDITOR'S DESK

Obstetric Research That Addresses Health Care Disparities

Corey D. Fogleman, MD, FAAFP
Editor in Chief

We are excited to feature several important articles in this issue of *JLGH.* From our nursing colleagues comes a report of a project conducted at the Ann B. Barshinger Cancer Institute, demonstrating that trauma-informed care education can positively impact the attitudes of clinicians. Our colleagues in the Penn Medicine Lancaster General Health Research Institute describe the new collaborative relationship being built with the University of Pennsylvania Office of Clinical Research, under the umbrella of One Penn Medicine.

Further, one of our Philadelphia colleagues, who gave the Larry Carroll memorial lecture earlier this year at LG Health, offers thoughts on the adverse outcomes of accountable care in our hospitals and society. Health care policies presumably designed to level the playing field in fact may be eliminating care opportunities. Dr. Rachel Werner's eloquent analysis reinforces the need on our part to be always mindful, to reexamine our system and practices. Even the best of intentions may have negative impact.

Regarding thoughtful reexamination of practices that have broad implications, three provocative studies are soon to be launched at Women & Babies Hospital, led by both local and national research teams.

In the first, "Optimizing Outcomes for Patients with Pre-Viable PROM," Drs. Sarita Sonalkar and Rachel McKean will conduct a qualitative analysis of patient care in cases of premature rupture of membranes. Rupture in the second trimester can be devastating, forcing parents to make challenging decisions about termination and the birthing person's own health. The management of these circumstances can vary greatly depending on local protocols and resources, as well as provider and patient needs. These researchers aim to determine best practices and barriers to care; their long-term hope is to establish a standardized and evidence-based protocol that can be implemented broadly.

The second study, "Disrupting Obstetric Racism — Evaluating Interventions That Mitigate Harm to Black Birthing People," aims to decrease the impact of systemic racism as a source of our national Black maternity care crisis. Dr. Crista Johnson-Agbakwu, of UMass Memorial Health, leads a team that includes Dr. Cherise Hamblin. This team notes that non-Hispanic Black birthing patients suffer the worst mortality among any racial group in the United States, with 69 deaths per 100,000 live births.[1] They propose a change in culture and practice and are preparing to launch a study with two variables: implementing anti-racism training at the systemic level, as well as employing doula care to help support Black birthing persons at the individual level.

Anti-racism training is designed not to blind us to color differences, but to help us see the root causes of inequity and look for solutions to a system that may subtly reinforce substandard care for one group of patients. This can and should happen at many levels, including the individual, interpersonal, systemic, community, and organizational levels.[2] Doula support during pregnancy and labor has already been shown to result in fewer cesarean deliveries and higher birth weights, increase rates of breast feeding, and improve the health of the mother.[3]

This study will have a qualitative component to characterize usual care received by Black patients, as well as a comparative effectiveness component to determine morbidity outcomes achieved by the above interventions. With plans to study implementation at four sites in Massachusetts as well as here in Lancaster at Women & Babies Hospital, the researchers will recruit 600 patients; the total sample will be 3,000 birthing mothers, and Dr. Robert Faizon will be the local principal investigator.

Finally, a third study aims to decrease morbidity and cesarean deliveries associated with prolonged and failed labor induction. Penn Medicine's Dr. Rebecca Hamm will head a quality improvement team that has developed a cesarean risk calculator for patients undergoing labor induction.

While we already know that across medicine increasing objectivity and standardizing decision-making

limit the effects of bias, the team hopes that use of their calculator will decrease disparities specifically associated with labors that are actively initiated. Nationally, more than 20% of birthing patients undergo labor induction; at Women & Babies Hospital, during both fiscal years 2023 and 2024, the rate was 33%. What's more, as many as a third of these inductions end in cesarean delivery nationally; at our institution it's 20%. These surgical deliveries can result in an increased risk of morbidities such as hemorrhage and surgical site infection.

The cesarean risk calculator requires data on height, body mass index, parity, gestational age, and cervical exam at the start of induction. Development of this risk predictor has already yielded encouraging outcomes: in a single-site prospective cohort study of 1,600 patients, use of the calculator was associated with a 6% absolute risk reduction in maternal morbidity and an 8% absolute risk reduction in cesarean delivery.[4] Further, it has been shown to reduce disparities in dissatisfaction with induction that otherwise correlate with race.[5]

In a stepped-wedge randomized roll-out trial to determine obstetric outcomes overall and specifically among patients who are Black, indigenous, and other people of color, the study team will oversee implementation at 14 labor and delivery sites, with the goal of developing and studying tailored implementation plans. The long-term hope is to implement at a national scale, consistent with a goal of the National Institute of Child Health and Human Development's "Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE)" initiative.[6]

We wish these researchers success in conducting their trials and look forward to reporting on what societal changes may be born of these groundbreaking endeavors.

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Letter to the Editor

To the Editor:

I am a retired family doctor in Harrisburg, and I have been reading *JLGH* for six to eight years. Even though I'm retired for four years, the journal maintains my interest because the articles are so practical.

I think it should be required reading for all the residents at UPMC and CGOH hospitals.

Regarding the lead article on clinical inertia [vol. 19, no. 1], I've witnessed this problem in colleagues. I think the solution is regular peer review and feedback, as suggested in the article. Keep up the good work!

— Robert Little, MD

Response from the editor in chief:

I was pleased to receive Dr. Little's letter and kind words. CGOH is now named UPMC Community Osteopathic. We have reached out to UPMC Lititz and UPMC Central PA with complimentary copies of JLGH *for their internal medicine and family medicine residency programs.*

Thank you, Dr. Little, for your suggestion to better spread the word about the good work being done here in Lancaster.

– Corey Fogleman, MD

To send a letter to the editor, visit our website at jlgh.org/Contact-Us.aspx

JLGH Spring 2024 Recap

Q&A for Extended Learning

The Spring issue of The Journal of Lancaster General Hospital *offered articles on clinical inertia and medication treatment plans for type 2 diabetes mellitus, a risk-benefit analysis of duloxetine, and other practice recommendations. Review the questions and answers below to see how much you remember from the issue. Need a refresher? All issues of* JLGH *are available online at JLGH.org.*

Q **What is clinical inertia?**
How can the medical community reduce its risk in patient care?

A Clinical inertia is the failure to accelerate or change therapy to meet the standard of care. Solutions can include targeted guidance, ongoing peer review, and studies focused on how to better serve patients.

Q **American Diabetes Association (ADA) guidelines suggest a patient-centered, collaborative, multidisciplinary care team of pharmacists, nurses, or dieticians, among other health care professionals, that prioritizes timely follow-up and medication adjustments in patients with type 2 diabetes mellitus and an A1C not at goal. How soon do the ADA guidelines recommend treatment initiation or intensification?**

A The guidelines recommend treatment initiation or intensification within three months of findings.

Q **Although the side effect profile and other potential adverse effects of duloxetine warrant consideration, this drug remains effective for what clinical syndromes?**

A Duloxetine is approved for the treatment of mental health disorders such as major depression and generalized anxiety disorder, as well as pain syndromes such as fibromyalgia, chronic musculoskeletal pain, and diabetic neuropathy.

Q **List some practical applications of text message reminders in outpatient practices.**

A Text message medical reminders (TMMRs) can help improve compliance with preventive screenings, wellness checks for pediatric patients, and annual physicals for adults. TMMRs might also help increase vaccination rates for yearly inoculations, such as the flu vaccine.

Q **In patients with repetitive monomorphic ventricular tachycardia who have symptoms of palpitations but are not ready for ablation, what medical treatment can be offered?**

A Although radiofrequency ablation may resolve the symptoms, patients may be treated with beta-blockers, calcium channel blockers, or antiarrhythmic medications.

Q **Why might we consider continuing the outpatient dose of buprenorphine in a patient being admitted to an inpatient service?**

A Patients who continue their outpatient dose of buprenorphine in the inpatient setting have overall lower morphine milligram equivalents (MME) needs while inpatients. They also require significantly fewer MME to achieve similar pain scores, have reduced opioid prescription rates at discharge, and may avoid problems associated with buprenorphine reinitiation.


Bush


Nguyen

Polypharmacy and Deprescribing Implementation in Practice

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Adults 65 years and older — 55 million individuals — make up almost 17% of the U.S. population, per the 2020 Census.[1,2] Polypharmacy is defined as taking five or more medications, and more than 40% of geriatric adults do so. This article describes concerns associated with polypharmacy and strategies for deprescribing.

Deprescribing techniques and resources can help minimize the harms of high pill burden in the geriatric population. The following is an illustrative case.

CASE VIGNETTE

An 81-year-old male presents for a new patient visit to establish care. His past medical history includes chronic pain with opiate dependence, multiple joint replacements several years ago, recurrent deep vein thromboembolism (DVT), hypertension, post-surgical seizures following meningioma resection, depression, anxiety, and mild leg edema. The patient's medication list is presented in Table 1.

The patient notes that he has frustrations with how many pills he is taking and how often he takes them. He is not taking omeprazole, cyclobenzaprine, and diphenhydramine every day due to not having symptoms and not remembering to use them. Of note, the patient's phenytoin level has been subtherapeutic for several years, but he has not had any seizures. He reports experiencing sedation when his phenytoin was therapeutic in the past.

POLYPHARMACY AND DEPRESCRIBING

Polypharmacy is defined as the use of five or more medications. Over time, patients taking five medications will average one significant drug problem, including adverse events, undesired side effects, or drug interactions.[2] Older age also correlates with increased medical complexity, and a prescribing cascade to mitigate side effects from previous prescriptions can occur.[2,3]

Retention of these medications poses a higher risk of morbidity and mortality. A patient's changing physiology, social situation, and goals of care must be considered, as polypharmacy may put our geriatric patients at greater risk of adverse drug reactions (ADRs), serious complications, or death.[3]

The act of removing or reducing the dose of medications to avoid unnecessary adverse effects, reduce medication burden, and improve quality of life is called *deprescribing.* Patients also have a desire to reduce their medications; one study demonstrated 92% of older adults would be willing to stop one or more of their medications if their physician felt it was possible.[4] Oftentimes, patients may be more resistant to deprescribing with long-term use, continued effectiveness, or physical dependence.

Effective deprescribing in patients with polypharmacy starts with recognition that this population is at high risk for ADRs. Critical and holistic review of patient medications should occur during any hospitalization, as well as at least every six months in outpatient settings, especially in frail or elderly populations.[5] We should ask our patients to bring all medications, including over-the-counter (OTC) medications and supplements, to each appointment and perform a formal medication reconciliation.

During medication reconciliation, it is helpful to assess for adherence to medications and frequency of use, particularly with "as needed" medications. Medicines the patient is not frequently using or that no longer serve their intended purpose are often good medications to deprescribe if they are not providing the medical benefits needed.

Other priorities should include identification of drug-drug interactions, medications without indication(s), and evidence of class duplication that may have additive side effects.

Clinical decision support tools such as the Screening Tool of Older Persons' Prescriptions/Screening Tool to Alert to Right Treatment (STOPP/START), Anticholinergic Burden Scale, and other drug-drug interaction databases can be helpful in identifying drug-drug or drug-disease interactions.[5-7]

Determining the need for routine lab monitoring in the management of warfarin, lithium, amiod-

arone, and phenytoin is important, as is assessing if the treatment regimen can be simplified by choosing treatments that do not require monitoring. Supplements and OTC medications are often overlooked, but discontinuing these can also help reduce total pill burden.

BEERS CRITERIA

Since 1991, the Beers Criteria has served as a resource to guide prescribing practices to identify medications with potential harm that outweigh the expected benefit in nursing home residents. Formally known as the American Geriatrics Society (AGS) Beers Criteria® for Potentially Inappropriate Medications (PIM) in Older Adults, the Beers Criteria has now morphed into a multidisciplinary-reviewed document.

The 2023 update identifies PIMs for older adults in all care settings, except for hospice and end-of-life care. It is a tool for evaluation and consideration for health care practitioners and is not intended to serve as a binding guideline, recognizing that geriatric care means being thoughtful about a wide range of ages, health care statuses, and goals of care.[8]

The Beers Criteria is divided into five sections:

1. Medications considered to be potentially inappropriate.
2. Medications potentially inappropriate in patients with certain diseases or syndromes.
3. Medications to be used with caution.
4. Potentially inappropriate drug-drug interactions.
5. Medications whose dosages should be adjusted based on renal function.

Table 1. Example Patient's Medication List

Aspirin	81 mg daily
Clindamycin	600 mg prior to dental procedure(s)
Cyclobenzaprine	10 mg at night as needed
Warfarin	5 mg daily
Phenytoin	100 mg three times daily
Furosemide	40 mg daily
Diphenhydramine	25 mg daily
Metoprolol succinate ER	25 mg daily
Naloxone	4 mg/0.1 mL nasal liquid, one spray in a nostril as needed
Oxycodone	5 mg every 4 hours as needed
Potassium chloride ER	20 mEq daily
Duloxetine	30 mg three times daily
Escitalopram	10 mg at night
Omeprazole	40 mg daily

Section 1: Medications Considered to Be Potentially Inappropriate

This section covers common drugs to avoid in geriatric patients grouped by organ systems and therapeutic class. Commonly thought of medications within this first section are outlined in a-b. Recommendations c-f are notable updates. These recommendations include:

a. Avoid first-generation antihistamines due to anticholinergic properties and reduced clearance.
b. Avoid non-selective peripheral alpha-1 blockers as antihypertensives due to a risk of orthostatic hypotension and benzodiazepines, which can cause increased risk of sensitivity, cognitive impairment, delirium, falls, fractures, and motor vehicle crashes.
c. Aspirin can cause bleeding. There is lack of evidence of benefit and evidence of potential harm when used for primary prevention of cardiovascular disease.
d. Warfarin, when used for management of nonvalvular atrial fibrillation or venous thromboembolism (VTE), should be avoided as initial therapy unless alternative anticoagulants are contraindicated or there are other barriers to use. It would be appropriate to continue therapy if the international normalized ratio (INR) has been within range 70% of the time and there have not been adverse effects.
e. Rivaroxaban, when used for treatment of nonvalvular atrial fibrillation or VTE, can cause major, including gastrointestinal (GI), bleeding. This treatment option may be reasonable for treatment if daily dosing is needed.
f. All sulfonylureas are now discouraged due to the risk of cardiovascular (CV) events, all-cause mortality, and hypoglycemia compared to other available medications for type 2 diabetes management. In previous editions of the Beers Criteria, glipizide was not included.

Additional language and clarification of certain drug classes were revised in the 2023 update, including:

- Regarding proton pump inhibitors and the risks associated with C. *difficile* infection, bone density loss, and fractures, it is strongly recommended they be used for no more than eight weeks.
- Non-COX-2 selective oral NSAIDs may be reasonable for short-term use when other agents are inappropriate or ineffective.
- Skeletal muscle relaxants can cause anticholinergic effects, sedation, and fractures. The criteria differentiate between those used for musculoskeletal complaints, which are considered PIMs, and

those used for treatment of spasticity, which may be appropriate.

Section 2: Medications Potentially Inappropriate in Patients with Certain Diseases or Syndromes

The 2023 update added that dextromethorphan and quinidine should be avoided in the setting of heart failure, anticholinergics should be avoided in patients with cognitive impairment or a high risk of falls and fractures, and opioids may exacerbate delirium.

Section 3: Medications to Be Used with Caution

Sodium-glucose cotransporter-2 (SGLT-2) inhibitors are now widely used. While they can provide cardiovascular and renal benefits, SGLT-2 inhibitors were added to the list due to the risk of urogenital infections and euglycemic diabetic ketoacidosis. Prasugrel and ticagrelor were also included because of emerging evidence that these antiplatelet agents increase the risk of major bleeding in comparison to clopidogrel.

Regarding anticoagulation, while warfarin and rivaroxaban were identified as PIMs, dabigatran is regarded as one to use with caution due to the risk for GI bleeding when compared to warfarin and apixaban.

Other notable medications to use with caution include those medications that increase the risk for hyponatremia or syndrome of inappropriate antidiuretic hormone secretion (SIADH), including antidepressants such as mirtazapine, tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), as well as antiepileptics such as carbamazepine and oxcarbazepine, antipsychotics, diuretics, and tramadol. These have historically been listed in prior Beers Criteria, while SGLT-2 inhibitors and ticagrelor were new additions.

Section 4: Potentially Inappropriate Drug-Drug Interactions

Among updates are the recommendations to avoid the concomitant use of:

- Skeletal muscle relaxants added to any combination of three or more central nervous system (CNS) active drugs.
- Lithium with angiotensin receptor blockers and angiotensin receptor-neprilysin inhibitors.
- Warfarin with SSRIs.

Previous notable interactions identified in the Beers Criteria that remain in the most recent update include:

- Opioids and benzodiazepines, gabapentin, or pregabalin.

Table 2. Risks Associated with Example Patient's Medication List

Medical Issue	Medication	Medication Class	Adverse Reactions/ Side Effects	Lab Monitoring
Chronic pain	Oxycodone*	Opiate	**Sedation,** physical dependence	
	Cyclobenzaprine*	Muscle relaxant	**Sedation, anticholinergic properties**	
	Naloxone	Opiate antagonist		
Joint replacement	Clindamycin	Antibiotic	**Stomach upset,** diarrhea, increased risk of *C. diff* infection	
Seizure	Phenytoin	Anti-epileptic	Sedation, increased fall risk, **strong inducer of CYP450**	
Recurrent DVT	Warfarin*	*Anticoagulant*	**Increased bleeding risk** or increased risk of VTE if subtherapeutic, metabolized by CYP450	INR
	Aspirin*	*Anti-platelet*	**Increased bleeding risk**	Platelets
Lower extremity edema	Furosemide	Diuretic	**Hypotension, electrolyte disturbance**	Electrolytes, renal function
Depression/anxiety	Duloxetine	*SNRI*	**Headache, stomach upset**	Electrolytes, renal function
	Escitalopram	*SNRI*	**Headache, stomach upset**	Electrolytes, renal function
Hypertension	Metoprolol succinate ER	Beta blocker	**Hypotension, bradycardia**	
No diagnosis to associate from given past medical history	Omeprazole*	Proton pump inhibitor	Increased risk of *H. pylori* infection, vitamin and mineral deficiency	Vitamin D, vitamin B12, magnesium
	Diphenhydramine*	Antihistamine	**Sedation,** headache, anticholinergic side effects	
	Potassium chloride ER	Electrolyte	**Cardiac arrhythmia, muscle cramping**	Electrolytes

Medications included in updated Beers Criteria; **bolded side effects denote duplicate side effect of multiple medications; italicized items under medication class denote duplicate therapeutics; CYP450 = cytochrome P450, DVT = deep vein thromboembolism, VTE = venous thromboembolism, INR = international normalized ratio.*

Table 3. Proposed Changes to Example Patient's Medication List

Original Medication List		Revised Medication List	
Aspirin	81 mg daily	DISCONTINUE	
Clindamycin	600 mg prior to dental procedure(s)	DISCONTINUE	
Cyclobenzaprine	10 mg HS prn	DISCONTINUE	
Warfarin	5 mg daily	Apixaban	5 mg BID
Phenytoin+	100 mg TID	Levetiracetam	500 mg BID
Furosemide	40 mg daily	DISCONTINUE	
Diphenhydramine+	25 mg daily	DISCONTINUE	
Metoprolol succinate ER	25 mg daily	Chlorthalidone	25 mg daily
Naloxone	One nasal spray prn	Naloxone	One nasal spray prn
Oxycodone+	5 mg q4h prn	Buprenorphine patch	One 10 mcg/hr patch weekly
Potassium chloride ER	20 mEq daily	DISCONTINUE	
Duloxetine+	30 mg TID	Duloxetine	90 mg daily
Escitalopram	10 mg daily HS	DISCONTINUE	
Omeprazole+	40 mg daily	DISCONTINUE	
Total Medications	**14**	**6**	

+Medication notes: when changing from phenytoin, cross taper to minimize chance of breakthrough seizure; regarding diphenhydramine, if a patient has allergic symptoms after discontinuation, a second-generation antihistamine is preferred; oxycodone, 30 MME/day equivalent dose; max daily dose of duloxetine = 120 mg; if GERD symptoms return after discontinuing the proton pump inhibitor, an H2 blocker would be preferred.

- Two or more anticholinergic agents.
- Three or more CNS active agents.
- Warfarin and several antibiotics, including ciprofloxacin, macrolides (excluding azithromycin), and trimethoprim sulfamethoxazole.
- Warfarin and any SSRI.

Section 5: Medications Whose Dosages Should Be Adjusted Based on Renal Function

Notable updates to this section include an item regarding the anticoagulant apixaban. Previously, this medication was to be avoided in patients with a creatinine clearance <25 mL/min; however, emerging data regarding its use in patients with low renal function suggest it can be reasonable, thus it is no longer listed in this section of the Beers Criteria.

Renal dosage adjustments based on kidney function (eGFR) are recommended in patients using baclofen as an antispasmodic skeletal muscle relaxant.

Other medications in which impaired renal function increases the risk for side effects include gabapentin, duloxetine, pregabalin, tramadol, famotidine, levetiracetam, and colchicine, among others.

CLINICAL INERTIA

With the use of the Beers Criteria and an awareness regarding polypharmacy concerns, judicious deprescribing may be appropriate.

Clinical inertia is defined as "the lack of treatment intensification in a patient not at evidence-based goals for care."[9] Several causes, including complexity of polypharmacy, lack of awareness or training, systemic barriers, and patient factors, may contribute.

Fortunately, using resources appropriately can combat clinical inertia and provide better outcomes for the patient. A clinical pharmacist is recommended to help deprescribe medications.[10,11]

CASE VIGNETTE: MEDICATION CHANGES

Returning to our 81-year-old male who presented as a new patient, we note he has symptoms related to his polypharmacy. He is frustrated with the timing of medications, as well as his pill burden.

Complex patients require a holistic approach to better assess for medication necessity, streamline evaluation of side effect profile, and determine clinical adherence feasibility. Table 2 demonstrates one approach to synthesizing this patient's information.

The goal of a revised medication list is to safely discontinue or reduce doses, or to transition medications to safer or more effective alternatives. Table 3 represents a proposed improved medication list, including drug removal, substitutions, and dosing changes.

The proposed improved medication list was determined using a 10-step methodology and approach to deprescribing (see Table 4 on page 40).

Table 4. Ten-Step Methodology and Approach to Deprescribing	
1	Match diagnosis with medications.
2	Identify high-risk medications.
3	Assess for any duplicate medications.
4	Assess for drug-drug interactions.
5	Assess for drug-disease interactions.
6	Review OTC and supplement necessity.
7	Assess for needed lab monitoring.
8	Assess for drug adherence.
9	Assess for necessity of medications.
10	Optimize medications and simplify regimen.

Step 1: Match Diagnosis with Medications

Omeprazole, diphenhydramine, and potassium chloride were not associated with a specific diagnosis in this example. Table 2 on page 38 demonstrates which medications do and do not have a current diagnosis association.

Step 2: Identify High-Risk Medications

Particularly high-risk medications in the vignette include oxycodone and cyclobenzaprine. Regarding this patient's history of chronic pain and opiate dependence, tapering narcotic medications is preferred due to sedating side effects, but doing this quickly is often not practical. Transitioning the patient to a morphine-equivalent buprenorphine patch is preferable for more consistent pain control and to simplify the regimen.

In addition, this patient would likely benefit from discontinuation of cyclobenzaprine as it is not being used regularly, has great potential for side effects, and can interact negatively with other medications on the list. Other high-risk medications that will be discussed in more detail below include phenytoin and warfarin.

Step 3: Assess for Any Duplicate Medications, and Step 4: Assess for Drug-Drug Interactions

Duloxetine and escitalopram represent similar medication classes; SSRI and SNRI medications should not be taken simultaneously, as this increases the risk of hyponatremia and additive side effects. Maximizing the patient's SNRI dosage will allow discontinuation of the SSRI since duloxetine alone could treat chronic pain and mood issues in this case.

Phenytoin is known to react with warfarin as it is a cytochrome (CYP) P450 inducer. In this patient, subtherapeutic levels are of concern. Levetiracetam was chosen as an alternative as it has an easier dosing schedule and does not require blood monitoring. It is also worth considering that in the setting of subtherapeutic anti-epileptic drug levels and no recent history of seizure, this patient may not need an anti-epileptic drug.

Low-dose aspirin is no longer recommended for primary prevention of atherosclerotic cardiovascular disease; however, in this case it could be considered secondary prevention.[12] While this patient has had a DVT, he could be anticoagulated with a direct oral anticoagulant (DOAC). The benefit of aspirin would be modest and in the setting of a DOAC would pose an increased risk of bleeding.

Low-dose aspirin has been studied as an alternative for the extended prevention of VTE, yet DOACs decrease rates of recurrence and are therefore preferred.[13]

Step 5: Assess for Drug-Disease Interactions

Utilizing the side effects of one medication as a treatment for a secondary medical problem can be one strategy to reduce medication burden. In this patient case, transitioning from metoprolol succinate to chlorthalidone would remove an agent that is not considered a first-line agent for hypertension.[14]

Thiazide diuretics, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blockers may be more helpful with mild leg swelling. The Dietary Approaches to Stop Hypertension (DASH) diet is also a consideration for adjunctive nonpharmacological management of hypertension and leg edema. In this patient's case, we would avoid calcium channel blockers, which can exacerbate leg swelling. Given that the leg swelling has been mild, the patient likely can discontinue his furosemide and potassium chloride by changing the antihypertensive.

Step 6: Review OTC and Supplement Necessity

This patient does not take over-the-counter medications or supplements.

Step 7: Assess for Needed Lab Monitoring

Changing warfarin to apixaban will negate the need for regular INR checks. Similarly, changing phenytoin to levetiracetam for seizure prophylaxis eliminates the need for drug concentration monitoring.

Step 8: Assess for Drug Adherence, and Step 9: Assess for Necessity of Medications

The patient was not taking omeprazole, diphenhydramine, and cyclobenzaprine regularly and therefore they were discontinued.

In elderly patients, medications such as dental prophylaxis and aspirin commonly linger on the medication list. Antibiotic therapy is no longer recommended routinely with dental work in a patient with stable joint replacements.[15,16]

There are always exceptions to this rule, however in this case clindamycin can be safely discontinued. Collaboration with specialists is encouraged when determining medication necessity.

Step 10: Optimize Medications and Simplify Regimen

Several changes were made to simplify the regimen, including a once-weekly buprenorphine patch and daily dosing of duloxetine instead of three-times-daily dosing. Twice-daily dosing of levetiracetam is also an improvement over that needed for phenytoin.

CONCLUSION

Polypharmacy is quite common among patients and creates risks for ADEs, as well as drug-disease and drug-drug interactions, especially in the geriatric population.

Routine hands-on medication reconciliation during patient follow-up is crucial in identifying opportunities to deprescribe.

Various resources, such as STOPP/START, the Anticholinergic Burden Scale, and the Beers Criteria, are available to help identify high-risk medications in older adults. Active discussion with patients and caregivers is encouraged during the deprescribing process.

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A Review of Novel Pharmacotherapeutic Agents for the Management of Type 2 Diabetes Mellitus

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The National Institute of Diabetes and Digestive and Kidney Diseases estimates the prevalence of diabetes in the United States was 37.3 million in 2019, and global estimates suggest 537 million adults live with diabetes.[1,2] Novel agents for managing diabetes are efficacious and offer cardiovascular (CV) and renal benefits that make them important in management. Additionally, ultra-long-acting and highly concentrated insulins make flexible dosing and lower injection volumes possible.[3,4]

Studies demonstrate sodium-glucose cotransporter type 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) can reduce major adverse cardiac events.[5-12] These are now considered first-line agents in patients with atherosclerotic cardiovascular disease or high CV risk, patients with established kidney disease, and those with heart failure, regardless of the glycosylated hemoglobin (HbA1C) at the initiation of therapy.[13]

In addition, a novel GLP-1/glucose-dependent insulinotropic polypeptide (GIP) dual agonist, tirzepatide, was approved by the Food and Drug Administration (FDA) in 2022. Despite final cardiovascular outcome trial (CVOT) data in progress, this agent has been shown to improve diabetes control and promote significant weight loss compared to other therapeutic options. A review of these agents follows.

SGLT2 INHIBITORS

SGLT2 inhibitors are relatively novel oral agents that have intermediate to high efficacy in lowering HbA1C. Currently available therapies include canagliflozin, dapagliflozin, and empagliflozin; new agents include bexagliflozin and ertugliflozin. SGLT2 inhibitors work in the apical membrane of the proximal tubule of the kidney, blocking glucose reabsorption from glomerular filtration by the SGLT2 receptor, reducing glycemia by causing glycosuria; this primarily affects fasting blood glucose.[14] Other than lowering HbA1C by approximately 1%, these once-daily medications modestly reduce body mass and blood pressure, thus addressing numerous comorbidities within the population affected by diabetes.[15]

Due to efficacy and their ability to reduce CV and renal risks, SGLT2 inhibitors are now considered one of the first-line agents for type 2 diabetes mellitus (T2DM).[13] Cardiovascular benefits include decreased likelihood for heart failure-related hospitalizations, as well as a potential reduction in major cardiovascular events (MACE) and CV-related deaths. Renal benefits include decreased albuminuria, a reduced need for renal replacement therapy, stabilization of estimated glomerular filtration rate (eGFR), and reduced risk for disease progression.[5-8,12,15-19]

Although there are eGFR cut-offs at which initiation of SGLT2 inhibitor therapy is not recommended, these agents may be continued until initiation of dialysis in those established on therapy.[20] Additionally, newer research proposes that, because SGLT2 inhibitors lower blood pressure without raising heart rate, they decrease sympathetic overactivity, subsequently causing reductions in blood pressure, heart rate, and edema, which may be the partial etiology of therapeutic benefit seen in heart failure.[16]

SGLT2 inhibitors do have risks that may preclude their use. Due to the mechanism of action, SGLT2 inhibitors may cause acute kidney injury, volume depletion, and fluctuations in serum electrolytes, which is more important if patients are taking other antihypertensives or diuretics.[21-25] Electrolytes and renal function should be monitored at baseline and periodically during treatment.

These agents may cause an increased risk of diabetic ketoacidosis, and even euglycemic diabetic ketoacidosis, so it is recommended to hold therapy three to four days prior to planned surgeries depending on the agent.[26,27] Additionally, they increase the risk of developing a urinary tract infection or genitourinary fungal

infection; rarely, Fournier's gangrene can occur.[21-25] Furthermore, canagliflozin, bexagliflozin, and ertugliflozin may increase the risk for lower limb amputation in clinical trials. Canagliflozin previously held a black box warning for lower limb amputations, but this was removed from the product labeling in 2020.[23]

SGLT2 inhibitors can be used as monotherapy or add-on therapy. Cost may limit access.

GLP-1 RECEPTOR AGONISTS

GLP-1 RAs are another burgeoning class of agents for the treatment of T2DM. Agents in this class include dulaglutide, exenatide, liraglutide, and semaglutide. While all these medications are given via subcutaneous injection, semaglutide is also available as an oral preparation. GLP-1 is an incretin hormone that increases glucose-dependent insulin secretion, decreases glucagon secretion, delays gastric emptying, and increases satiety, thereby decreasing food intake among other effects.[28]

GLP-1 RAs enhance these pleiotropic effects and primarily act on post-prandial blood glucose. They are highly effective for the treatment of T2DM, with HbA1C reductions of 1% to 2%.[13,15] While native GLP-1 is typically short-lived due to enzymatic degradation by dipeptidylpeptidase-4 (DPP-4) and renal elimination, synthetic GLP-1 RA peptides have altered amino acid profiles that cause them to stay active longer, allowing for either daily or weekly administration.[28]

GLP-1 RAs lower HbA1C and also have cardioprotective and renoprotective effects; therefore, they are also considered first-line options for T2DM depending on patient risks.[13] Specifically, these agents decrease the risk for MACE, including CV death, nonfatal myocardial infarction, and nonfatal stroke.[9-11,29] Renal benefits include reduced albuminuria, slowed decline in eGFR, as well as a reduced risk of renal replacement therapy.[30-33] With currently available data, the American Diabetes Association highlights dulaglutide, liraglutide, and semaglutide (injection) as having cardiac and renal benefits.[13] Though all of these agents share a similar mechanism of action, it is noteworthy that exenatide has a different chemical structure and is not approved for CV risk reduction.

In addition to cardiorenal benefits, numerous GLP-1 RAs also have been shown to produce at least

Table 1. SGLT2 Inhibitor Dosing and Labeling

Agent	Starting Dose	Maximum Dose	Dose Adjustments	FDA Labeling for CV Benefit	FDA Labeling for HF Benefit	FDA Labeling for Renal Benefit
Bexagliflozin (Brenzavvy™)	20 mg PO daily in the morning	20 mg daily	eGFR <30: use not recommended	No	No	No
Canagliflozin (Invokana®)	100 mg PO daily	300 mg daily	eGFR 30 to <60: max 100 mg daily eGFR <30: do not initiate Child-Pugh class C: not studied Use with concomitant UGT inducers (e.g., phenytoin, phenobarbital, rigampin, ritonavir): increase to 300 mg daily if eGFR ≥60, otherwise consider alternative	Yes	No	Yes
Dapagliflozin (Farxiga®)	5 mg PO daily	10 mg daily	eGFR <25: do not initiate	Yes	Yes	Yes
Empagliflozin (Jardiance®)	10 mg PO daily	25 mg daily	eGFR <30: do not initiate	Yes	Yes	Yes
Ertugliflozin (Steglatro®)	5 mg PO daily	15 mg daily	eGFR <45: do not initiate Child-Pugh class C: not studied	No	No	No

PO = "by mouth"; eGFR = estimated glomerular filtration rate (mL/minute/1.73 m²); UGT = uridine 5'-diphospho-glucuronosyltransferase.

a 5% weight reduction from baseline; liraglutide and semaglutide are each approved for weight loss at higher doses than used for T2DM.[34,35] When used with therapeutic lifestyle modifications, these medicines have been revolutionary in the management of patients who are overweight and obese. Studies demonstrate weight loss delays the progression from prediabetes to T2DM and improves glycemia, reducing the need for other glucose-lowering therapies.[13] In regard to further metabolic benefits, GLP-1 RAs may reduce morbidities in patients with non-alcoholic fatty liver disease.[13,36]

The most recent GLP-1 RA to come to market is semaglutide, available as a once-weekly subcutaneous injection and a once-daily oral tablet.[37,38] With both formulations, the lowest dose is not considered an effective dose for blood glucose lowering and is meant as a "step up" to the next dose to limit potential side effects. It is unclear whether one formulation is more effective than the other, but both reduce HbA1C compared with placebo.[39,40]

In numerous trials, weekly subcutaneous semaglutide 1 mg helped patients decrease their HbA1C by 1.5% to 1.8% compared with sitagliptin, liraglutide, exenatide extended release, dulaglutide, canagliflozin, or insulin glargine; various doses were used among the comparator medications.[41] In further trials, oral semaglutide 14 mg reduced HbA1C levels by 1% to 1.4% compared with sitagliptin or empagliflozin.[41] A randomized controlled trial demonstrated that subcutaneous semaglutide yields cardioprotection, and a pooled analysis of previous trials demonstrates it yields renoprotection as well.[10,33,42] Oral semaglutide is safe for use in moderate renal impairment and was non-inferior to placebo in terms of CV outcomes.[29,32] In obesity studies, both injectable and oral semaglutide significantly reduced body weight compared with placebo by at least 5% from baseline.[35,43]

One of the primary challenges for patients with this class of medications is gastrointestinal side effects, such as nausea, vomiting, diarrhea, constipation, and slowed gastric emptying,[37,38,44-47] which can exacerbate gastroparesis and other gastrointestinal disorders. These side effects appear to be a class effect, likely partially due to the mechanism of action.

To combat this, it is recommended to start at the lowest dose and titrate slowly with at least four weeks between each dosing increase for once-weekly GLP1 medications. As noted above, the lowest doses of both oral and injectable semaglutide are meant as tolerability doses and are not expected to lower blood

Table 2. GLP-1 RA and GLP-1/GIP Agonist Dosing and Labeling

Agent	Starting Dose	Maximum Dose	Dose Adjustments	FDA Labeling for CV Benefit	FDA Labeling for Weight Loss
Dulaglutide (Trulicity®)	0.75 mg subQ weekly	4.5 mg weekly	None	Yes	No
Exenatide (Byetta®)	5 mcg subQ twice daily before meals	10 mcg twice daily	Avoid if CrCl <30 or end-state renal disease	No	No
Exenatide ER (Bydureon®)	2 mg subQ weekly	2 mg weekly	Avoid if CrCl <30 or end-state renal disease	No	No
Liraglutide (Victoza®)	0.6 mg subQ daily	1.8 mcg daily	None	Yes	Yes (Saxenda®)
Semaglutide Injectable (Ozempic®)	0.25 mg subQ weekly	2 mg weekly	None	Yes	Yes (Wegovy®)
Semaglutide Oral (Rybelsus®)	3 mg PO daily	14 mg daily	None	No	No
Tirzepatide (Mounjaro™)	2.5 mg subQ weekly	15 mg weekly	None	No	Yes (Zepbound™)

subQ = subcutaneously; PO = "by mouth"; CrCl = creatinine clearance (mL/minute); eGFR = estimated glomerular filtration rate (mL/minute/1.73 m²).

glucose, though they could have a mild effect in some patients.

Other potential adverse effects of this class include acute kidney injury in the setting of dehydration due to gastrointestinal side effects, gallbladder and biliary diseases, and acute pancreatitis, especially if the patient has comorbid hypertriglyceridemia. Additionally, GLP-1 RAs are contraindicated (black box warning) in patients with a personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, as this is a rare, dose-dependent, and duration-dependent complication that appeared in mice and rats treated with GLP-1 RAs, with the exception of exenatide daily injection.[37,38,44-47]

Lixisenatide was discontinued from the U.S. market in 2023 but is still available in a combination product with insulin glargine.[48] Fortunately, since these agents cause glucose-dependent insulin secretion, they have a low risk for causing hypoglycemia as monotherapy, which makes them a favorable option for many T2DM patients.[13]

Generally, GLP-1 RAs are a highly effective option for T2DM, with numerous agents as options for comorbid atherosclerotic CV disease or chronic kidney disease, as well as for providing dose-dependent weight reduction.[13] While cost may limit their use, GLP-1 RAs are another effective first-line option for T2DM, as either monotherapy or add-on therapy.

GLP/GIP DUAL RECEPTOR AGONIST

A newer, dual incretin (twincretin) protein agonist for GLP-1 and GIP, tirzepatide is now available for patients with T2DM. Similar to GLP-1 RAs, tirzepatide is a once-weekly subcutaneous injection, with its first dose as a "step-up" dose, not meant for providing glycemic control.[49]

Tirzepatide works similarly to GLP-1 RAs, but with added GIP agonism, allowing for a synergistic effect on both glycemic control and weight reduction.[50,51] Theoretically, dual agonism of GLP-1 and GIP could make tirzepatide superior in HbA1C lowering compared with GLP-1 RAs, and trials suggest that it can lower HbA1C as much as 2%.[51]

A head-to-head study compared three different doses of tirzepatide to 1 mg of semaglutide but did not include the maximum dose of semaglutide (2 mg); yet all three doses of tirzepatide used in the study were non-inferior and superior to 1 mg semaglutide for reductions in HbA1C.[52]

Similar to its monotherapeutic target counterparts, tirzepatide can facilitate weight reduction of at least 5% from baseline and 15% on average.[50] In a head-to-head trial of tirzepatide versus semaglutide for diabetes, all three doses of tirzepatide resulted in more weight loss than 1 mg of semaglutide.[52]

Tirzepatide was also approved in November 2023 for use in the treatment of patients diagnosed as overweight and obese. Unfortunately, there are no published data to elucidate CV and renal outcomes in patients taking tirzepatide. A study is ongoing, and this trial may help delineate whether tirzepatide has the same cardioprotective effects as other GLP-1 RAs.

INSULIN

While human insulin analogues have been available since 1982, there have been several updates in the last decade. Insulins are often categorized based on duration of action and concentration. In 2015, two new insulin preparations became available in the United States: insulin degludec (U-100 and U-200) and insulin glargine (U-300).

Insulin degludec is the first ultra-long-acting insulin available in the United States. It has a terminal half-life of approximately 25 hours and a duration of action exceeding 42 hours. Once injected, insulin degludec is slowly absorbed following zero-order kinetics, providing consistent glucose-lowering and low patient-to-patient pharmacokinetic variation. The extended duration of action allows for flexible dosing, meaning patients may wait 8 to 40 hours between doses without compromising patient safety.[3,53]

A study of a forced-flexible dosing schedule for insulin degludec demonstrated similar safety and efficacy compared to standard dosing of insulin degludec and insulin glargine.[54] Participants in the forced-flexible dosing group administered insulin degludec on an alternating morning and evening schedule in which there was a minimum of eight hours and a maximum of 40 hours between injections. This highlights insulin degludec as a preferred basal insulin option for patients in which schedule conflicts or other barriers make it difficult to administer insulin at the same time each day.

Another benefit of insulin degludec is lower rates of nocturnal hypoglycemia.[55-58] A meta-analysis of seven clinical trials including over 3,300 participants with T2DM showed patients using this medication had lower rates of nocturnal hypoglycemia compared

to patients using insulin glargine. In participants with T2DM not on bolus insulin, nocturnal hypoglycemia rates ranged from 6.1% to 20.4% with insulin degludec versus 8.8% to 24% with insulin glargine (rate ratio = 0.68; 95% CI = 0.57-0.82). Patients using insulin degludec also had a lower fasting plasma glucose.[58]

Insulin glargine U-300 contains 300 units for every milliliter, compared to 100 units per milliliter for U-100 insulin glargine. This allows for decreased injection volumes and differences in pharmacokinetics and pharmacodynamics compared to U-100 insulin glargine. U-300 insulin glargine has an onset of action of six hours and duration of action of up to 36 hours, compared to U-100, which takes effect within three hours and lasts for up to 24 hours.[4]

Despite having the same active ingredient as insulin glargine U-100, prescribers should be cautious when switching between products, as the dosing conversion is not necessarily 1:1. Thus when switching from insulin glargine U-100 to U-300, higher doses may be needed to achieve glycemic goals. In reverse, when switching from insulin glargine U-300 to U-100, the dose should initially be reduced by 20%. Dose titrations should be limited to every three to four days.[4]

A study investigating the safety and efficacy of insulin glargine U-300 in patients with T2DM demonstrated patients needed higher doses of insulin glargine U-300 to achieve similar efficacy compared to U-100; however, hypoglycemia rates were similar or lower regardless of the definition of hypoglycemia. Despite higher insulin requirements in patients receiving U-300 compared to patients receiving U-100, participants receiving insulin glargine U-300 either lost more weight or gained less weight compared to those on U-100.[59-62]

Several head-to-head trials have compared insulin glargine to insulin degludec. One such crossover study, in which patients used continuous glucose monitors, demonstrated that patients using insulin degludec U-100 had greater time in range and reduced incidences of hypoglycemia and nocturnal hypoglycemia.[63] A treat-to-target trial comparing insulin degludec U-200 to insulin glargine U-300 showed no difference in safety or rates of hypoglycemia.[64]

Similarly, a 24-week trial comparing insulin glargine U-300 to insulin degludec U-100 showed similar improvements in HbA1C and rates of hypoglycemia. Mean insulin doses among patients using insulin glargine U-300 were higher than those in patients using insulin degludec U-100 (0.54 units/kg versus 0.43 units/kg, respectively).[65]

Insulin degludec and insulin glargine are both valuable options for managing T2DM. More highly concentrated insulin degludec U-200 or insulin glargine U-300 are reasonable options if a patient's insulin requirement exceeds 60 units per dose. Switching to these agents may improve adherence by reducing the need to split the basal insulin dose into two daily injections.

Patients in need of flexible insulin dosing may benefit from insulin degludec U-100 or U-200. Although clinical factors should be evaluated in determining the appropriate product, medication access and cost may influence insulin selection.

KEY TAKEAWAYS

- *SGLT2 inhibitors have intermediate to high efficacy in lowering HbA1C.*
- *GLP-1 RAs and SGLT2 inhibitors can be used as mono- or add-on therapy.*
- *The altered amino acid profile of GLP-1 RAs allows them to stay active longer for weekly administration. They may produce at least 5% weight reduction from baseline.*
- *Newer preparations of insulin may allow for weekly or even monthly administration.*

T2DM MEDICATION PIPELINE

Sotagliflozin is a novel dual SGLT1-SGLT2 inhibitor currently approved in the United States for use in heart failure, as well as for CV risk reduction in patients with T2DM and CKD (with or without albuminuria). It is available as 200 mg tablets, and the dose may be increased to 400 mg after at least two weeks.[66]

In the European Union, sotagliflozin has already been approved in the treatment of type 1 diabetes mellitus.[67] The inhibition of SGLT1 in the intestines slows intestinal glucose absorption and is therefore a mechanism for reducing post-prandial glucose levels.[68,69]

A study published in *Diabetes Care* in 2022 comparing sotagliflozin to empagliflozin in patients with T2DM showed sotagliflozin reduced postprandial glucose, insulin, and GIP, and increased GLP-1. These

benefits waned after lunch and dinner.[70] The mechanism for this change is not fully understood.

A 26-week phase III study of sotagliflozin 400 mg monotherapy in patients with T2DM not otherwise treated with antidiabetic therapy showed reductions in A1C of 1.03% compared to only 0.34% with placebo. Diarrhea, urinary tract infections, and headaches were the most reported adverse effects. At the time of this writing, this study was not yet published, but results of the trial are available on clinicaltrials.gov (NCT02926937).

Danuglipron (PF-06882961) is a small-molecule, oral GLP-1 RA in development for the treatment of T2DM and obesity. At this time, only phase I and phase II studies have been published. A phase IIb study investigating danuglipron in patients with T2DM with or without metformin demonstrated it reduced A1C and fasting plasma glucose at 16 weeks at doses ranging from 2.5 mg to 120 mg. This medication is administered orally twice daily with food, and doses are escalated with a target dose of danuglipron 40 mg or more twice a day. Similar to other GLP-1 RAs, this medication can cause adverse effects such as nausea, diarrhea, and vomiting.[71]

Insulin icodec is a novel basal insulin under investigation for use in both type 1 and type 2 diabetes. Its half-life exceeds 196 hours and reaches steady state after three to four weekly injections. Two trials of insulin icodec have been published. The first was a 26-week open label randomized controlled trial, which demonstrated that insulin-naïve participants had similar improvement in their HbA1C and no increased risks — that is, incidence of hypoglycemia — compared to decludec.[72,73]

The second trial was a 26-week, randomized, open-label treat-to-target trial in which participants with baseline HbA1C from 7% to 10% were assigned to once-weekly icodec or once-daily insulin glargine U-100, which was combined with two to four daily bolus insulin injections. Insulin icodec was non-inferior to insulin glargine U-100 in HbA1C lowering at 26 weeks. Participants in the icodec group needed fewer bolus insulin doses and experienced similar rates of hypoglycemia compared to participants using insulin glargine U-100.[74]

CONCLUSION

Type 2 diabetes mellitus remains a threat to global health despite the continued expansion of therapeutics available for its management. SGLT2 inhibitors, GLP-1 RAs, and a novel GLP/GIP agonist offer clinicians and patients many new options, while newer insulin formulations can change the landscape of T2DM management.

Additionally, several novel agents — including a dual SGLT1-SGLT2 inhibitor and a once-weekly basal insulin option — are in development.

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Visit jlgh.org/T2DM or scan the QR code below to view the references for this article.

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A Trauma-Informed Care Educational Program for the Staff of an Outpatient Cancer Center


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Trauma is a global problem with life-altering effects that can impact the health and well-being of individuals and families for generations. Each year, the United States spends $4.2 trillion on trauma expenses due to work losses and trauma-related medical costs associated with cancer, heart disease, chronic respiratory disease, liver disease, and diabetes.[1] At the same time, trauma-related grant funding through the National Institutes of Health is only 0.02% of its budget.[2] Compounding the problem, evidence shows that health care providers lack the knowledge and skills to assess and treat patients with a recent or remote history of trauma.[3] Trauma-informed care should be implemented as a universal precaution to help ameliorate the risk of re-traumatization among patients with a lifetime history of trauma.

Trauma can negatively impact health. As the Center for Health Care Strategies explains, "Experiencing trauma, especially in childhood, can change a person's brain structure, contributing to long-term physical and behavioral health problems."[4] The landmark study on adverse childhood experiences (ACEs) in 1998 showed correlations between childhood trauma and chronic health problems, including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease.[5] Some studies have revealed an intersection between adverse childhood experiences, breast cancer, elevated stress levels, fatigue, and depression.[6] Moreover, the experience of trauma at any age can lead to specific behaviors — such as substance use, poor diet, and high-risk sexual behaviors — that predispose an individual to a cancer diagnosis.[6]

The health care system must have a plan in place to respond to patients who positively screen for trauma and must provide trauma-informed universal precautions in all patient encounters. Trauma-informed care should be the lens through which all care is administered as the standard of care. Trauma-informed practices can improve patient engagement, treatment adherence, health outcomes, and provider and staff wellness.[2] Trauma-informed health care professionals understand that any individual utilizing the health care system could have trauma in their history and staff must be prepared to prevent re-traumatization.[7]

Despite the high rates of trauma in the United States and globally, many patients do not reveal a history of trauma.[8] And although many health care providers lack the knowledge and skills to assess and treat patients with a recent or remote history of trauma,[8] research shows that implementing a trauma-informed care (TIC) educational program improves provider knowledge and comfort in providing trauma-informed care.[9] Recent work demonstrates that implementing a trauma-informed educational program can improve provider knowledge and attitudes about providing trauma-informed care.[8,10]

METHODS

This quality improvement project aimed to improve staff attitudes and readiness to provide trauma-informed care among staff at an outpatient cancer center that did not already have a TIC educational program for staff. The center's administration identified a need for a trauma-informed educational program to improve the care for the population they serve.

The Attitudes Related to Trauma-Informed Care (ARTIC) Scale, created by the Traumatic Stress Institute, was used to determine the impact of this educational program. The ARTIC-10 version used in this program contains 10 questions in a seven-point Likert scale format.[11] The mean score of each participant's pre-test is compared to the mean score of each participant's post-test. The ARTIC-10 is a validated tool that measures professional attitudes in support of or

unsupportive of TIC. This tool was developed to objectively measure the degree to which an individual or a system is trauma informed.

Additionally, a program evaluation tool was developed using the Proctor framework to measure participants' feelings about the educational program's effectiveness.[12] The program evaluation survey was a six-question, five-point Likert scale with one open-ended question.

Project Setting and Population

The educational program was created for the staff at the Ann B. Barshinger Cancer Institute (ABBCI), which employs more than 500 individuals in Lancaster. The oncology center — a prominent, suburban, not-for-profit, multidisciplinary, community-based, outpatient cancer center — is affiliated with a large tertiary academic hospital system.

The nurse managers for each of the units of the cancer center advertised the educational sessions to the patient care staff via email. In addition, an advanced practice provider (APP) at the center, who served as a liaison for the project, notified the APPs and physicians of the center about the educational program. A total of 76 employees attended the educational sessions.

Advertising for the sessions was directed toward registered nurses (RNs), patient care assistants (PtCAs), advanced practice providers (APPs), and physicians. The RNs and PtCAs that provide direct patient care were required to attend the sessions as part of their annual competencies. Team members from other disciplines who were not required to attend included social workers, a chaplain, a financial counselor, dieticians, and nursing management. Most participants were RNs (see Fig. 1).

Participants represented eight departments in the cancer center: Medical Oncology, Radiation Oncology, Surgical Oncology, Hematology Oncology, Social Work, Dietary, Chaplaincy, and Palliative Care. A virtual platform was offered, however no one participated in the educational sessions remotely.

Procedure

Two identical, one-hour educational sessions on TIC were offered during two separate lunch hours to maximize attendance. At the beginning of each educational session, each participant completed the paper-and-pen version of the ARTIC-10 Scale. Licensing for this version permits up to 200 copies of the scale, therefore the study accommodated up to 100 participants. The questionnaire takes approximately five minutes to complete.

The ARTIC-10 surveys were de-identified using a unique numerical identification system. Each participant was asked to write the last four digits of their phone number and the two digits of their birth month on the top of their survey. This unique number was used to label both the pre-tests and post-tests. The pre-tests were printed on pink paper, the post-tests on blue paper. The pre- and post-program surveys were linked numerically.

An attendance record was kept for each session. Immediately following the educational session, each participant completed the program evaluation tool. Two weeks later, a second ARTIC-10 Scale was disseminated by nursing management to each participant. Both sessions were recorded for future educational opportunities.

The educational program (see Table 1 on page 50) utilized a PowerPoint presentation, including didactic and interactive teaching techniques. Six weeks before the educational sessions, ABBCI staff received an email invitation introducing the TIC educational program. Staff selected their session using a survey emailed by nursing management. The educational programs were recorded for later viewing during onboarding of new staff. The sessions, advertised as "Lunch and Learn," were held during a sitewide lunch break from 12:00 noon to 1:00 p.m.

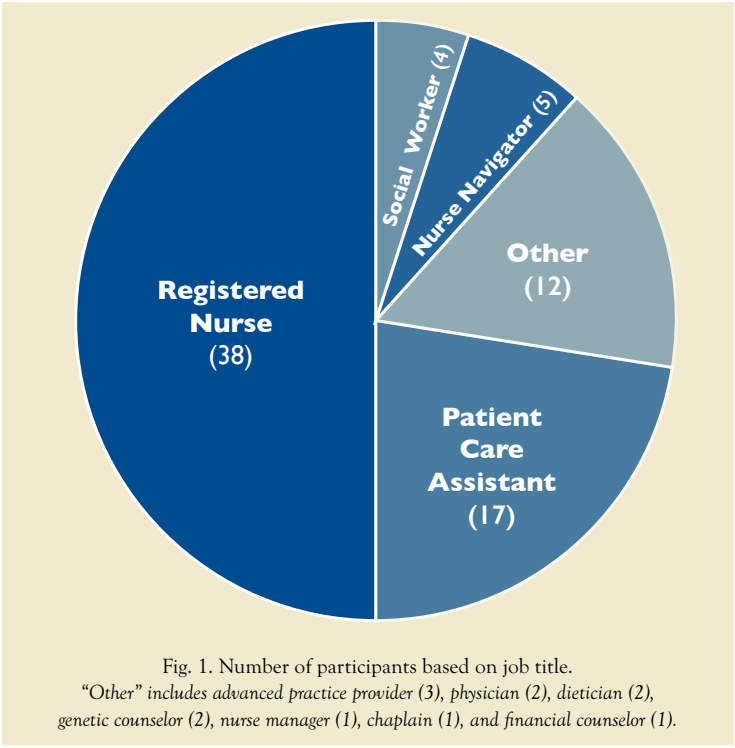

Fig. 1. Number of participants based on job title.
"Other" includes advanced practice provider (3), physician (2), dietician (2), genetic counselor (2), nurse manager (1), chaplain (1), and financial counselor (1).

An evidence-based curriculum for TIC provided the foundation for program development. The educational program was guided by the principles of TIC published by the Substance Abuse and Mental Health Services Administration (SAMHSA) in 2014. SAMHSA's framework for TIC includes behaviors staff must demonstrate, which are designated using a protocol called the "Four Rs: Realization, Recognize, Respond, and Resist." In addition, TIC curriculums must adhere to six generalizable principles: Safety; Trustworthiness and Transparency; Peer Support; Collaboration and Mutuality; Empowerment, Voice, and Choice and Culture; and Historical and Gender Issues.[13] Due to the lack of standardization in TIC training programs, these educational sessions were created by the first author utilizing PowerPoint slides to present the information.

Outcomes Measured

The results of the ARTIC-10 Scale were entered manually into an Excel spreadsheet. The Traumatic Stress Institute, the creator of the ARTIC Scale, provided detailed scoring instructions. A paired t-test compared the pre- and post-educational program mean scores, and the author then used Statistical Package for the Social Sciences (SPSS) software to complete statistical analysis. Descriptive statistics were collected to analyze the participant's level of care and the department of employment.

Additionally, a program evaluation tool was developed to collect qualitative data on the program's effectiveness. This seven-question, Likert-scale survey uses elements of the Proctor Model[9] to measure outcomes such as program acceptability, appropriateness, effectiveness, equity, and participant satisfaction. The results of the program evaluation survey, which helped assess the program's value, were tabulated.

RESULTS

A total of 76 attendees were at the educational sessions; 44 staff members participated on February 7, 2023, and 32 staff members participated on February 16, 2023. Of the 76 employees participating in the educational sessions, 38 correctly labeled the pre- and post-tests with their unique identification number described above. Twenty-six pre-tests could not be paired with a post-test, and 11 pre-tests were not labeled. Further, eight post-tests could not be paired with a pre-test, and seven post-tests were not labeled. In summary, 50% of the participants correctly labeled their pre- and post-surveys.

To assess the normal distribution of the dependent variables between the pre/post responses, the Shapiro-Wilk test of normality was completed in SPSS.[14] The results indicate a normal distribution, which suggests that a parametric test such as a t-test is appropriate for these data.

The paired t-test was run using the SPSS software to compare the mean value between the pre-session ARTIC-10 Scale and the post-session ARTIC-10 Scale. The results showed the mean score between the ARTIC-10 tool differed before ($M = 5.485$, $SD = 0.6975$) and after ($M = 5.818$, $SD = 0.7486$) the TIC educational session at the 0.05 level of confidence, $t(37) = -3.44$, $n = 38$, $p < 0.05$, 95% CI for mean difference: -0.5143 to -0.1330. On average, the mean score on the ARTIC-10 Scale was 0.333 points greater after the TIC educational session. A higher score reflects a positive change in attitude about providing TIC, showing that the educational session improved attitudes and readiness about providing TIC.

Seventy-five of the 76 participants anonymously completed the program evaluation survey. Five-point responses — Strongly agree, Somewhat agree, Neither agree nor disagree, Somewhat disagree, Strongly disagree — followed six statements about the program. The qualitative results from the survey show that the program was effectively implemented and well received by the participants:

- Sixty-two participants (83%) thought that a Lunch-and-Learn style education session was an acceptable way to receive TIC information.

Table 1. Outline of Educational Program and Learning Objectives

Educational Program

Introduction to and completion of ARTIC-10 Scale.

Description of trauma effects on the brain.

Description of TIC, including:
- Four-minute TED Talk.
- SAMHSA guidelines on TIC: the 4 Rs to TIC and six guiding principles.

Case studies and group role-playing.

Learning Objectives

1. Participants should be able to provide examples of trauma, its effects on the brain, and long-term health problems associated with trauma.
2. Participants should be able to summarize the principles of TIC.
3. Participants should be able to apply TIC principles if a patient discloses a history of trauma.

- Thirty-five participants (47%) said they would like more information about trauma-informed care.
- Fifty-seven participants (76%) said that they would "use TIC principles in my interactions at work with my patients and team members."

DISCUSSION

Despite the prevalence of lifetime traumatic experiences within the general population, with some groups at greater risk for a lifetime history of trauma than others, many health care systems lack trauma-informed policies and educational programs for staff. To address this knowledge gap, a quality improvement educational program on TIC for the staff of a free-standing cancer center was developed. The targeted audience for the educational program was RNs, PtCAs, APPs, and physicians.

An unexpected outcome regarding the study sample was the surprising number of employees who attended who were not initially recruited to participate. Employees attended from a wide variety of departments within the cancer center. This demonstrates an interest in trauma-informed care among professionals with diverse skill sets and working backgrounds at this site.

A paired t-test was run on SPSS software to evaluate the mean difference in pre- and post-ARTIC scores. The paired t-test results showed that the program improved staff attitudes about providing TIC. The qualitative data indicate that the program was well received by the attendees, with some narrative comments requesting more training on the subject.

Limitations

Although this quality improvement project demonstrates that a one-hour Lunch-and-Learn style educational session is an effective way to introduce TIC to multidisciplinary staff at a cancer center, there were some limitations. This was a small study; a larger sample size of paired pre- and post-surveys may have resulted in more confidence in the statistical outcome of this study.

Also, a time constraint was placed on the educational sessions since the intervention targeted front-line workers with limited time to devote to off-the-floor education. Ideally, trauma-informed principles should be part of an ongoing conversation. While the educational sessions positively improved staff attitudes and readiness to provide TIC among its participants, more than a one-hour intervention is needed to provide sustainable trauma-informed practice change within the organization.

In addition, the ARTIC-10 Scale and the program evaluation survey rely on self-reporting methods for data collection. Self-reporting could introduce bias into the results. Further, gender was not considered in the demographic collection, and thus, there would have been gender bias. The study's sample was also a mix of employees required to meet continuing education competencies and employees who attended voluntarily. This sampling outcome could introduce selection bias.

Finally, errors occurred with the numerical labeling of the pre- and post-ARTIC-10 surveys. While 76 employees attended the two educational sessions, only 38 pairs of pre- and post-ARTIC-10 surveys were correctly labeled. Consequently, we were unable to analyze the data of those participants whose ARTIC-10 surveys were not correctly labeled because we were not able to pair their pre- and post-tests.

The pairing of pre- and post-ARTIC-10 surveys is the only way to assess the pre/post mean scores. Written and verbal labeling instructions were provided after the mislabeling was discovered following the first session, and more time was spent giving labeling instructions to participants before the second session. The additional instruction time improved mislabeling errors.

The robustness of the results of the paired t-test is impacted by the loss of half of the data due to incomplete or incorrect labeling. This loss of data could lead to non-response bias.

Practice Recommendations

The favorable results from this quality improvement intervention could catalyze dialogue and education on trauma-informed care. With the center's administrative support for a trauma-informed approach to care and the positive feedback from the educational sessions, this site is well positioned to align the organization with SAMHSA's six key principles to a trauma-informed approach.

The cancer center where this study was conducted has an opportunity to build off the educational program's success by adding trauma-informed practice initiatives into its training and practice models. System-level changes should include trauma-informed language written into their mission statements, hiring practices, annual competencies, and employee evaluation procedures.

The administration could identify trauma-informed "champions" at all levels and within each department who could create trauma-informed organi-

zational practices that align with the six key principles. In addition, the TIC champions could provide ongoing training and peer support for staff.

The center's technical support personnel where this study was conducted did record the educational sessions to be used to onboard new staff. This exposure to TIC at the time of hire would help create a workforce where every employee would be trained in some level of trauma-informed care, and that training would be ongoing.

Sustainability Plan

This quality improvement TIC educational program aimed to implement trauma-informed care principles into the continuing education competencies of staff at all levels of the organization at a regional cancer center. As noted above, the educational program was archived for future educational opportunities.

Knowledge Link, the organization's learning management system that provides classroom and web-based training for the health system, could serve as a platform to introduce TIC education to staff within a health system at large. Further, trauma-informed practice champions could provide ongoing peer support and disseminate TIC guidelines through weekly huddles and staff meetings.

CONCLUSION

Trauma impacts individuals across all demographic groups. At times, the systems put in place to help our population can also be a source of trauma or cause re-traumatization for patients with a history of trauma. Implementing a TIC educational program for staff at outpatient health centers could help address this pervasive problem.

As noted, leadership at all levels of care must support trauma-informed initiatives, from mission statements to bedside care practices. Moreover, trauma-informed health care staff should be the standard of care across all health care organizations.

Finally, a TIC educational session for multidisciplinary staff can be an effective way to improve attitudes and readiness to provide TIC. More research is needed to help establish evidence-based practice guidelines and reliable, valid tools for measuring TIC.

In 1927, Dr. Francis Peabody famously wrote, "One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient."[15] These words are timeless and echo the principles of trauma-informed care.

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Intentions of Virtue

Quality Improvement and Health Equity

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Editor's note: The following is a transcript of the Laurence E. Carroll, MD 2024 Lecture, held on April 1, 2024, at Penn Medicine Lancaster General Health. The Laurence E. Carroll, MD Lecture Endowment was established by gifts from friends and family of Dr. Carroll to honor his memory, legacy, passion, and lifelong commitment to medical ethics and continuing medical education. To make a gift to the endowment in Dr. Carroll's memory, call 717-544-7126.

In 1999, concerns about patient safety and health care quality rose to the nation's consciousness. In September of that year, the Institute of Medicine released a report called, "To Err Is Human."[1] This report made front-page news across the United States, partly because it quantified for the first time the degree to which we have a problem with medical errors in this country.

The report estimated almost 100,000 deaths annually from medical errors — that's more than twice the number of deaths from the next most common cause of accidental deaths, which is vehicles. By providing a number to this problem of medical errors, the report brought to attention a problem that many people — not only policymakers, health care workers, and administrators, but also the public — didn't even know we should be worried about. It began an important policy discussion around the frequency of deaths from medical errors.

Around the same time, there emerged the beginning of a reckoning over unequal health care treatment in the United States. Again, a report from the Institute of Medicine, called "Unequal Treatment,"[2] drew attention to the fact that quality-of-care in the United States is not uniformly low; rather, it is differentially low across certain racial and ethnic groups. The report demonstrated that Black and Hispanic patients have higher rates of uninsurance. It also demonstrated that Black and Hispanic patients have decreased access to care compared to white patients and higher rates of death.

Since that time, a significant body of research has documented the problem we have with low and variable quality-of-care in this country and has prompted a discussion about how to improve quality-of-care.

Many quality improvement efforts have focused on restructuring the way we deliver quality care, often using financial incentives aimed at providers. It has often been assumed that these efforts will result in better quality-of-care for everybody and might decrease health care disparities, but our experience has demonstrated that that is not the case. Policies aimed at improving quality-of-care rarely also reduce disparities and may in fact worsen disparities.

To understand why disparities might worsen, it is helpful to first understand why quality-of-care is low. Health care suffers from a problem that economists call "asymmetric information." Health care is a technical field. It requires a specialized knowledge, and patients don't typically have complete knowledge about their medical condition or what the best treatment is, and so, understandably, they rely on their physicians and other providers to make decisions on their behalf.

However, patients can't easily observe the quality of their physicians, so they don't always choose a physician that may be highest quality or best able to make those decisions. As a result, physicians may be unresponsive to patients' demand for high-quality care.

This problem is exacerbated by the way we have historically paid for care in this country, through a fee-for-service payment system. Physicians, for many years, have been compensated for the quantity or intensity of care they provide, rather than the quality of that care. This often results in problems like overuse of care, unnecessary care, and high costs of care.

To correct the problem of asymmetric information leading to low quality-of-care, the solution, according to economists, is to change the incentives: high-quality care should be financially rewarded, regardless of whether patients can directly observe it. There have been two general approaches to try to implement this in practice — using targeted payment incentives and global payment incentives.

TARGETED PAYMENT INCENTIVES

Going back to the 1990s, Medicare led the way in changing payment in a very targeted way, using public-reporting of quality (report cards) or using "pay-for-performance," which is a more direct way to tie payment to quality.

Public-reporting offers a straightforward way to improve quality through selection. The idea is that, if we give patients more information about the quality of medical providers, they can use that information to preferentially select high-quality providers. This can shift patients from lower quality providers to higher quality providers, but alone it doesn't do anything to incentivize the low-quality physicians to improve quality-of-care.

That's where the second pathway — the "change" pathway or the "quality improvement" pathway — comes in. Here, two things happen.

First, when we measure quality and report it to the public, we also let physicians know what their quality is. Just as patients can't easily observe quality-of-care, physicians often don't know their own level of quality or how it compares to their colleagues and peers.

Next, and perhaps more importantly, making information about quality-of-care available to the public gives physicians the incentive to compete on quality, so they might then put more effort into improving their quality-of-care in an effort to maintain or improve their market share. This is a very economic view, but it is, I think, a simple and elegant solution to the problem of low quality-of-care in the setting of asymmetric information. If only it worked that well.

In reality, we've often found that public-reporting alone is insufficient to change the behavior of physicians, in part because the incentives are too weak. It relies on consumers being able to find and use the information. There are a lot of competing reasons that patients choose a physician, and it's not always because of the grade they get on a report card. And so, without consumer choice, providers may not have as much motivation to improve.

Thus, soon after public-reporting started, Medicare and other payors began to add pay-for-performance, which directly adjusts fee-for-service payments to be higher when higher quality-of-care is provided. It can also include penalties for providing poor care.

So, what do we know about public-reporting and pay-for-performance and how effective they are in improving quality? One study completed shortly after these incentives were put into place demonstrates that pay-for-performance has a stronger effect on improving quality-of-care compared to public-reporting.[3] While this is encouraging, over the years we've found that this effect is quite variable and that the effect of pay-for-performance is often quite small: physicians will improve their quality-of-care for the discreet things for which we are paying them, but often not for other related items. For instance, hospital outcomes or patient mortality rates may not improve.

There are also other shortcomings that limit the effectiveness of pay-for-performance. The incentives are often too small, the rewards are received long after care is delivered — so not salient to providers — and the biggest rewards tend to go to providers who were already doing well. Thus, around the time that the Affordable Care Act was passed, there was an increased interest in using strategies that more fundamentally altered the payment system.

GLOBAL PAYMENT INCENTIVES

The second approach, "global payment incentives," moves away from the pay-for-performance piecerate system. Global payment shifts the focus to managing health populations or an episode of illness. It holds providers accountable for the costs of care across the episode or population, and often includes shared savings or shared risks. This means, if a clinical provider can manage the health of their population for less than a benchmark set by the insurers, the provider can keep some of that savings for themself.

This doesn't just reduce costs; providers are also held accountable for the quality-of-care. The idea is to achieve high-quality care at lower cost.

A bundled payment is a common type of global payment incentive. While fee-for-service pays hospitals, radiologists, surgeons, and anesthesiologists separately for the care of each patient hospitalized for surgery, in a bundled payment, a single payment is divided across all the different providers for all the different services. This incentivizes individual providers and organizations to work together to provide high-quality care at a lower cost, therefore providing high-value care.

Another common approach to global payment is through accountable care organizations. Accountable care organizations bring providers together to agree that they're going to care for a defined population — for example, nursing home patients — to manage the care across space and time. They hold themselves accountable for the overall quality and costs for this defined group of members. Yet, when we look at whether these approaches are working, we see mixed results.

EFFECT OF VALUE-BASED PAYMENT ON HEALTH EQUITY

If we take a step back and think about how these value-based payment (VBP) programs affect disparities, we recall there's been a general assumption that improving quality will help everybody without exacerbating existing inequities. The idea is that rising tides lift all boats. And it is certainly possible that the lowest quality providers may respond to these financial incentives; as a result, it may improve or reduce health care disparities.

The flipside is, VBP programs may not do that. Providers are relatively risk averse and may avoid complex patients if their salary is tied to the outcomes of high-risk patients.

VBP may also worsen disparities due to differences in provider resources. Safety-net hospitals and clinics operate with low financial margins; they don't have a lot of financial resources because the payment systems don't provide them. They also typically have lower quality-of-care in the absence of quality improvement incentives — that may be related to the complexity of the patients they care for, which in turn may be related to their patients' poor financial conditions.

VBP disproportionally penalizes safety-net hospitals, taking resources from organizations that need them the most while giving to organizations that need them the least. Pay-for-performance and other payment models tend to be rolled out in a cost-neutral way, so there's a fixed pot of money distributed based on quality or value. For example, Medicare may withhold 2% of payment and then reallocate that money to hospitals based on performance scores.

If you are a safety-net hospital and have lost 2% of your payment when you don't meet quality benchmarks — because that payment is now going elsewhere — you may find yourself in a cycle of poverty. This cycle can result in decreased quality and may lead to hospital closure. This has, in fact, occurred frequently in rural areas, reducing access to care for at-risk patient populations; it probably ultimately worsens patient outcomes.

A lot of evidence collected over the last decade suggests that VBP programs are not helping health disparities and in many cases seem to be worsening them. The question remains, how can we redesign payments to advance the goal of health equity?

REDESIGNING PAYMENT TO ADVANCE EQUITY

There's been significant attention focused on the problem of payment incentives and health care disparities in the last five years. Medicare, to their credit, has taken the evidence produced by researchers very seriously, and has tried to advance an agenda that will address and reduce racial disparities. Medicare and the Center for Medicare and Medicaid Innovation have made an explicit goal of addressing disparities and increasing participation of safety-net providers in VBP programs.

There are four approaches to modifying the current VBP program to more purposefully advance health equity. The goal of these is to not just avoid harm, but to improve disparities. I've ordered them here from what I think are the weakest incentives, or the least likely to work, to the strongest incentives, the most likely to advance health equity.

Create Accountability for Equity

The idea here is to modify existing VBP programs to include metrics focused on disparities and equity. Instead of just measuring admission rates or the rate of use of home dialysis, we can also include measures of disparities and equity. Other approaches in this area are to meaningfully reward providers for reducing disparities and achieving equity, and also ensure that health equity performance — and payment for that performance — represent a significant percentage of a provider's overall quality score.

Account for Social Risk in Performance Measurement

The incentives we have used for the past couple of decades have differentially penalized providers who take care of a high number of patients at social risk. Another approach is to level the playing field in a more meaningful way and not financially penalize those providers.

This is an excellent idea in theory, but it's harder to implement. It may be done by rewarding providers for improving their performance and stratifying performance to compare providers with others who have a similar makeup of patients. Another option is adjusting performance measures for social risk — that is, using statistical techniques to "level the playing field" and account for difference in social risk across providers.

One very recent study seems to suggest that, if implemented today, adjusting performance based on social risk would result in a substantial increase in the likelihood that safety-net hospitals and minority-serving hospitals receive a bonus. That would be progress in the right direction.

Financially Support Under-Resourced Providers

Another step in the right direction is for VBP programs to direct financial support to under-resourced providers serving low-income patients through upfront payments that are not tied to performance or

equity. Sometimes called "equity pools," these payments support capacity building and practice transformation. Though there are barriers to widespread implementation like this — to many politicians and policymakers, the unrestricted funds can be perceived as being politically unpalatable — such programs are likely to have a larger effect than the other approaches, which are less about providing additional funding and more about improving quality-of-care.

Address Drivers of Inequities

But if we *really* want to improve health equity, we need to take a step back and think about what's driving health *inequity.* It's a myriad of things, such as economic opportunity and having access to healthy food, a safe environment, insurance, and health care providers. Some of these are being addressed through VBP programs, but fundamentally the ability of those programs to have a meaningful impact on health inequities is low.

But there are approaches I'm optimistic about. In work I've been doing over the past year, my colleagues and I have been thinking about how to implement VBP programs in a way that makes sense in community health centers. We've been spending time talking to community health center providers to understand the barriers they face in participating in VBP programs and the modifications that would be needed for those programs to be successful in that setting.

What we hear from them is that the activities they engage in and the care they provide are often so upstream to the health care delivery being targeted by VBP programs, it's hard for them to fit into current program frameworks. These organizations often prioritize finding stable housing, addressing food insecurity, job training, and stable sources of health insurance for their patients. We know these activities affect the health and long-term outcomes of patients, yet we don't have a system in place that rewards providers for addressing them.

I am optimistic that if we find a path forward that meaningfully addresses these drivers of health inequities, we can make meaningful progress to advance the goal of health equity. I'm less optimistic that there's anything we can do to the *existing* VBP structures that's going to meaningfully address these inequities.

It's a hard problem to solve, and it's not surprising in some ways that in the past 20-plus years we've been working on this, we've made very little progress. The good news is, we are doing much better in terms of reducing the harms that come from VBP programs.

There are things we can do to make the existing system work better for everybody, putting patients at the center of what we do. Stakeholder input — including patient input — throughout the policy process, would be helpful. We should be building equity directly into the policy process.

It's a complex health system that we work in — it often responds in ways that are surprising and unintended. All new policies need to be monitored for their impact on equity. This is something that didn't used to happen routinely; it happens relatively routinely now.

We need to build in the ability to pivot policies quickly as more data become available. It's hard for large insurers like Medicare to do that; it's easier in small settings. But the inflexibility that's built into traditional Medicare makes this kind of pivoting very hard, which is why it takes decades to try to get to these solutions.

These kinds of activities are being adopted more and are important next steps in the goal of taking the existing system and improving it to decrease disparities. Thinking more about how we can more meaningfully affect these drivers of health inequities would have a longer term, more valuable impact on quality-of-care.

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PHOTO QUIZ FROM URGENT CARE

Acute Abdominal Pain Followed by a Rash

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CASE HISTORY

A 17-year-old male initially presents to Urgent Care for evaluation of a lesion behind his knee with no known trigger or trauma. A single plaque measures approximately 3 mm, but he is otherwise asymptomatic.

Several days later, the patient develops severe abdominal pain with CT-confirmed duodenitis. He then develops a similar but more prominent rash on the lower extremities (see Fig. 1), particularly around the ankles (see Fig. 2). A few areas present with a target appearance; joint pain continues, mainly in the bilateral knees.

These symptoms and the progression of disease lead to a diagnosis of Henoch-Schönlein purpura (HSP).

QUESTIONS

1. What is the typical age distribution of HSP?
2. What are the signs and symptoms, as well as the diagnostic criteria, of HSP?
3. What is the significance of HSP, and what organ is most important to monitor?
4. What is the treatment for HSP?

ANSWERS

1. HSP generally occurs in children and teens 3-15 years of age and is seen less commonly in adults.
2. Signs and symptoms include rash presenting as palpable purpura, which may or may not be itchy; arthralgia; and acute abdominal pain. Diagnostic criteria include purpura (usually palpable and in clusters) or petechiae, with lower limb predominance with or without thrombocytopenia or coagulopathy.
3. HSP can cause kidney involvement and may lead to kidney deterioration.
4. Supportive care includes having patients stay well hydrated, and they can use NSAIDs for joint pain and prednisone for more concerning symptoms. Frequent monitoring of kidney function is important via blood pressure measurements, urinalysis, and sometimes bloodwork. A kidney biopsy is warranted in severe cases.

DISCUSSION

HSP is a relatively rare, often self-limiting condition that is almost always associated with skin

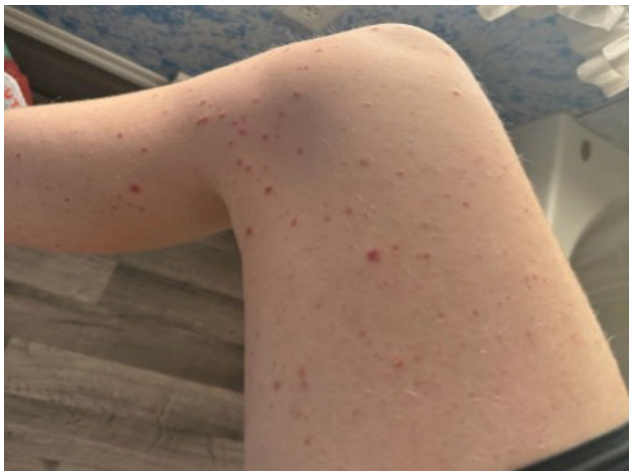

Fig. 1. Several days after a single plaque presents behind the patient's knee, a more prominent rash develops on the lower extremities.

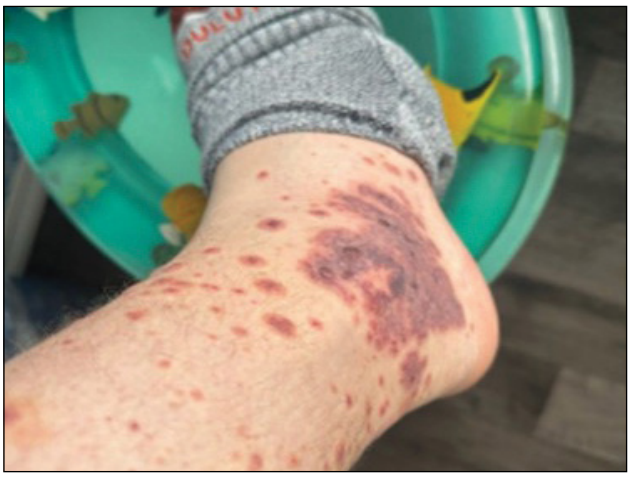

Fig. 2. Larger areas of rash also appear around the ankles after several days.

changes and can have significant implications for kidney health, potentially related to the age of onset.[1] Although it most commonly occurs in children aged 3-7 years old and teens with most cases occurring before age 17, HSP can present in adults as well.[2-4] A later age of onset is associated with adverse outcomes related to kidney function.

Because of its implications for kidney function, a prompt and accurate diagnosis is important for this condition.[5] Supportive care should accompany close monitoring of kidney health.[5,6] In this case, the rash was first diagnosed as erythema multiforme, as a few lesions were target-like. Serial trending of kidney function demonstrated deterioration.

This patient was referred to nephrology, and ultimately a kidney biopsy was performed. The skin changes around the ankles worsened, and skin grafts needed to be performed.

Subsequently, the patient fully recovered and is now in good health.

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One Penn Medicine. One Research.

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Editor's note: This is the 19th in a series of articles from the Penn Medicine Lancaster General Health Research Institute that describes ongoing research studies. Members of the LG Health staff who are conducting research and wish to have their studies described here are encouraged to contact the offices of JLGH *at 717-544-8004.*

In the summer of 2015, when Penn Medicine acquired Lancaster General Hospital, the future of what that partnership would look like was far from realized. We continue to see, even now, the development of that relationship through the five-year strategic plan and new collaborative pathways. One of those pathways is the One Penn Medicine. One Research, initiative that "drives integrated, innovative research across the Penn Medicine Health System, providing technology advancements and care for our patients and community."

Penn Medicine boasts a robust academic research center overseen by the Office of Clinical Research (OCR) at the Perelman School of Medicine within the University of Pennsylvania. OCR manages all clinical research at Penn and ensures it meets high levels of conduct, as well as maintaining compliance with all applicable regulatory and compliance standards. The University of Pennsylvania Institutional Review Board (IRB) maintains eight boards that review a wide variety of different types of research.

Lancaster General Health's research infrastructure, while smaller than Penn's, is well organized and comprehensive. The Research Institute employs a team of about 20 people, including clinical research nurses, research coordinators, research assistants, project managers, and administrative support staff. The oncology research program at the Ann B. Barshinger Cancer Institute is currently a distinct entity and not included in the Research Institute tally. Similarly, the trauma research team led by Lindsey Perea, DO, the nursing researcher program led by Christian Burchill, PhD, RN, and other independent practices conduct research projects within their specialties.

The Human Research Protection Program, the Compliance Department, and Business Intelligence are just a few of the departments that support research in invaluable ways at LG Health. The Lancaster General Hospital (LGH) IRB, which previously operated independently, is in the process of merging with Penn's IRB. Together, they will offer a more streamlined approach to collaborative studies and allow for consistency of processes (e.g., legal review, contract execution) without sacrificing the local expertise that LGH's IRB possesses.

The One Penn Medicine. One Research, initiative is an exciting aspect of the evolving relationship between Penn Medicine and LG Health. It will facilitate our access to Penn research projects and allow the LGH research community to be more involved in exciting academic studies.

Now, as more departments and groups merge across the health system, we are able to diversify how LG Health supports these studies. For example, there is a new Master Reliance Agreement between Penn's IRB and LGH's IRB that covers most research studies. This has shortened the start-up time required for collaborative studies and decreased the need for superfluous study documents.

For some studies, Penn continues to operate largely independently and the LG Health component is simply to provide regulatory oversight and local support as needed. For many others, there is a spectrum of involvement that could include an LG Health research coordinator conducting the informed consent process only, or it could see LG Health being an independent study site with its own study team and full participation in all aspects of the study. A small selection of current Penn studies taking place at LG Health is summarized in Table 1 on page 60.

One Penn Medicine. One Research, provides opportunities for our community in Lancaster County to access research studies at other Penn Medicine hospitals without needing to travel to Philadelphia or

surrounding areas. This not only benefits our patients, but also our providers and staff who are interested in getting involved in research. A collaborative study with a Penn team is a great way to ease into research for those who do not have prior research experience.

If you are interested in learning more about the research being done between LG Health and Penn Medicine, or if you want to get involved in a research study, contact the LG Health Research Institute at LGHResearch@pennmedicine.upenn.edu.

Table 1. Selection of Penn Medicine Studies Taking Place at Lancaster General Health

Study Name	Study Summary	LG Health Involvement
The Whole Health Study: Collaborative Care for OUD and Mental Health Conditions	This study compares three care conditions to determine which condition is best to help people with opioid use disorder (OUD) and mental illness reduce their drug use and improve symptoms. The collaborative care model uses a team-based approach in which a primary care physician (PCP) and a care manager coordinate care. As part of this study, care managers will monitor patients with mental health conditions in the primary care practice. Participants will be offered medication such as buprenorphine, which, in combination with counseling, provides a whole-patient approach to the treatment of OUD.	**Local Principal Investigator:** Caroline Barnhart, MSS, LCSW The local Behavioral Health study team manages all local aspects of the study from recruitment to follow-up, training of staff, and all other local needs. There is no involvement of operational staff from the LG Health Research Institute.
INFORM: Investigating and identifying the heterogeneity in COVID-19 misinformation exposure on social media among Black and Rural communities to inform precision public health messaging	This observational study is being conducted to understand how health information and misinformation are shared and interacted with through Facebook wall posts, X (formerly Twitter) posts, and Google and YouTube searches. We are interested in learning more about how people use information on social media and what people find the most interesting and useful.	**Local Principal Investigator:** Jean David Dumornay, MD, MBA The research assistant at the Research Institute provides operational support for this study at LG Health. He facilitates patient recruitment and follow-up communications as needed.
Healthy Heart: Reducing Atherosclerotic Cardiovascular Disease (ASCVD) Risk Through a Comprehensive Heart Disease Prevention Program (HDPP)	This study aims to leverage access to patients across the primary care network, Epic tools for identifying eligible patients, and the *Way to Health* platform to launch. Patients will enroll into the Penn Medicine Healthy Heart, a six-month program for reduction of hypertension and hypercholesterolemia grounded in behavioral economics insights. The goal is to increase uptake of and adherence to evidence-based interventions to reduce ASCVD risk. Penn Medicine Healthy Heart emphasizes proactive outreach and prevention outside of a traditional visit model using data assets to identify and risk stratify patients. The program aims to relieve overburdened PCPs through automated hovering technology coupled with a centralized, leveraged team of non-clinical navigators and nurse practitioners.	**Local Principal Investigator:** John Wood, MD LG Health personnel will help with administering the study, as well as collect and maintain data and provide study data to the Penn team. There is no involvement of operational staff from the Research Institute.
Cognitive Function, Self-Management and Health Outcomes Among Liver Transplant Recipients: The LivCog Cohort	This study seeks to characterize cognitive, psychosocial, and health trajectories in liver transplant recipients (LTRs), identifying those at higher risk of impairment. The Penn study team plans to enroll 450 LTRs and their care partners across diverse sites over a five-year timeline. The investigation includes assessing cognitive trajectories, identifying risk factors, and evaluating associations between cognitive function and various post-transplant experiences. The comprehensive study measures cover patient and care partner aspects, with a timeline spanning preparation, enrollment, and follow-up phases. The ultimate goal is to inform interventions that enhance self-management, health behaviors, and care partner support for optimal health outcomes in LTRs.	**Local Principal Investigator:** Marina Serper, MD, MS No recruitment takes place at LG Health. However, many of the participants enrolled in the study receive follow-up care at LG Health. To allow for the study-specific follow-up to take place here, LG Health was added as a study site. There is no involvement of operational staff from the Research Institute.

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Osteoporosis, Cardiovascular Disease, Urinary Tract Infection, Radon Exposure

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TREATMENT OF PRIMARY OSTEOPOROSIS TO PREVENT FRACTURES IN ADULTS[1]

A new guideline from the American College of Physicians (ACP) updates its 2017 recommendations on pharmacologic treatment of primary osteoporosis or low bone mass to prevent fractures in adults.

The ACP Clinical Guidelines Committee based these new recommendations on an updated systematic review of evidence and evaluated them using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system.

Recommendation 1: ACP recommends that clinicians use bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in:

a. Postmenopausal females diagnosed with primary osteoporosis (strong recommendation: high-certainty evidence).
b. Males diagnosed with primary osteoporosis (conditional recommendation: low-certainty evidence).

Recommendation 2: ACP suggests that clinicians use the RANK ligand inhibitor (denosumab) as a second-line pharmacologic treatment to reduce the risk of fractures in:

a. Postmenopausal females diagnosed with primary osteoporosis who have contraindications to, or experience adverse effects of, bisphosphonates (conditional recommendation: moderate-certainty evidence).
b. Males diagnosed with primary osteoporosis who have contraindications to or experience adverse effect of bisphosphonates (conditional recommendation: low-certainty evidence).

Recommendation 3: ACP suggests that clinicians use the sclerostin inhibitor (romosozumab, moderate-certainty evidence) or recombinant PTH (teriparatide, low-certainly evidence), followed by a bisphosphonate, to reduce the risk of fractures in females with primary osteoporosis with very high risk of fracture (conditional recommendation).

Recommendation 4: ACP suggests that clinicians take an individualized approach regarding whether to start pharmacologic treatment with a bisphosphonate in females over the age of 65 with low bone mass (osteopenia) to reduce the risk of fractures (conditional recommendation: low-certainly evidence).

AMERICAN HEART ASSOCIATION TOP CARDIOVASCULAR DISEASE ADVANCES FOR 2023[2]

Novel Antihypertensive May Boost Medication Adherence

Fewer than 25% of adults being treated for hypertension keep their blood pressure (BP) within the target range, often due to low compliance with daily oral medication. Zilebesiran, an investigational, subcutaneously administered RNA interference therapeutic targeting angiotensinogen, has the potential to change that.

In the Phase 2 KARDIA-1 study, a single injection of zilebesiran (Alnylam Pharmaceuticals) effectively lowered BP in adults with mild to moderate hypertension for up to six months, with an encouraging side-effect profile.

Thrombectomy Benefits Seen in Even the Most Severe Stroke Cases

Endovascular thrombectomy is a standard treatment of small or medium-sized strokes. Until recently, however, it wasn't clear if this minimally invasive approach would also benefit people with larger, more severe strokes, which account for up to one-quarter of all strokes.

The ANGEL-ASPECT trial and the SELECT II trial demonstrated that early endovascular thrombectomy following large cerebral infarction was superior to standard medical care. Those who received endovascular thrombectomy experienced fewer disabilities and were more functionally independent during the three months after treatment.

Imaging Advances Help Guide Stent Placement in Complex Coronary Artery Disease

A systematic review demonstrated that when compared with coronary angiography guided percutaneous coronary intervention, intravascular-imaging guided percutaneous coronary intervention is associated with significantly reduced cardiac death (rate ratio 0.53, 95% confidence interval 0.39 to 0.72) among other positive outcomes.[3]

Earlier Anticoagulation Safe in Stroke with AFib

In patients with an acute ischemic stroke with atrial fibrillation, European guidelines suggest starting direct-acting oral anticoagulant (DOAC) therapy three days after a minor stroke, six days after a moderate stroke, and 12 days after a severe stroke, while U.S. guidelines suggest waiting more than two weeks in some high-risk patients.

The ELAN study published in May 2023 showed that starting DOAC treatment sooner (within 48 hours of a minor or moderate stroke and on day 6-7 following a major stroke) was not associated with an increased risk for intracranial hemorrhage and is probably better at reducing ischemic events.[4]

Novel Diabetes Drugs in Obesity Without Diabetes

Multiple large trials have shown that sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists can reduce cardiovascular (CV) events and improve CV health in patients with diabetes. A growing number of studies suggest that these drugs may also improve parameters related to CV health such as body mass index, weight, and blood pressure in adults with obesity but without diabetes.[5]

See pages 42-47 for a comprehensive review of these new drugs by LG Health ambulatory pharmacist clinicians.

More Evidence Links Healthy Eating to Lower Risk for Premature Death

Findings from a large cohort study published early in 2023 provide support for the AHA's Food Is Medicine initiative.[6] Food Is Medicine encourages health care systems to help patients access and consume healthy foods based on scientific evidence that a healthy diet can prevent, manage, and treat chronic illness.

Less Invasive Treatment for Advanced Peripheral Arterial Disease

New research supports an endovascular approach over vein bypass surgery to address chronic, limb-threatening ischemia, an advanced form of peripheral arterial disease. In the BASIL-2 trial, patients who received vein bypass as the first approach were more likely to require a major amputation or to die during follow-up than those who received the endovascular approach as first strategy.

Dyspareunia Signals Urinary Tract Infection in 83% of Cases[7]

Dyspareunia (painful sexual intercourse) is a major indicator of urinary tract infections (UTIs), being present in 83% of cases. This symptom is especially accurate in identifying UTIs in non-menopausal women, researchers have found.

Among 5,500 patients studied, 83% of those who had UTIs experienced dyspareunia, while 80% of women of reproductive age with dyspareunia had an undiagnosed UTI. During the perimenopausal and postmenopausal years, dyspareunia was more often associated with genitourinary syndrome than UTIs. In the study, 94% of women with UTI-associated dyspareunia responded positively to antibiotics.

This is something that has apparently never been described before, yet dyspareunia is experienced by 10% to 20% of women in the United States. Thus, this is a reminder that clinicians should safely and compassionately inquire about their patients' sexual history.[8]

Increased Stroke Risk from Moderate Radon Exposure[9]

An analysis of radon exposures in more than 150,000 postmenopausal women in the Women's Health Initiative revealed a 14% higher stroke risk in those exposed to the highest concentrations of radon compared to those exposed to the lowest concentrations. Even moderate concentrations of radon were associated with a 6% higher stroke risk.

Radon is the second leading cause of lung cancer, but little was known about how exposure to the gas might affect stroke risk in women. This is concerning, considering radon levels in Lancaster County are about nine times the national average of 1.3pCi/L.[10]

The research found an increased risk of stroke among participants exposed to radon above 2 picocuries per liter (pCi/L). This is below concentrations that usually trigger Environmental Protection Agency (EPA) recommendations to install a home radon mitigation system.

Radon is a naturally occurring, odorless, radioactive gas produced when uranium or radium break

Choosing Wisely

Originally published in the Fall 2012 issue of JLGH in conjunction with the American Board of Internal Medicine's now-complete Choosing Wisely campaign, this edited reprint is offered to remind physicians of the importance of talking with patients about what tests, treatments, and procedures are needed — and which ones are not.

RECOMMENDATIONS FROM THE AMERICAN ACADEMY OF FAMILY PHYSICIANS

❶ **Do not perform imaging for low back pain symptoms within the first six weeks of the complaint.** Exceptions include so-called "red flag" signs, which include — but are not limited to — severe or progressive neurological deficits, or suspicion of a serious underlying condition such as osteomyelitis. Imaging of lower spine complaints before six weeks increases costs significantly but does not improve outcomes.

❷ **Do not routinely prescribe antibiotics for acute mild to moderate sinusitis unless symptoms last a week or more, or symptoms worsen after initial clinical improvement.** Though most sinusitis in the primary care setting is due to a viral infection that will resolve on its own, antibiotics are still prescribed in the majority of outpatient visits for acute sinusitis. The American Academy of Family Physicians advises that symptoms must include discolored nasal secretions (although we know from repeated studies that discolored nasal discretions do not necessarily mean bacterial infection), and facial or dental tenderness.

❸ **Do not use DEXA screening for osteoporosis in women younger than 65 or men younger than 70 with no risk factors.**

❹ **Do not order annual EKGs or any other cardiac screening for asymptomatic low-risk patients.** There is little evidence that detection of coronary artery stenosis in such patients improves health outcomes. The U.S. Preventive Services Task Force states that false-positive tests are likely to lead to harm through unnecessary invasive procedures, over-treatment, and misdiagnosis. Potential harms of routine annual screening exceed the potential benefit.

The American College of Physicians adds a corollary: "Don't obtain screening exercise EKG testing in individuals who are asymptomatic and at low risk for coronary heart disease," since it does not improve patient outcomes. They define low risk as a ten-year risk under 10%.

The American College of Cardiology recommends not performing stress cardiac imaging or advanced non-invasive imaging in the initial evaluation of patients without cardiac symptoms, since such patients account for up to 45% of unnecessary "screening." Testing should be performed only when at least one high-risk marker is present:

- Diabetes in patients older than 40 years of age.
- Peripheral arterial disease.
- Greater than 2% yearly risk of coronary heart disease events.

❺ **Do not perform pap smears in women younger than 21 or who have had a hysterectomy for a non-cancer disease.**

down in rocks and soil. Its presence is increasing as a result of climate change, and it is increasingly being found in people's homes. When inhaled, this air pollutant releases ionizing radiation into the lungs and is seen as second only to smoking as an established cause of lung cancer.

Compared with men, women have a higher rate of stroke and, in the United States, typically spend about 11% more hours per day indoors at home, which investigators note highlights a "potential role of the residential environment among other risk factors specific to women."

The highest radon exposure group resided in areas where average radon concentrations were greater than 4 pCi/L; the middle exposure group lived in regions with average concentrations of 2-4 pCi/L; and the low-

est exposure group lived in areas with average concentrations <2 pCi/L.

The incidence rates of stroke per 1,000 women in the lowest, middle, and highest radon concentration areas were 333, 334, and 349, respectively. Notably, stroke risk was significant even at concentrations ranging from 2-4 pCi/L (p = 0.0004) versus <2 pCi/L, which is below the EPA's Radon Action Level for mitigation.

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Lancaster Medical Heritage Museum

Museum Offers Monthly Webinar Series

Readers of *JLGH* are invited to join the Lancaster Medical Heritage Museum for its monthly webinar series, offered the first Tuesday of every month.

According to Kim Jovinelli, the museum's executive director, "These engaging sessions are led by seasoned professionals and experts in various fields, offering a wealth of knowledge and insight. Designed to fit into your lunch hour, these webinars provide an opportunity to delve into intriguing topics and expand your understanding of medical history and advancements. Best of all, attendance is completely free, although donations are warmly welcomed and appreciated to support our ongoing educational initiatives."

More information about the webinars and other museum events can be found on the museum's website at lancastermedicalheritagemuseum.org/events.

The museum is open Wednesday-Saturday, 11:00 a.m. to 3:00 p.m. Admission is free to LG Health employees with a badge and children under 3; $8:00 for all others.

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Cover photo of the Ann B. Barshinger Cancer Institute (ABBCI) by David Lang, physician assistant at LGHP Comprehensive Care and the Union Community Care School-Based Health Clinic at Carter & MacRae Elementary School, Lancaster.

ABBCI opened in 2013 and continues to offer exceptional care to the patients of Central Pennsylvania. We are pleased to feature a study on page 48 describing implementation of a trauma education program among the clinical staff at the Institute.

INTERESTED IN WRITING FOR *JLGH*?

The following is a summary of the general guidelines for submitting an article to *The Journal of Lancaster General Hospital*. Details are located online at JLGH.org.

- Scientific manuscripts are typically between 2,500-4,500 words. Perspective articles are usually shorter, and photo quizzes average about 725 words plus illustrations.
- Medical articles should report research, introduce new diagnostic or therapeutic modalities, describe innovations in health care delivery, or review complex or controversial clinical issues in patient care.
- Reports of research involving human subjects must include a statement that the subjects gave informed consent to participate in the study and that the study has been approved by the Institutional Review Board (IRB).
- Patient confidentiality must be protected according to the U.S. Health Insurance Portability and Accountability Act (HIPAA).
- The Journal of Lancaster General Hospital *does not allow chatbot tools such as ChatGPT to be listed as authors.* JLGH *editors warn authors that the use of these tools poses a risk for plagiarism with inappropriate use of citations, and we require that use of such tools be disclosed.*

Please contact the managing editor, Maria M. Boyer (717-544-8004), Maria.Boyer@pennmedicine.upenn.edu, to discuss submitting an article or for further information.

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EARN CME CREDIT

American Medical Association Category 2 activities consist of self-directed learning or courses that have not been through a formal approval process. According to the Pennsylvania State Board of Medicine, this includes "learning experiences that have improved the care [physicians] provide their patients." Reading authoritative medical literature — like medical journals — is one such activity.

For Pennsylvania physicians, more information and the Pennsylvania Board of Medicine CME Reporting Form are available at LGHealth.org/CME. *For advanced practice providers,* more information is available from credentialing organizations.

Physicians can also log credit and advanced practice providers can access transcripts through their eeds accounts online.

← Scan to access your eeds account.

← Scan for additional information and links to individual reporting instructions and forms.

Upcoming CME Offerings at LG Health

Pediatric Grand Rounds
June 11, August 13, September 10, 7:00-8:00 a.m.

Department of Medicine Grand Rounds
July 3, 12:00 noon-1:00 p.m.

Geriatric Fellowship Lecture Series

This series, offered Wednesdays from 7:30-9:00 a.m., focuses on skills and strategies useful in the care of geriatric patients. Topics include diagnosis and treatment of common conditions, effective patient communication skills, and guidelines on when to seek consult/make referrals.

Act 31 Mandated Training — In-Person Only

Offered August 19 from 6:00-8:00 p.m., this training is an in-person, live event for a limited number of LG Health medical and dental staff members. *License information is required for registration. ONLY individuals registered in eeds prior to the training are eligible for attendance/credit.* LG Health is not a state-approved provider of this education and therefore is not allowed to record the session. Register at LGHealth.org/CME under the "Register for Live Events" heading.

CME On Demand

On-demand CME programming, plus recordings of select Medicine, Family Medicine, and Pediatric Grand Rounds sessions, are available at LGHealth.org/CME.

Scan to visit LGHealth.org/CME. ↑